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Unsupervised Anomaly Detection in Digital Pathology Images

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Digital & Computational Pathology
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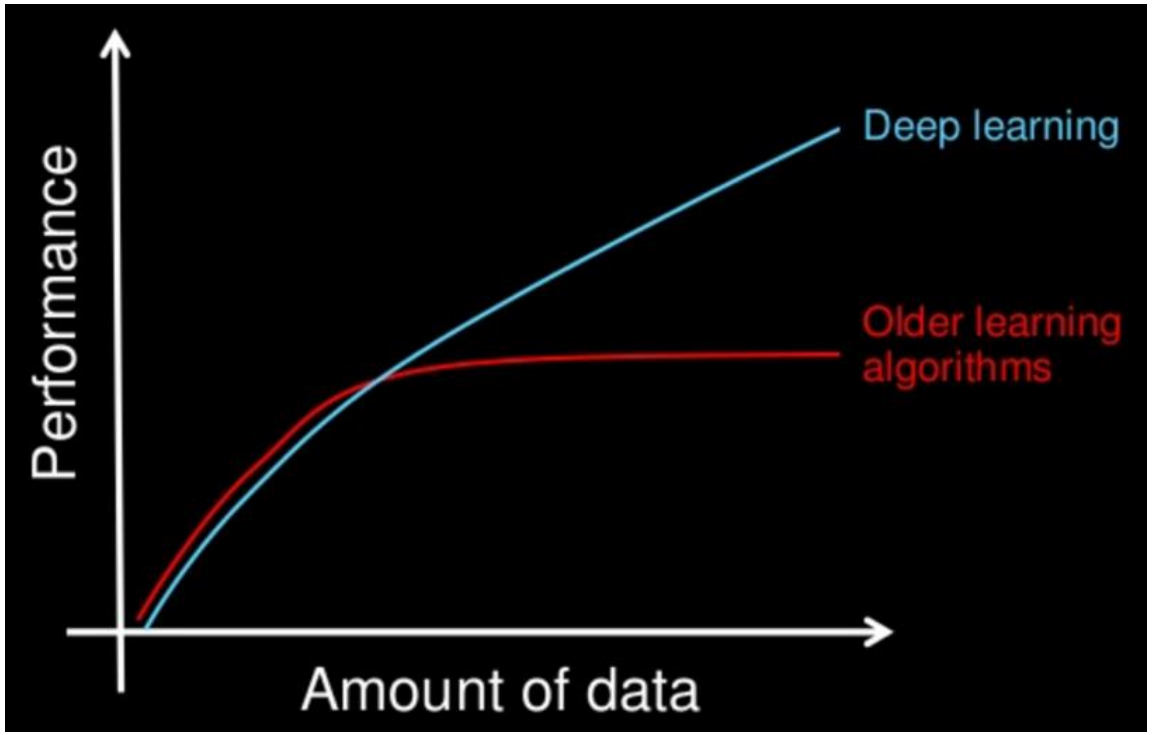
innovation you

Agenda

- Background
- Aim
- Approach
- Results
- Conclusion

Background

The building of deep learning models needs large amounts of data with annotated examples.



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Background

Obtaining expert labels for training deep learning models is difficult.

