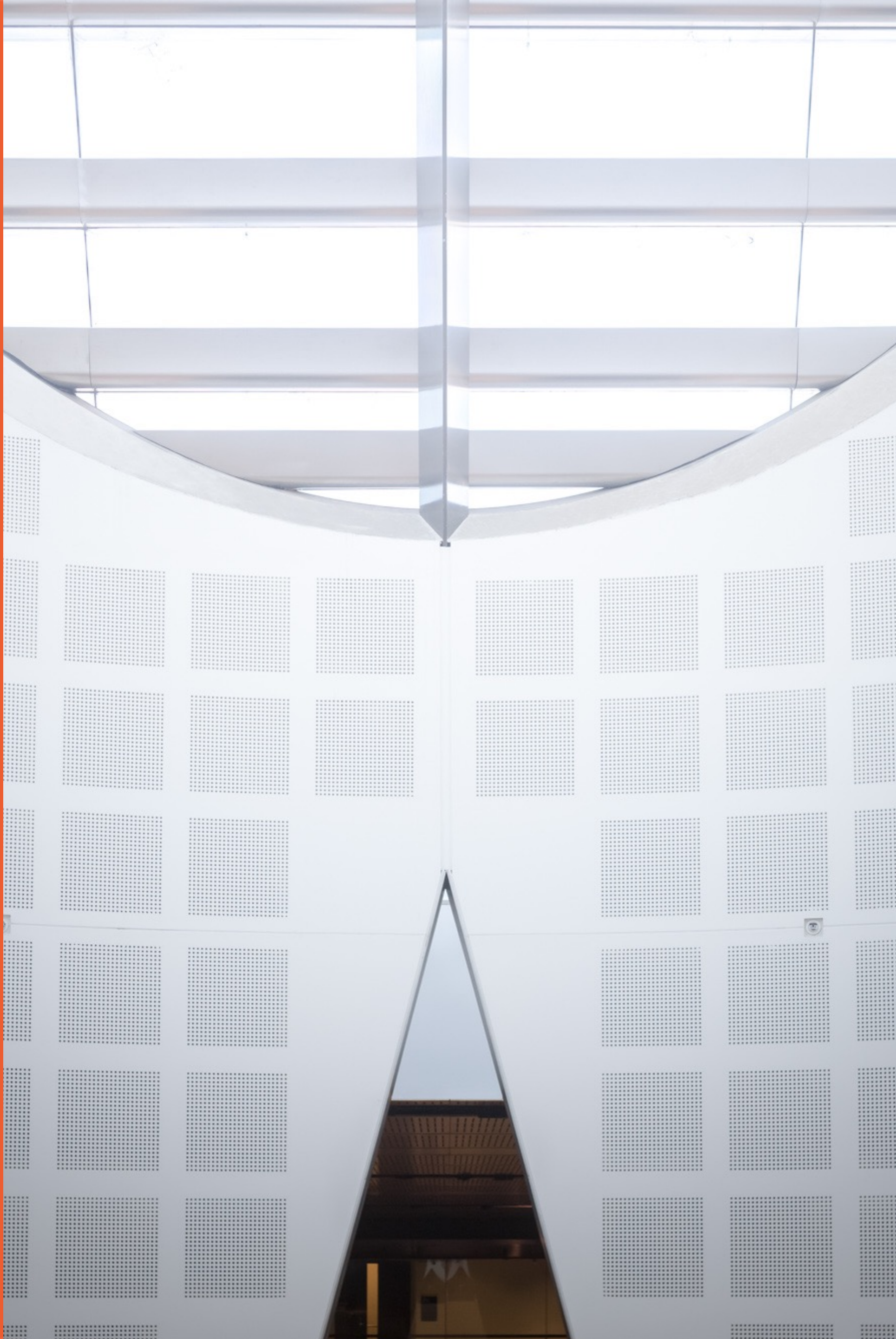
Biomedical Image Analysis

Reference: Healthcare Data Analytics, Chapter 3

THE UNIVERSITY OF SYDNEY



Daochang Liu

2022 - Now, Postdoc Researcher at University of Sydney
2017 - 2022, Ph.D. at Peking University, China
2013 - 2017, B.E at Tongji University, China

Research interests:

Human action and skill understanding

Generative learning using diffusion models

Surgical AI, Surgical Skill Assessment

AI vs. Human in Medical Image Analysis

	Sensitivity	**Specificity**
Deep learning models	**87.0%** (95% CI 83.0–90.2)	**92.5%** (95% CI 85.1–96.4)
Health-care professionals	**86.4%** (95% CI 79.9–91.0)	**90.5%** (95% CI 80.6–95.7)

"A comparison of deep learning performance against health-care professionals in detecting diseases from medical imaging: a systematic review and meta-analysis."

The lancet digital health 2019

Biomedical Images

An image is a spatial map of physical properties of a subject:

Natural Image:

Pixel value > Visible light intensity

Medical Image:

Pixel value > Invisible light intensity, Density, Blood flow, …

- Look inside of the body without hurting the subject
- View biological objects that are normally too small

Biomedical image analysis helps reduce human labor and errors when facing increasing data size and complexity

Challenges in Biomedical Image Analysis

Diverse modalities

CT, MRI, PET, Ultrasound, endoscopy, laparoscopy, microscopy, ...

Diverse structures of interest

Brain, Skin, Heart, Vessel, Cell, Eye Fundus, ...

Diverse analysis tasks

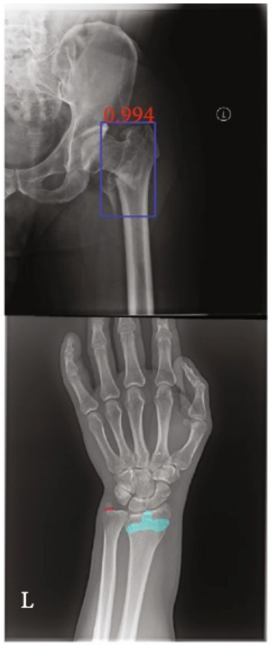
Segmentation, Detection, Reconstruction, Registration, ...

Diverse constraints

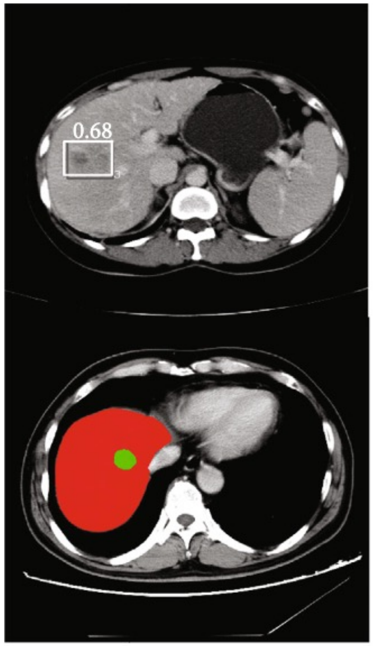
Interpretable, Calibrated, Privacy-preserving, ...

The domain knowledge about the modality, task, and structure is important for the model design!