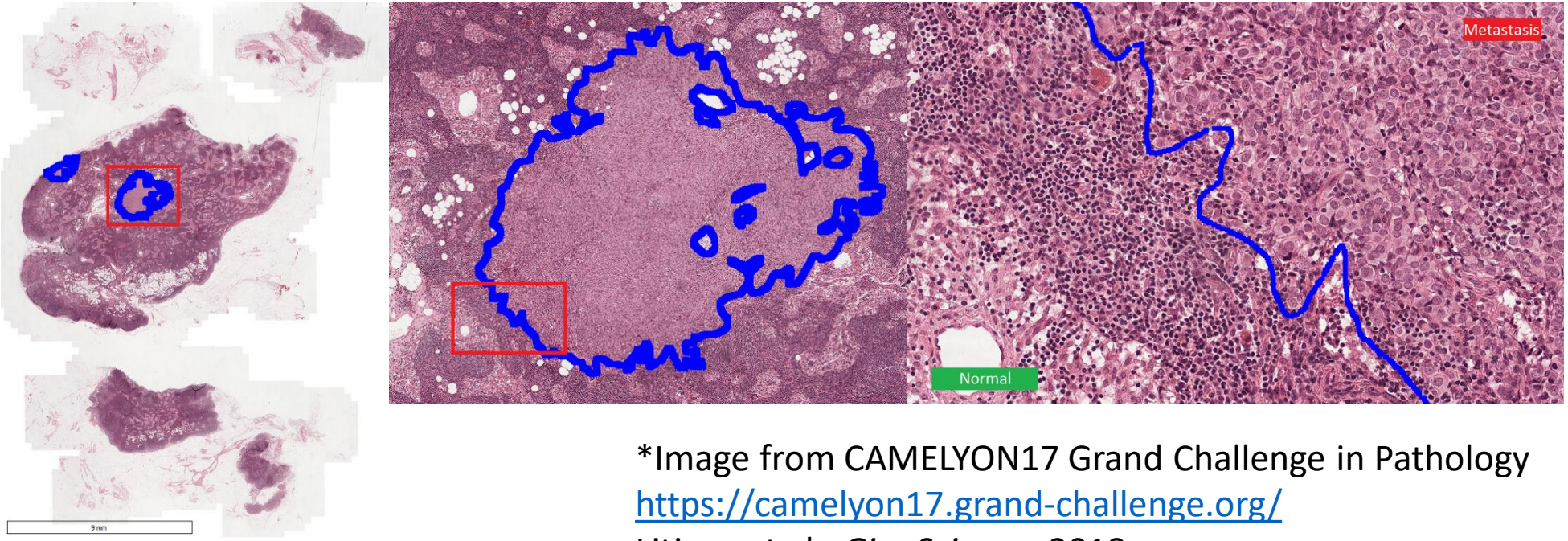

*Image from CAMELYON17 Grand Challenge in Pathology
https://camelyon17.grand-challenge.org/
Litjens et al., *GigaScience*, 2018

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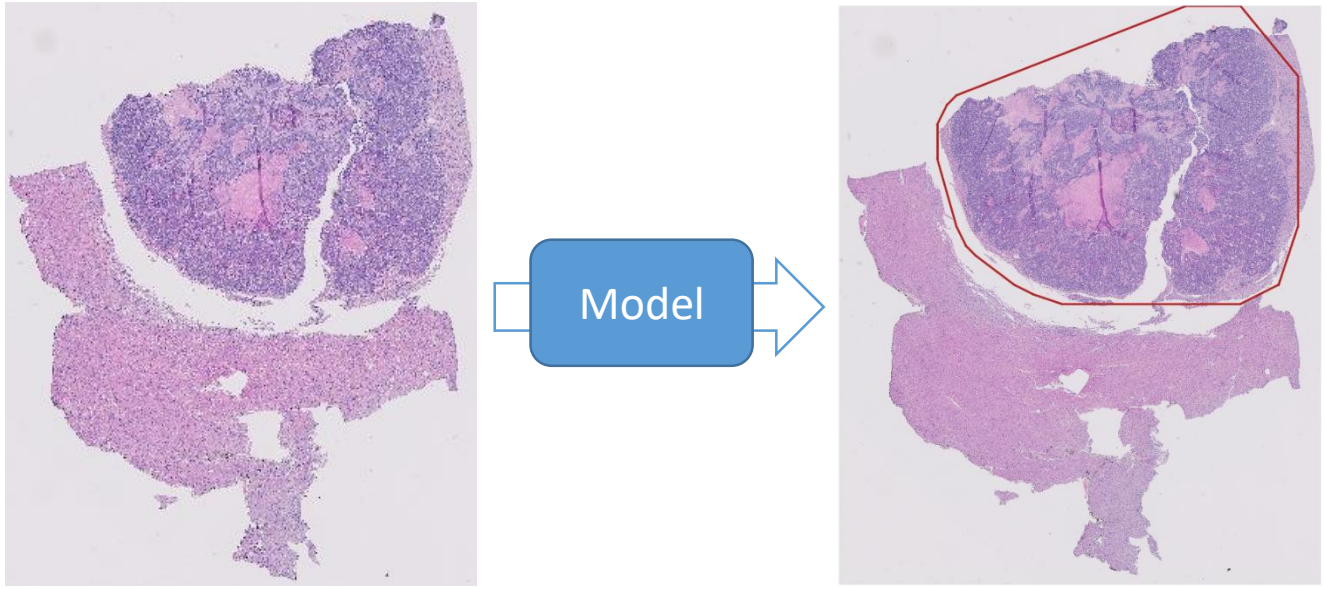
Aim

Build an **unsupervised learning** approach capable of identifying anomalous patterns for automated detection in diagnostics.



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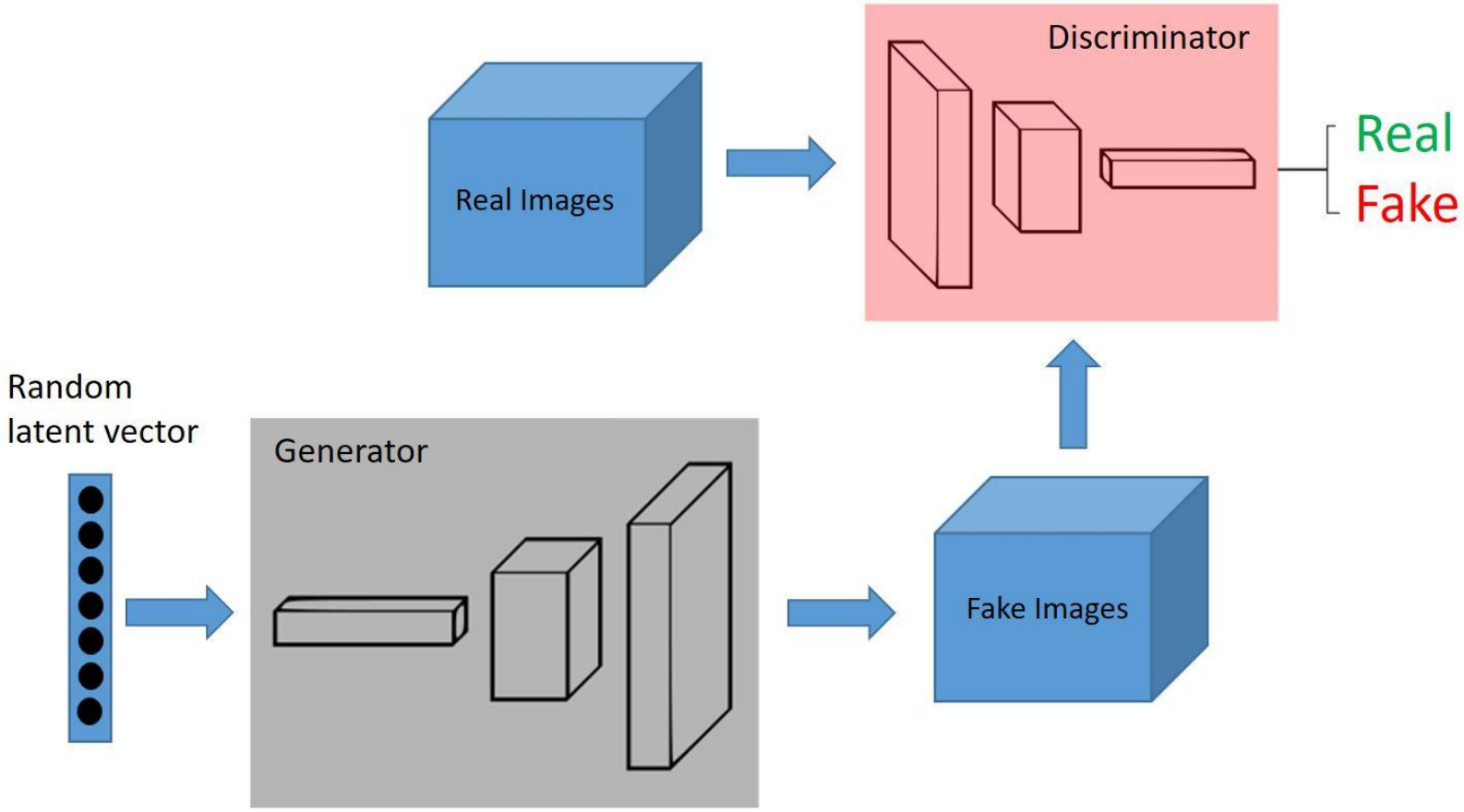
Generative Adversarial Networks (GANs)