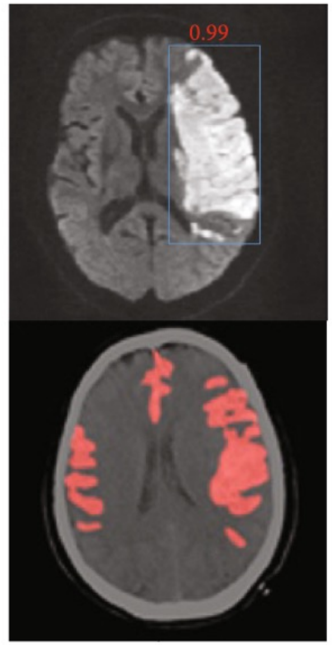
Biomedical Imaging Modalities



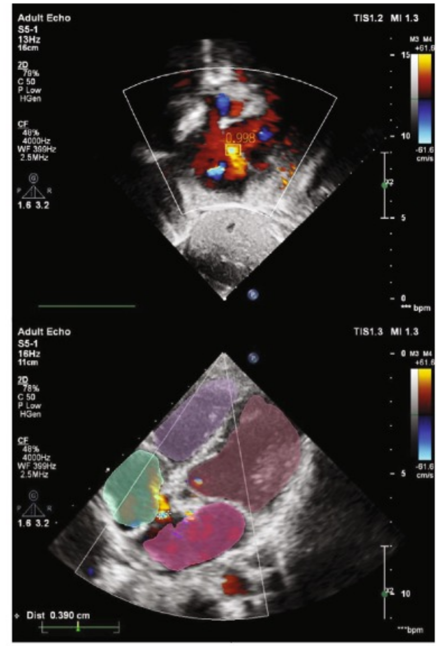
Bone X-ray



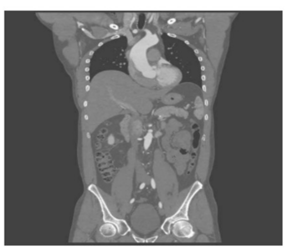
Liver CT



Brain MRI

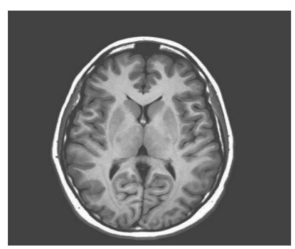


Cardiac ultrasound

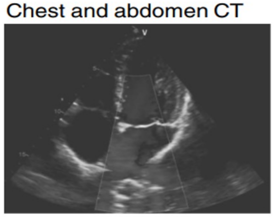


Chest and abdomen CT

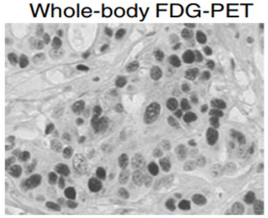
Whole-body FDG-PET



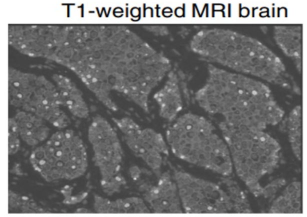
T1-weighted MRI brain



Cardiac ultrasound



Brightfield brown stain



Fluorescence microscopy

Advances in Deep Learning-Based Medical Image Analysis

Biomedical Image Analysis Tasks

Image Classification (Examples: disease classification, benign / malignant classification)

Image → Label

Object Detection (Examples: colonic-polyp detection, lung nodule detection)

Image → Bounding Box

Image Segmentation (Examples: lesion segmentation, anatomy segmentation)

Image → Mask

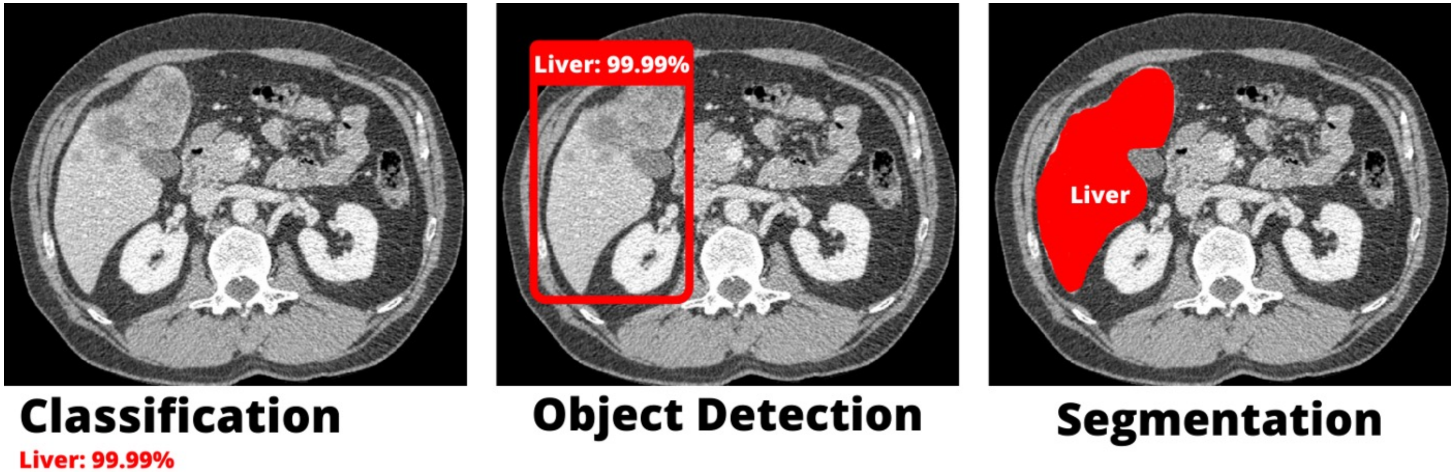


Image from: https://levelup.gitconnected.com/automatic-liver-segmentation-part-1-4-introduction-6fbae7a75bbd

Biomedical Image Analysis Tasks

Image Reconstruction (Examples: low-dose imaging, motion correction)

Corrupted Image High-Quality Image

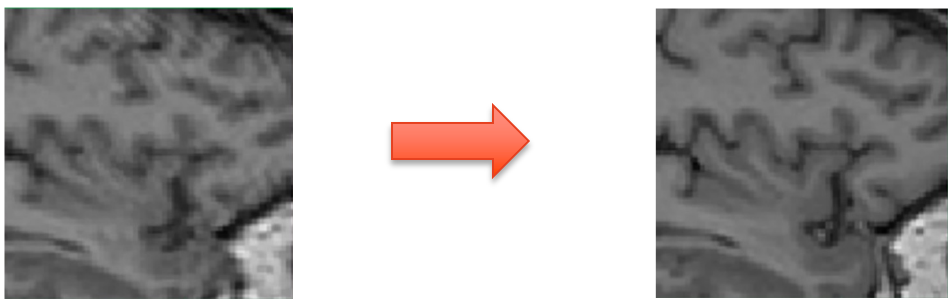
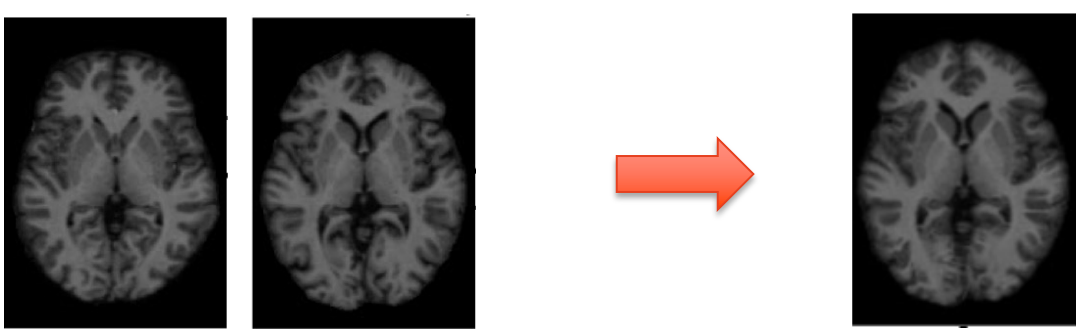


Image Registration (Examples: inter-subject comparison, CT-MRI registration)

Fixed Image + Moving Image Warped Moving Image



Reference: Suppressing motion artefacts in MRI using an Inception-ResNet network with motion simulation augmentation
Reference: Deformable Registration of Brain MR Images via a Hybrid Loss

Task-specific topics:

Biomedical image segmentation

Biomedical image registration

Task-agnostic topics:

Interpretability

Uncertainty

Task-specific topics:

Biomedical image segmentation

Biomedical image registration

Task-agnostic topics:

Interpretability

Uncertainty

Biomedical Image Segmentation

Segmentation is used to locate objects and boundaries in images.

Segmentation is one of the most important steps leading to the analysis of image data because it enables the further analysis.

Segmentation

Image from: https://levelup.gitconnected.com/automatic-liver-segmentation-part-1-4-introduction-6fbae7a75bbd

Biomedical Image Segmentation

Classical Methods:
only use single image
- Watershed Algorithm

Learning-based Methods:
require a separate training step with many images
- Convolutional Neural Networks and U-Net
- Segment Anything Model (SAM)

Biomedical Image Segmentation

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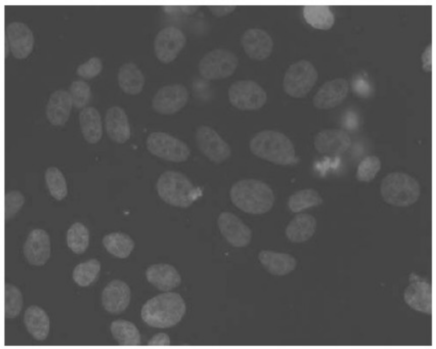
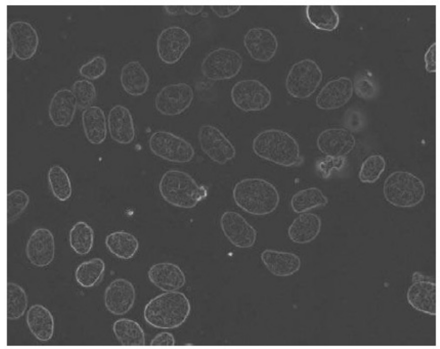
Watershed Algorithm

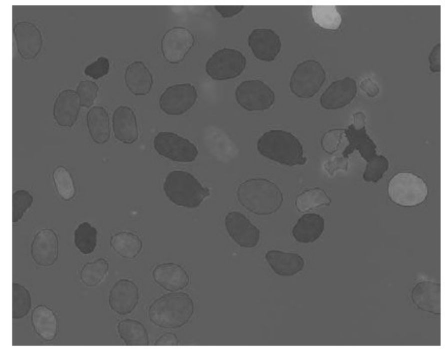
A classic algorithm commonly used for image segmentation and binary shape separation.