Goodfellow et al., NIPS, 2014

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Applications

Image generation

Impressive text to image results

Image inpainting

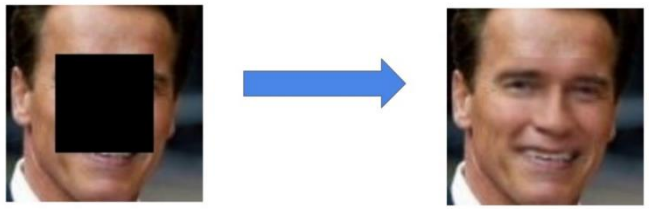

Image super resolution using SRGANs

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GANs and unsupervised learning techniques for anomaly detection in medical images

- Erfani et al. High dimensional and large-scale anomaly detection using a linear one-class SVM with deep learning. Pattern Recognit., 2016.
- Schlegl et al. Unsupervised Anomaly Detection with Generative Adversarial Networks to Guide Marker Discovery. IPMI, 2017.
- Akcay et al. GANomaly: Semi-Supervised Anomaly Detection via Adversarial Training. ACCV, 2018.
- Campanella et al. Clinical-grade computational pathology using weakly supervised deep learning on whole slide images. Nat. Med., 2019.

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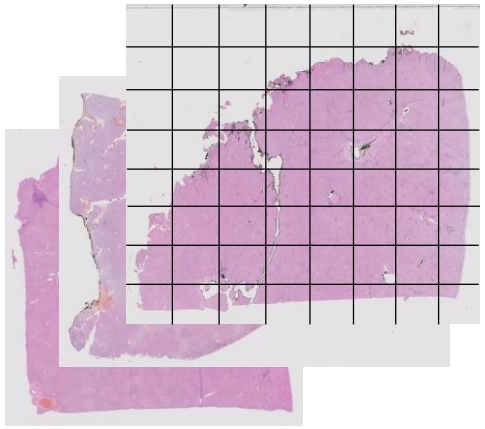
Anomaly Detection using GANs

Training



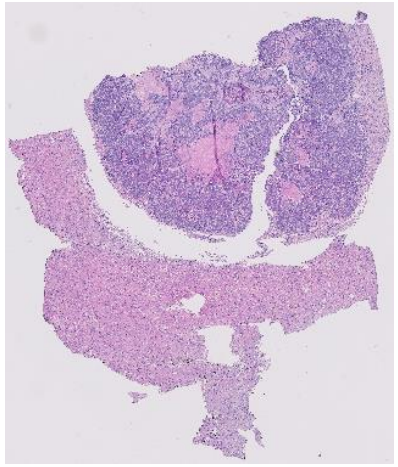
Normal/Healthy Data
'Unannotated'

GAN Model

Generator

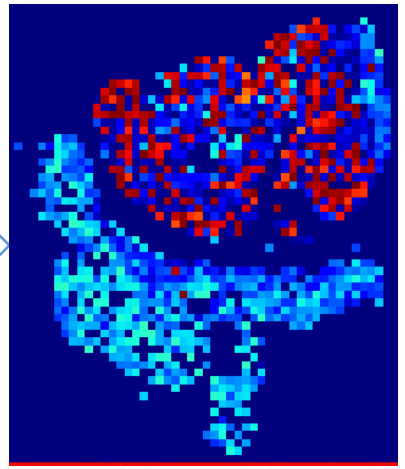
Discriminator

Identifying anomalies



Test Data

Model



Anomalies

Serag et al., Front. Med. - Pathology, 2019

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Anomaly Score

Anomaly Score is based on residual and discrimination losses:

- **Residual loss *R(x)*:** L1 distance between generated image and unseen test image.
- **Discrimination loss *D(x)*:** L1 distance between feature representations of generated and test image.

$$A(\mathbf{x}) = (1 - \lambda) \cdot R(\mathbf{x}) + \lambda \cdot D(\mathbf{x})$$