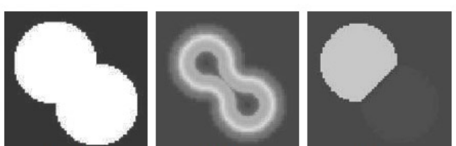
Input image



Edge image

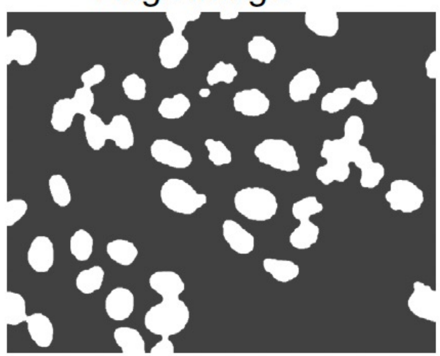


Marker-controlled watershed

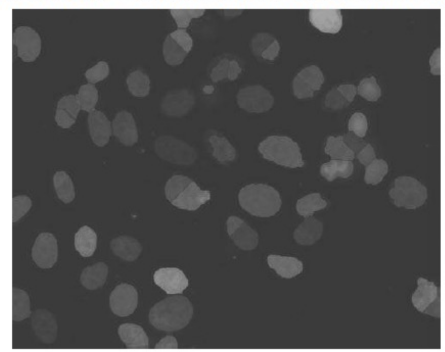


(a) (b) (c)

Toy example



Thresholded image



Shape watershed

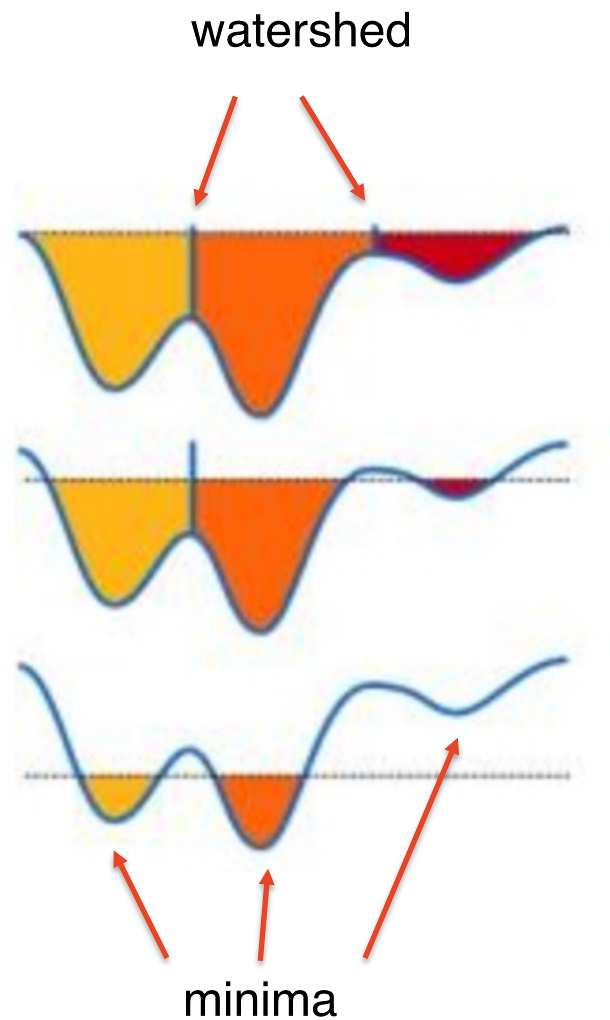
Give a unique index for each object

Watershed Algorithm

A flooding analogy:

Image > Landscape Surface
Pixel value > Altitude
Dark image regions > Valleys
Bright image regions > Hills

If we flood this surface from its minima and, if we prevent the merging of the water coming from different sources, we partition the image into different sets.



Reference: https://svi.nl/watershed

Watershed Algorithm

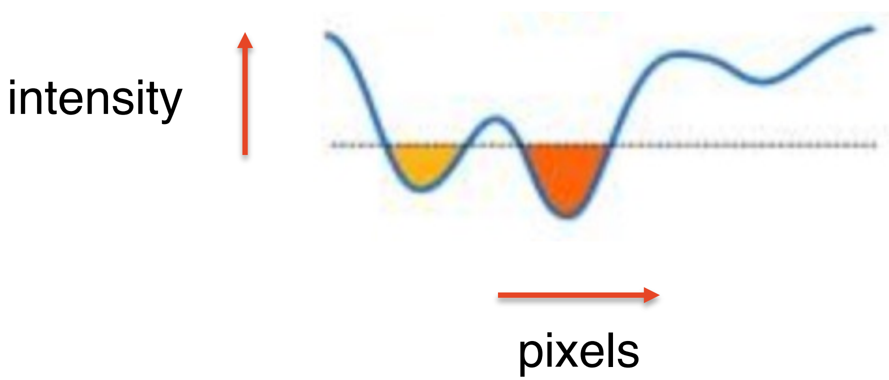
Suppose the image as a map of mountains and valleys, with the pixel intensity representing the altitude.

Reference: https://svi.nl/watershed

Watershed Algorithm

Suppose the image as a map of mountains and valleys, with the pixel intensity representing the altitude.

Let's look from its side view



Reference: https://svi.nl/watershed

Watershed Algorithm

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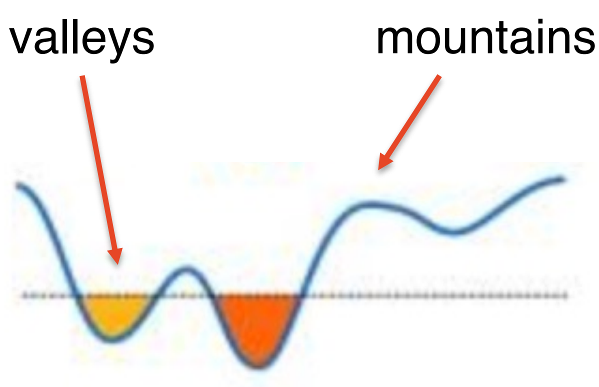
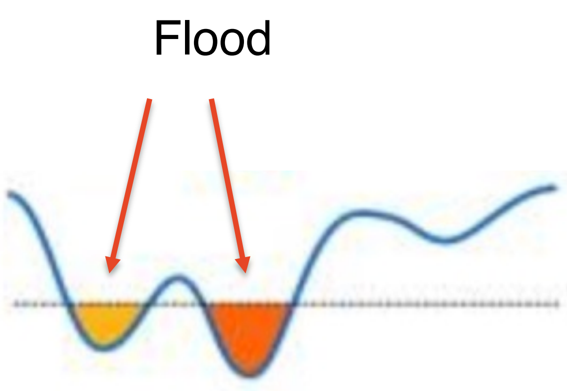


Reference: https://svi.nl/watershed

Watershed Algorithm

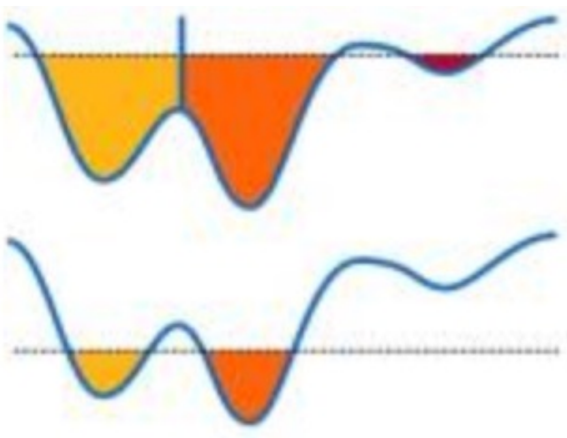
We flood this surface and the water start accumulating from the valleys



Reference: https://svi.nl/watershed

Watershed Algorithm

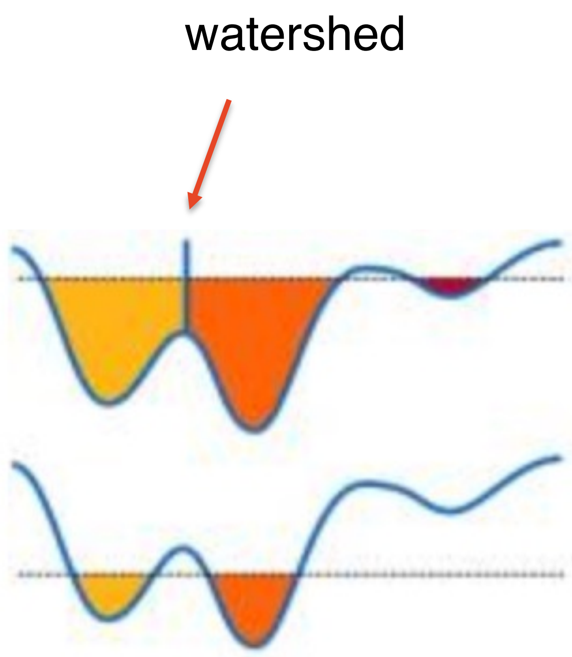
Keep flooding and the water continues to accumulate



Reference: https://svi.nl/watershed

Watershed Algorithm

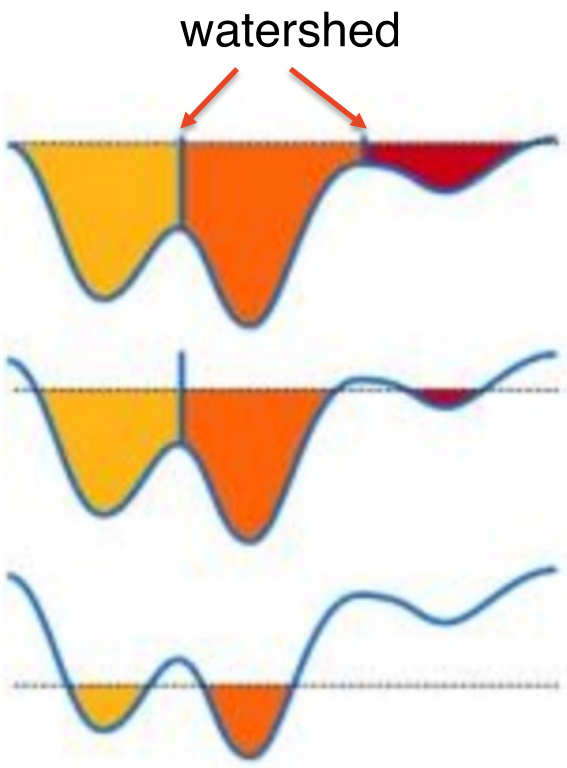
The water coming from different sources is prevented from merging with each other by watersheds



Reference: https://svi.nl/watershed

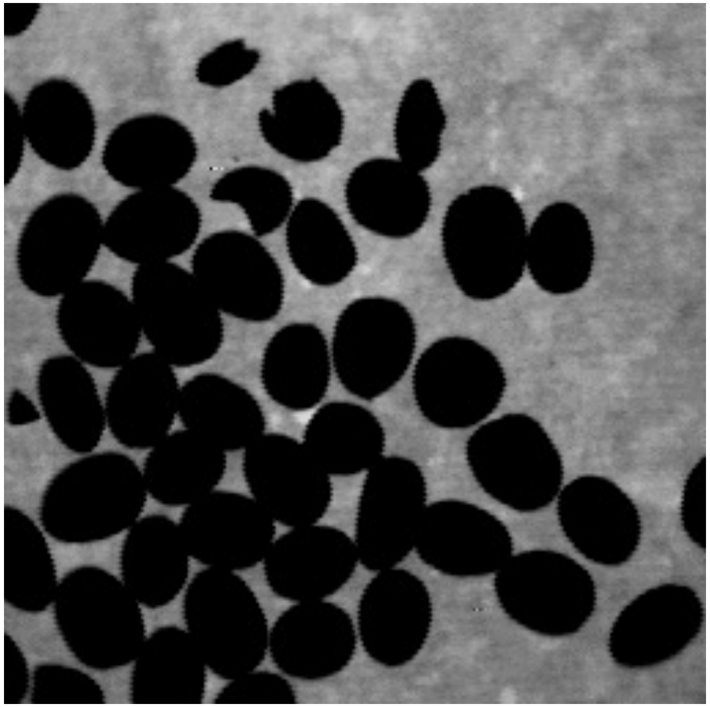
Watershed Algorithm

Finally, the images will be partitioned into different sets



Reference: https://svi.nl/watershed

Watershed Example with Seeds



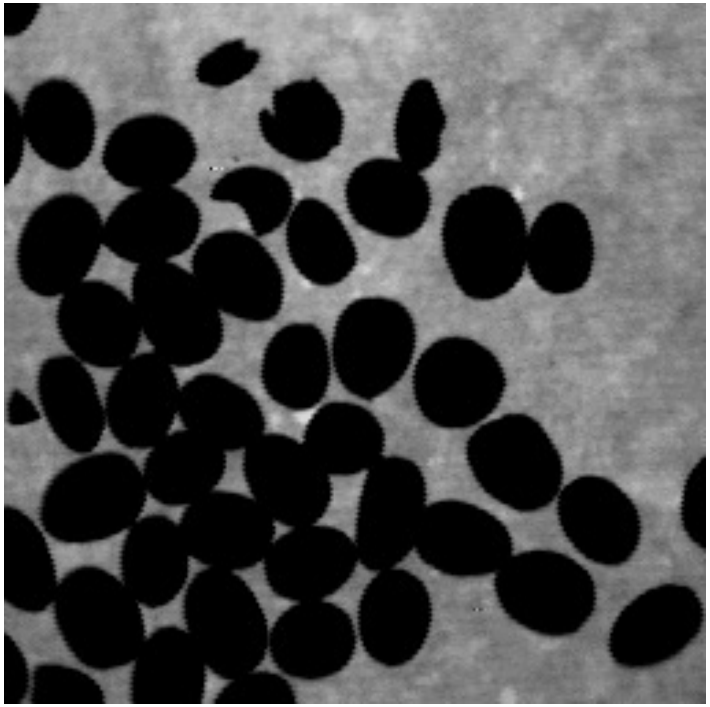
Image

Seeded Watershed

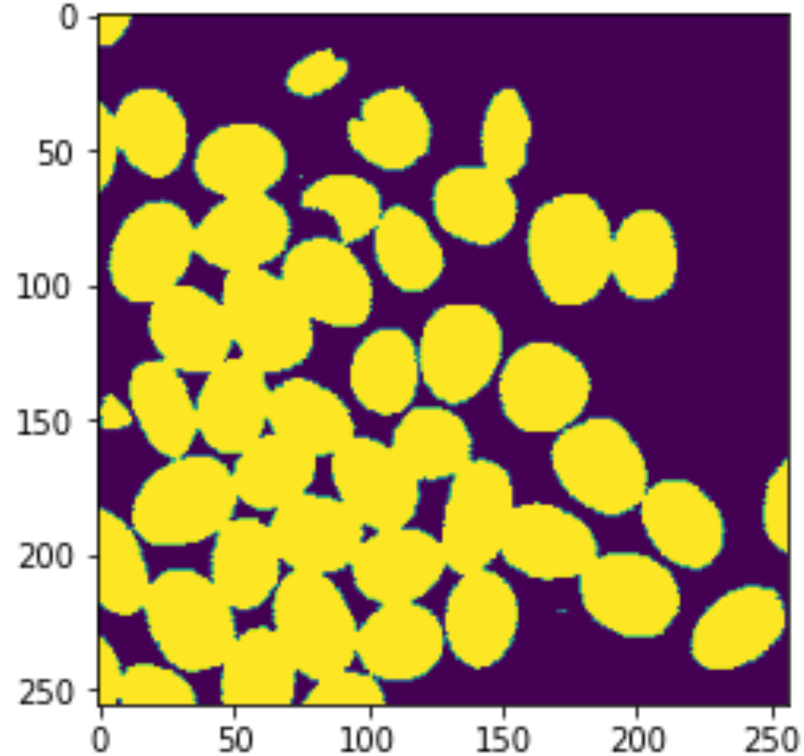
In this example, the water will be flooded from "seeds", corresponding to the objects to be segmented.