Schlegl et al., IPMI, 2017

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Results

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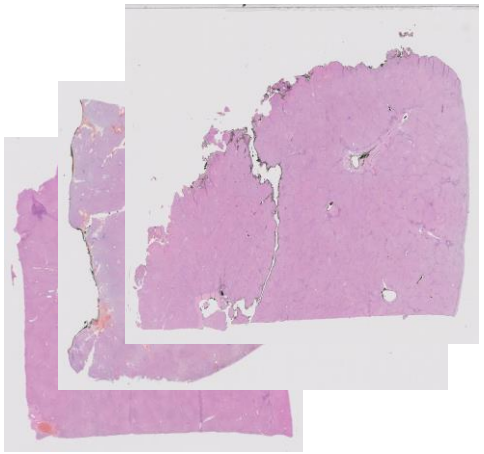
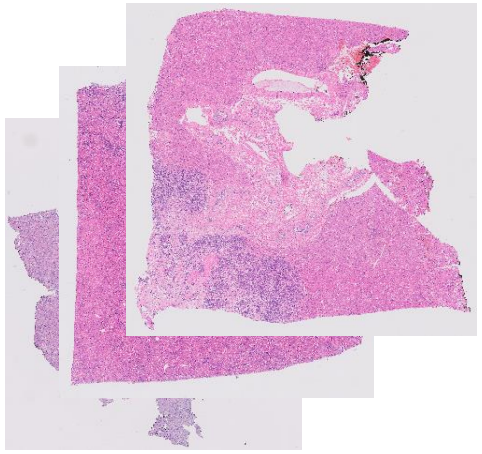
Liver metastasis from colon



50 slides of routinely taken section of macroscopically normal Liver.

100 H&E stained WSIs



50 slides of liver metastasis from colon.

- 64x64px patches were extracted at 2.5x (4MPP).
- For training: 43K patches from 40 non-tumor liver slides used (**No Annotations Needed**)
- For testing: 10k patches extracted from the remaining 10 non-tumor slides used.
- All 50 slides with metastasis used for testing.

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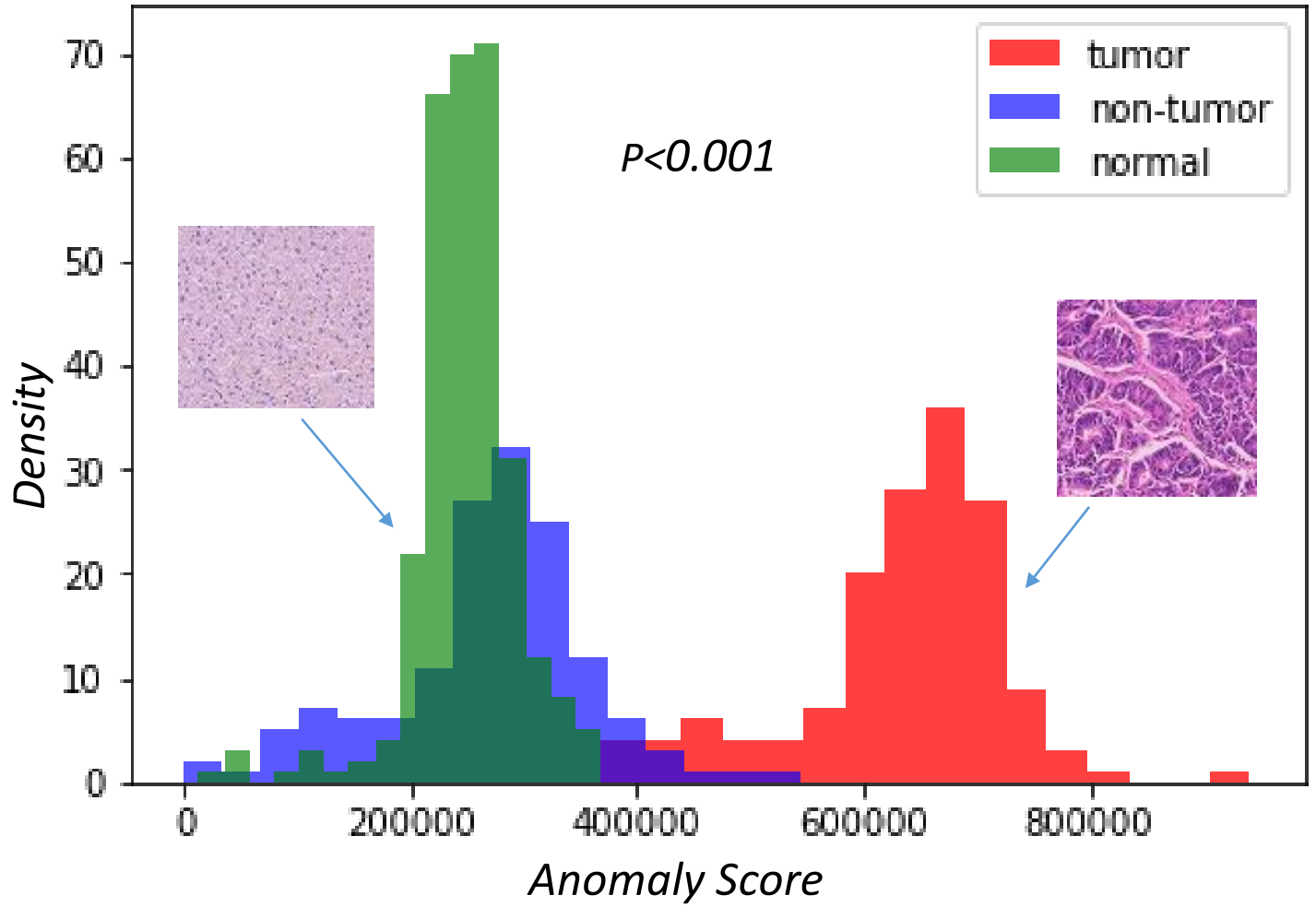
Results – Distribution of anomaly scores