Reference: https://people.cmm.minesparis.psl.eu/users/beucher/wtshed.html
Reference: https://docs.opencv.org/4.x/d3/db4/tutorial_py_watershed.html

Watershed Example with Seeds



Image



Thresholding
(Binary image)

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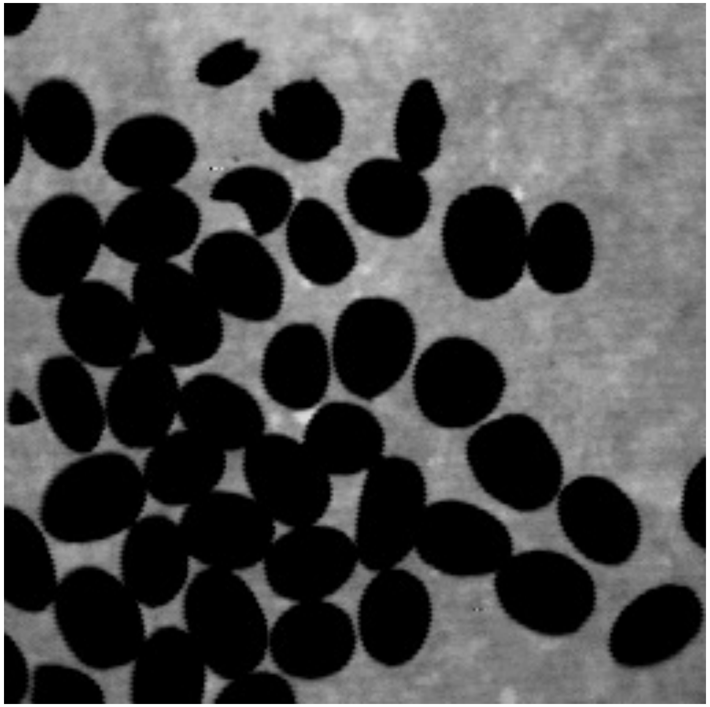
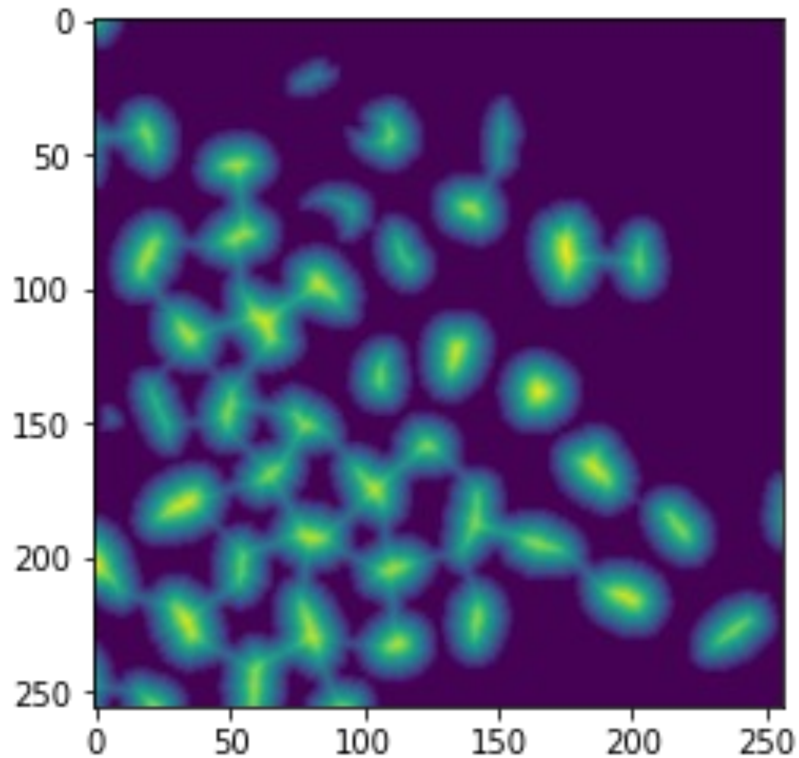
Reference: https://docs.opencv.org/4.x/d3/db4/tutorial_py_watershed.html

Watershed Example with Seeds



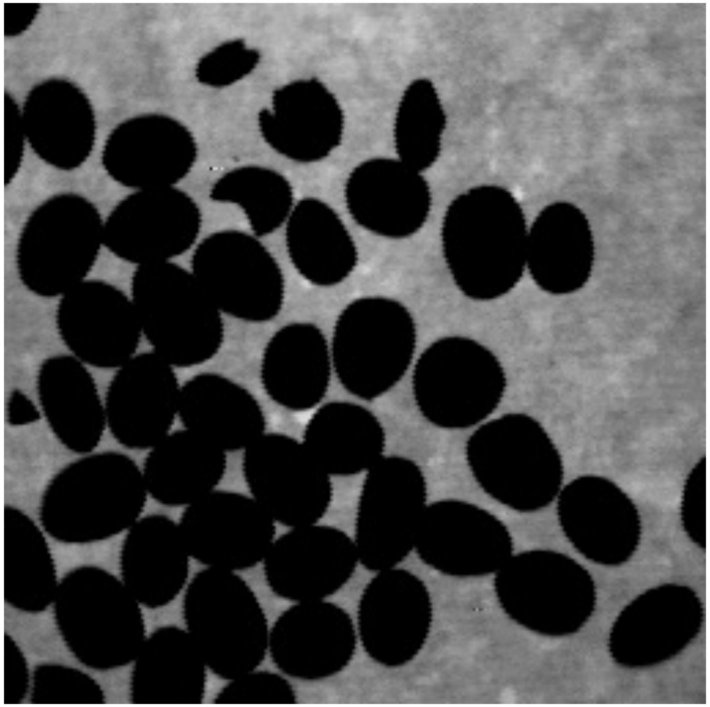
Image



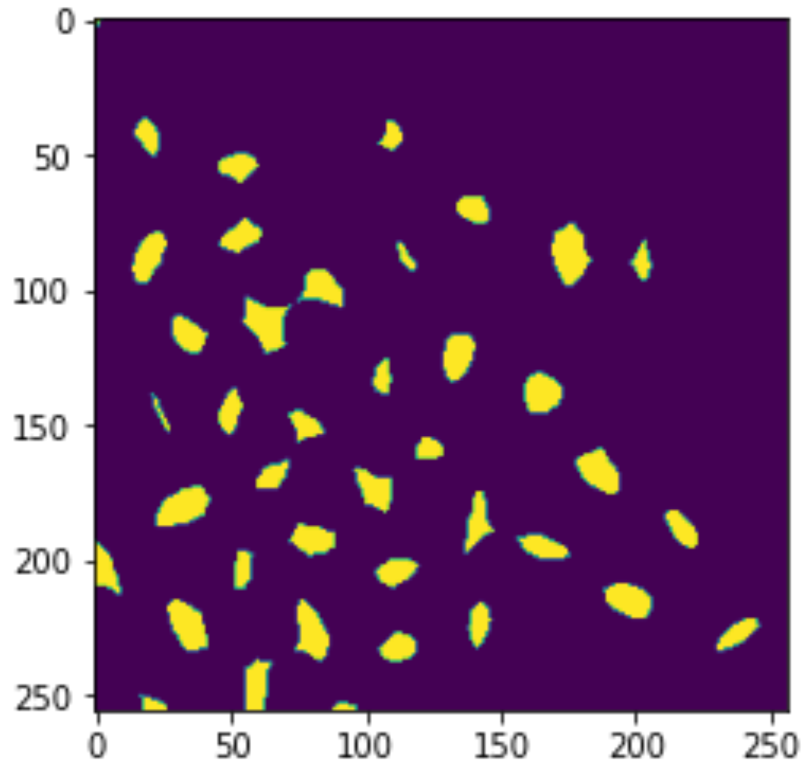
Distance Transform
(Distance to boundary)

Reference: https://people.cmm.minesparis.psl.eu/users/beucher/wtshed.html
Reference: https://docs.opencv.org/4.x/d3/db4/tutorial_py_watershed.html

Watershed Example with Seeds



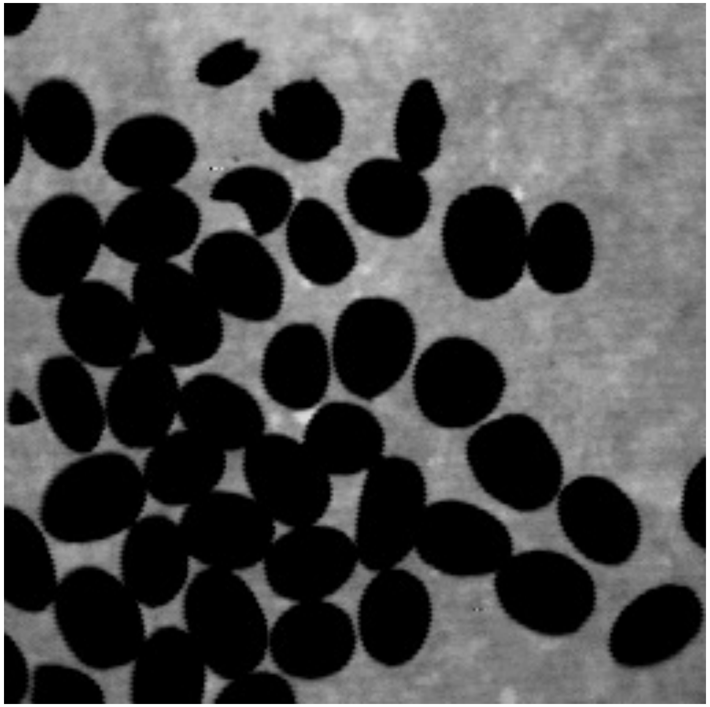
Image



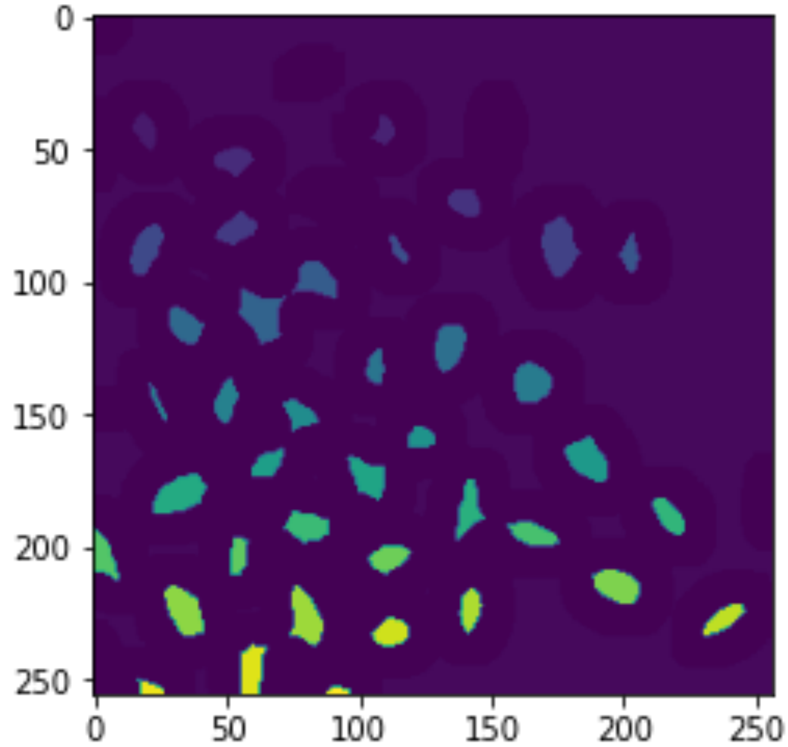
Sure Foreground by Thresholding
(Pixels far from boundary)

Reference: https://people.cmm.minesparis.psl.eu/users/beucher/wtshed.html
Reference: https://docs.opencv.org/4.x/d3/db4/tutorial_py_watershed.html

Watershed Example with Seeds



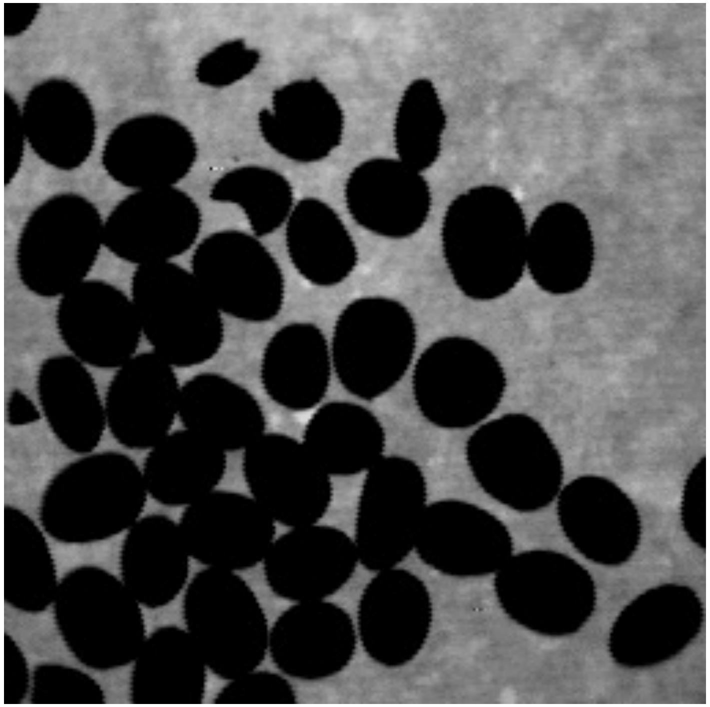
Image



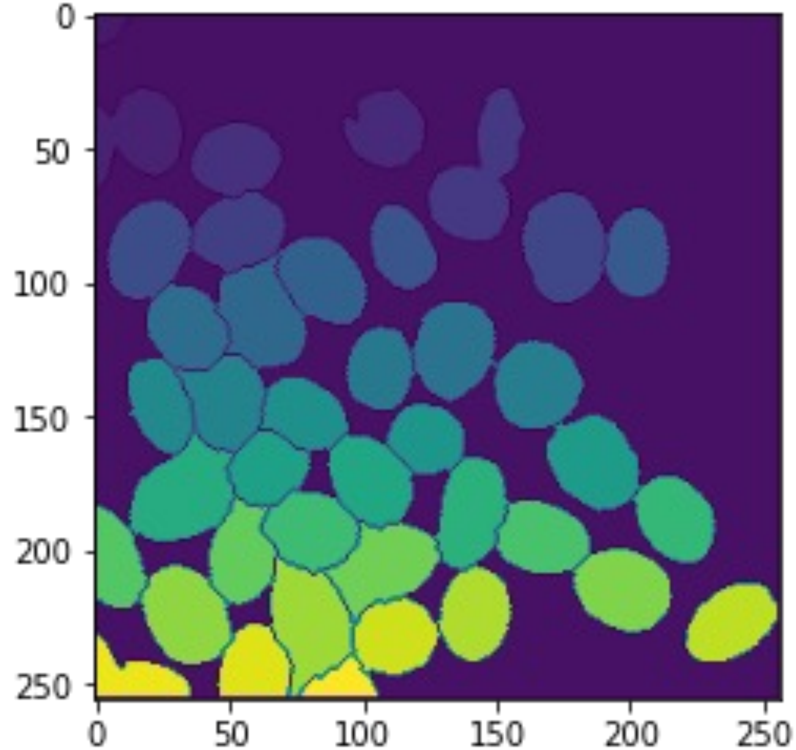
Use as Water Sources
(seeds)

Reference: https://people.cmm.minesparis.psl.eu/users/beucher/wtshed.html
Reference: https://docs.opencv.org/4.x/d3/db4/tutorial_py_watershed.html