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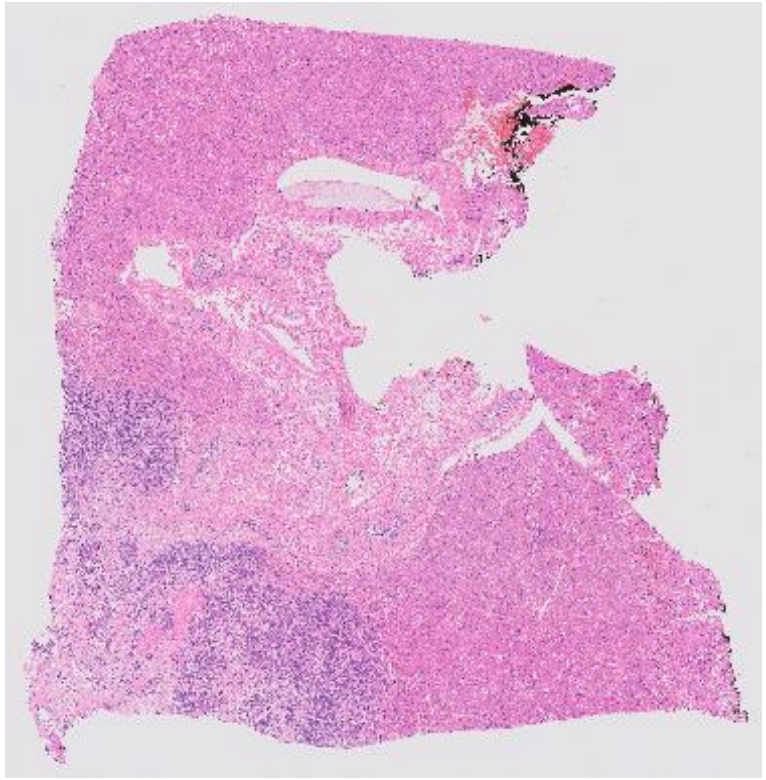
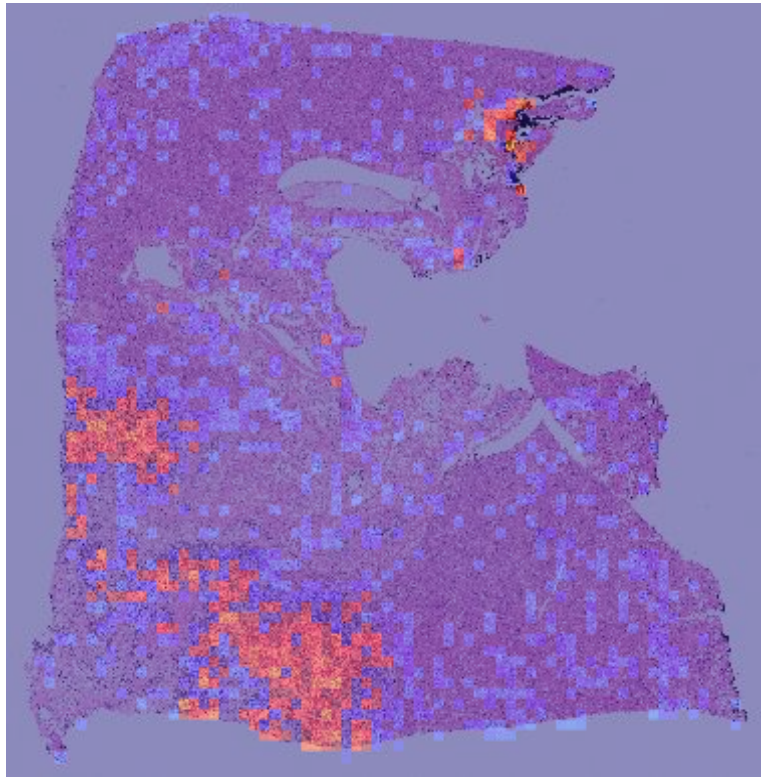
Results – WSI processing



Slide



Slide with overlaid anomaly heat map

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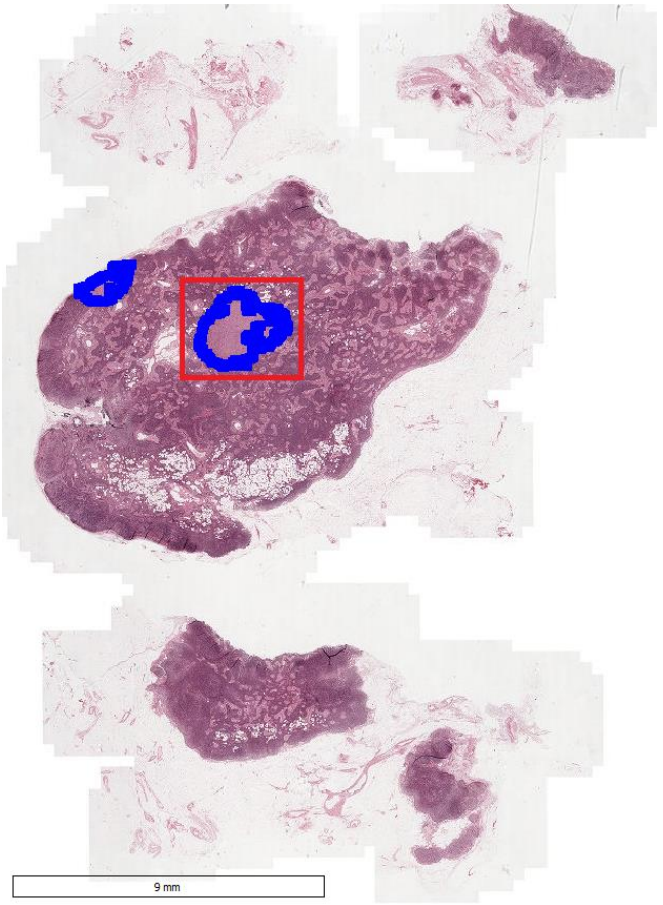
Breast lymph nodes metastasis

- Images from CAMELYON17* Grand Challenge used to test the scalability of the approach to higher resolution
- 64x64px patches were extracted at 10x.
- For training: 50K patches from 70 non-tumor slides used.
- For testing: 750 patches extracted from 10 slides (5 non-tumor and 5 tumor) used.