Watershed Example with Seeds



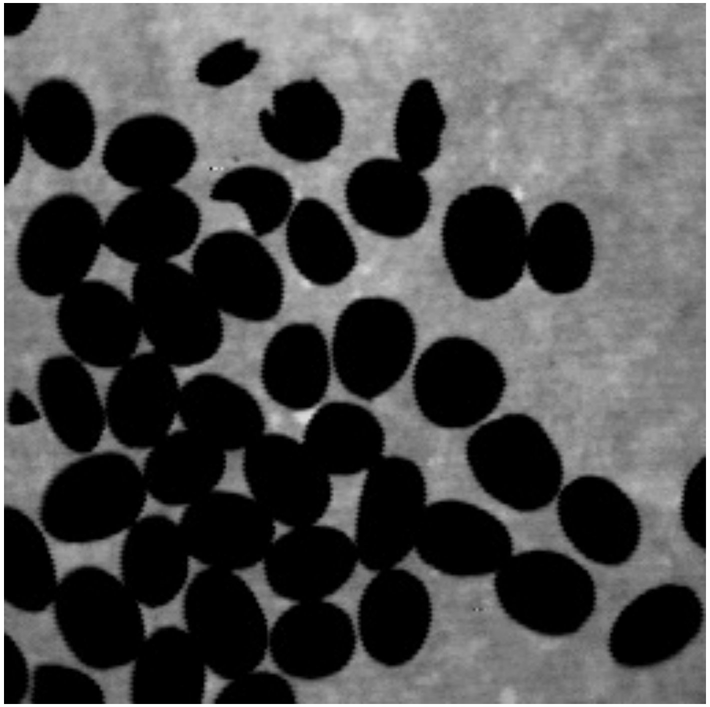
Image



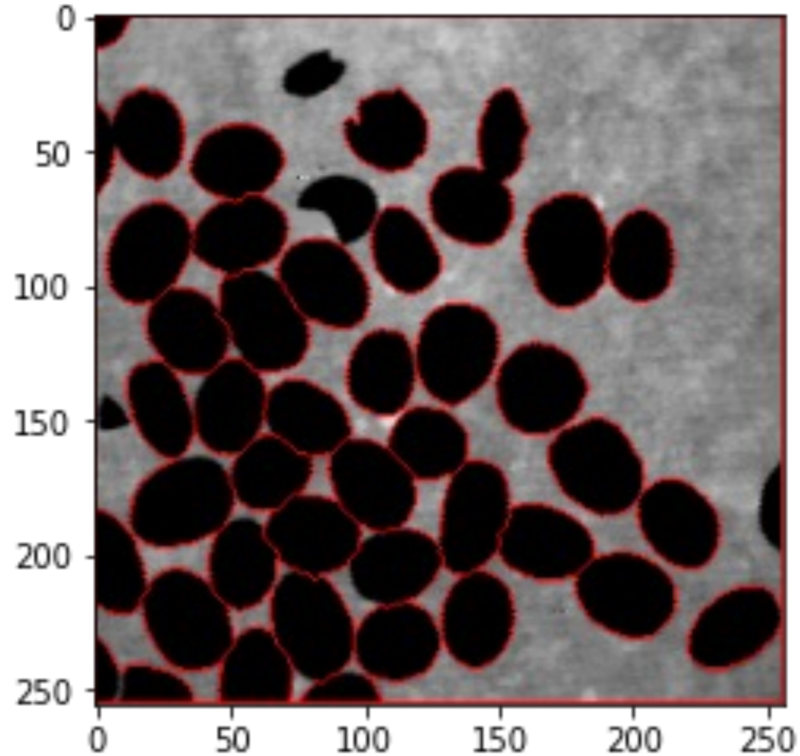
Get Watersheds
(flooding)

Reference: https://people.cmm.minesparis.psl.eu/users/beucher/wtshed.html
Reference: https://docs.opencv.org/4.x/d3/db4/tutorial_py_watershed.html

Watershed Example with Seeds



Image



Results

Reference: https://people.cmm.minesparis.psl.eu/users/beucher/wtshed.html
Reference: https://docs.opencv.org/4.x/d3/db4/tutorial_py_watershed.html

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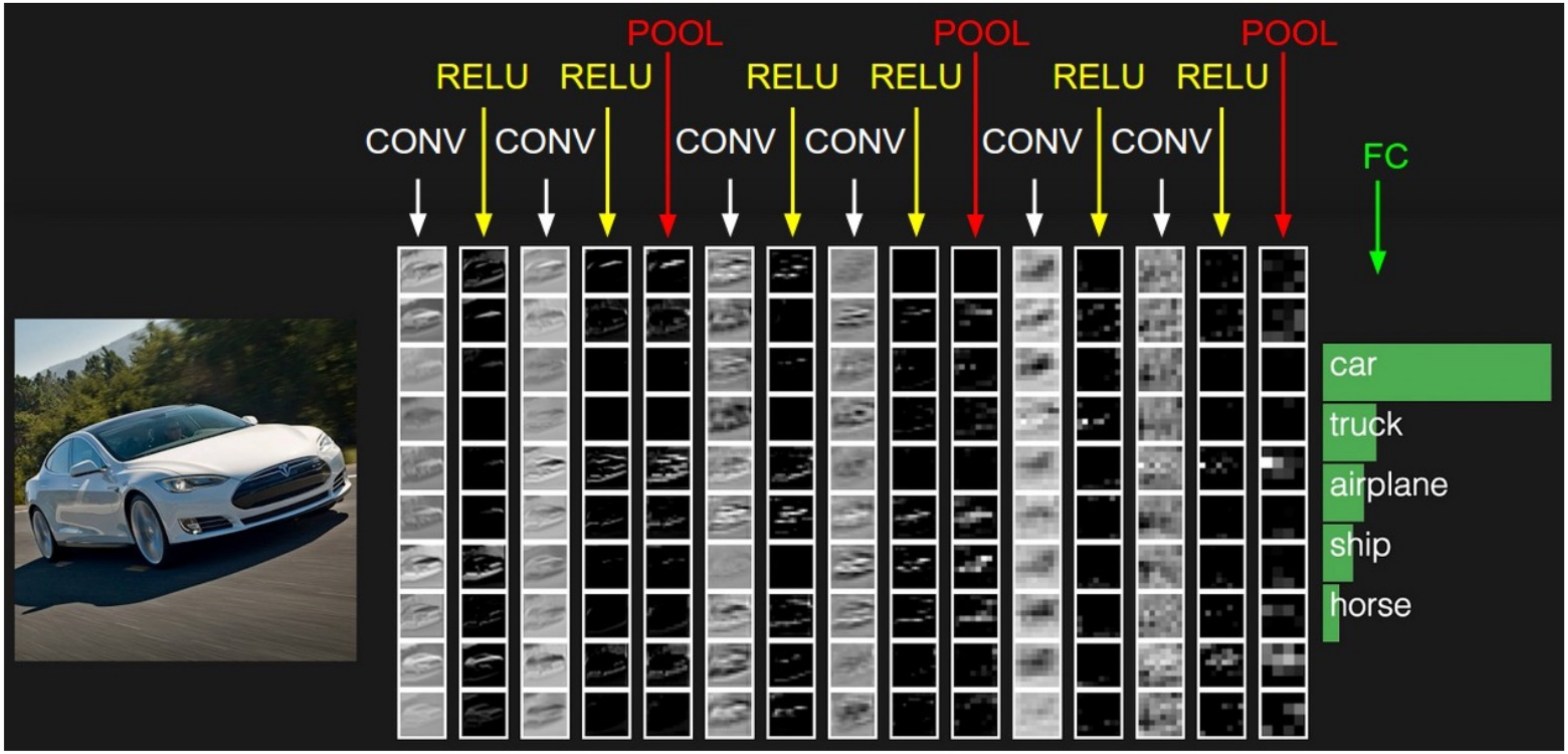
Convolutional Neural Networks