*Litjens et al., *GigaScience*, 2018
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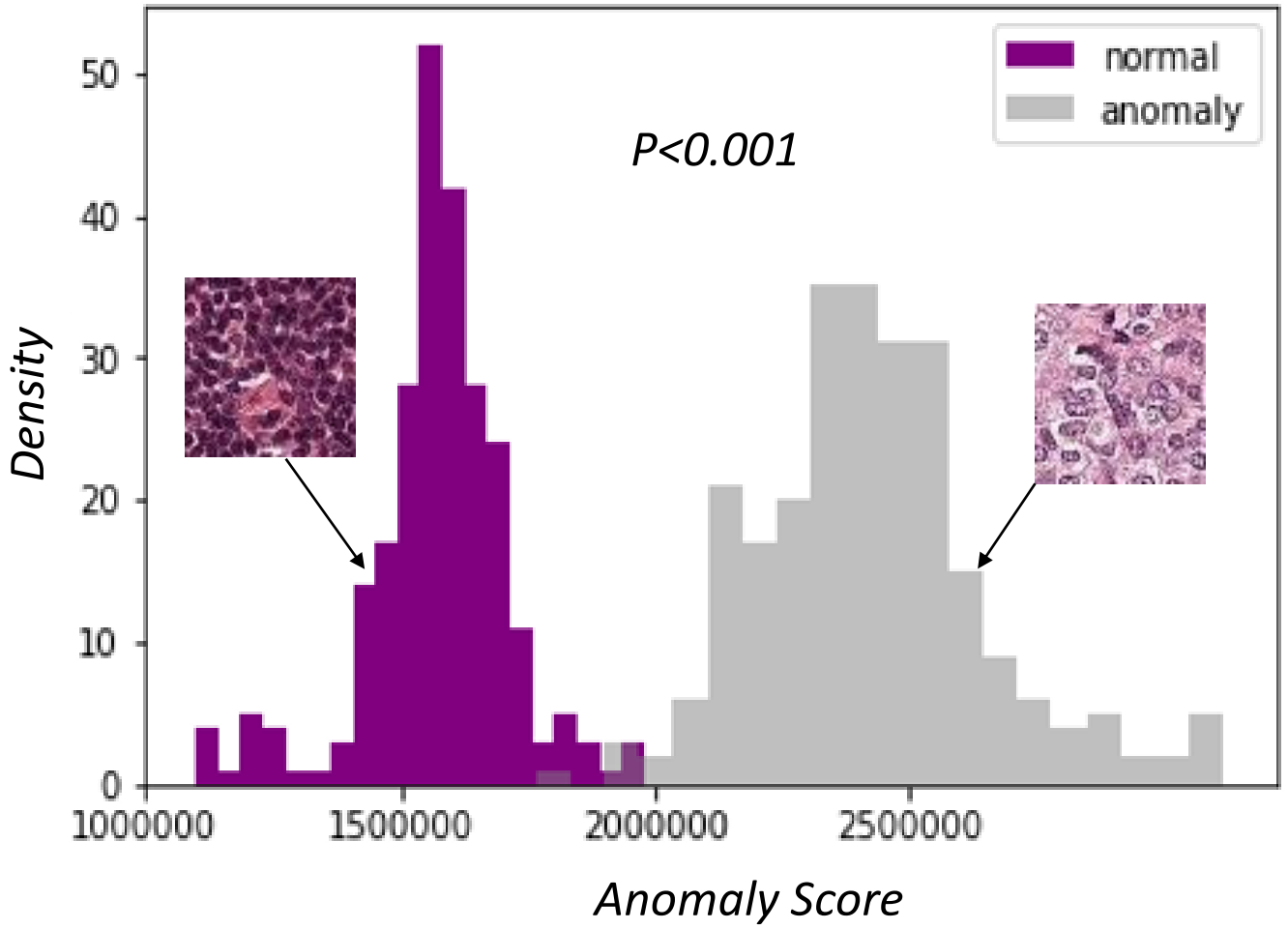
Results – Distribution of anomaly scores



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Conclusion

- We proposed an unsupervised learning approach capable of identifying anomalous patterns for automated detection in diagnostics.
- The approach was successfully applied for metastasis detection in liver biopsies and breast lymph nodes.
- Training patches were extracted from non-tumor images; avoiding the necessity of having detailed pathologist annotation.
- The approach may lead to substantial cost-reduction and time-saving in developing automated tools.

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Acknowledgment

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