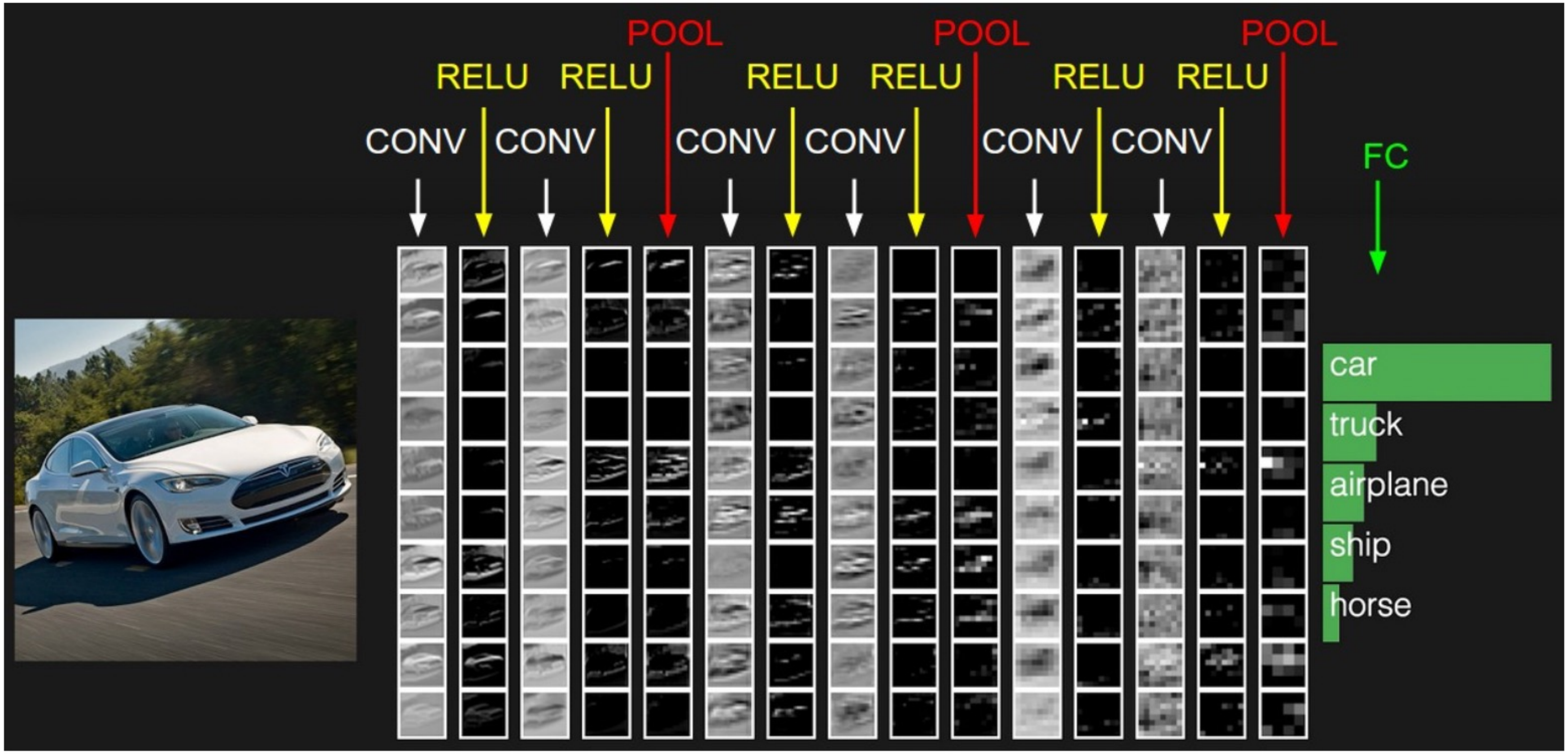
Convolutional neural networks (CNN) have shown superior performance on biomedical image analysis. A typical convolutional neural network consists of a series of convolutions (CONV), activations (e.g. RELU), and pooling layers (POOL)



Reference: https://cs231n.github.io/convolutional-networks/

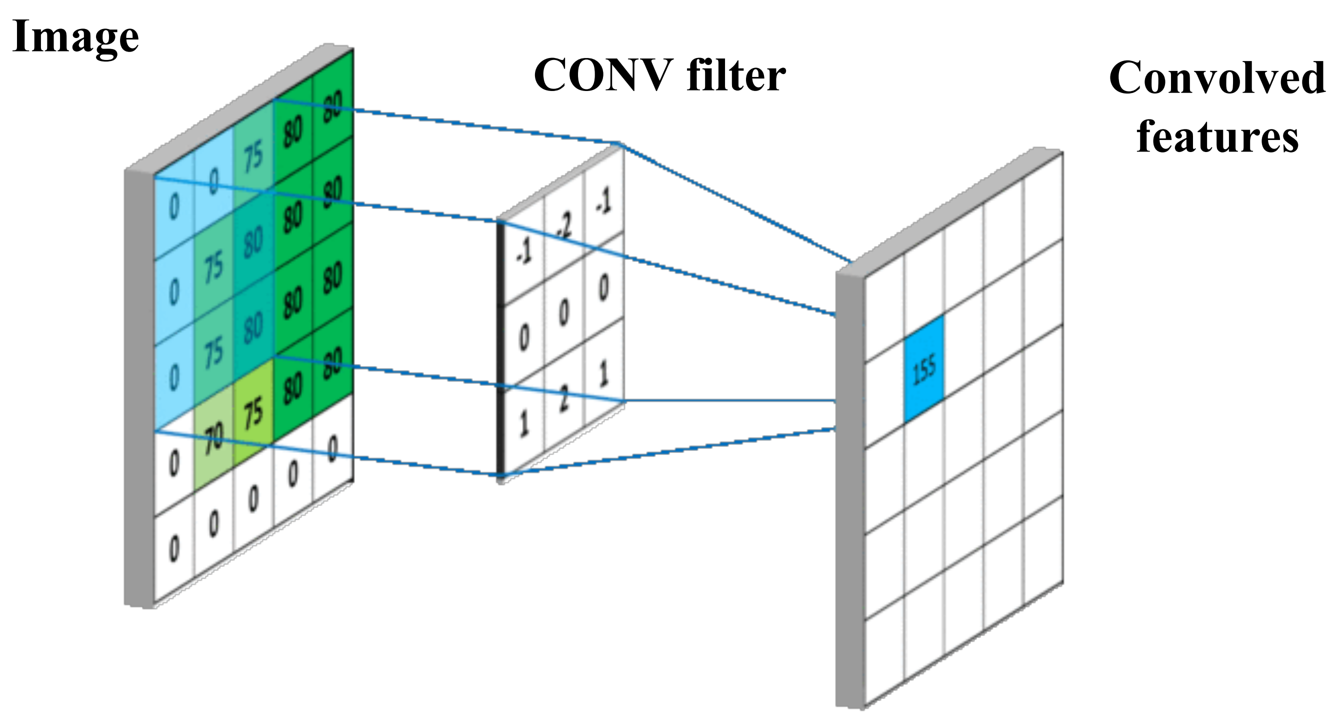
Convolutional Neural Networks

Convolution: Extract features for analysis
Activation: Apply the non-linearity
Pooling: Change the spatial size of image or features



Reference: https://cs231n.github.io/convolutional-networks/

Convolutions



Reference: www.cs.cmu.edu/~bhiksha/courses/deeplearning

Convolutions

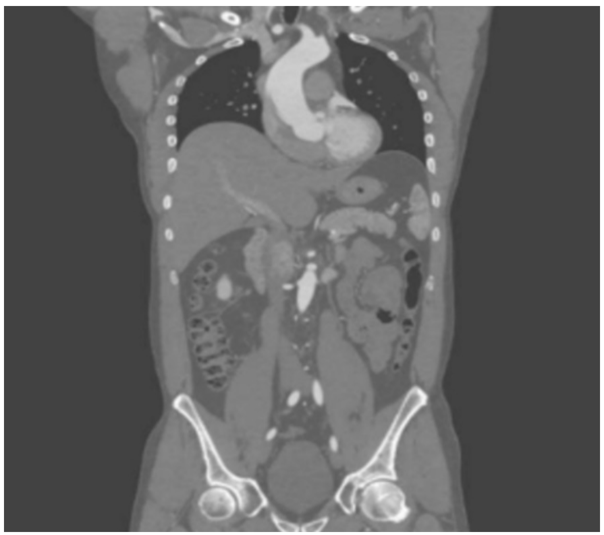
Convolution filters with different parameters could have different functions.

Reference: https://setosa.io/ev/image-kernels/

Convolutions

Convolution filters with different parameters could have different functions.

Here are some hand-crafted filters for example

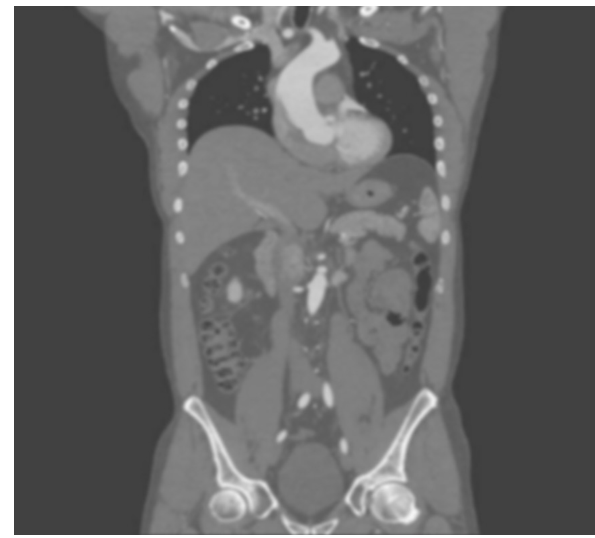


Input

0.11	0.11	0.11
0.11	0.11	0.11
0.11	0.11	0.11

Filter

Blur



Output

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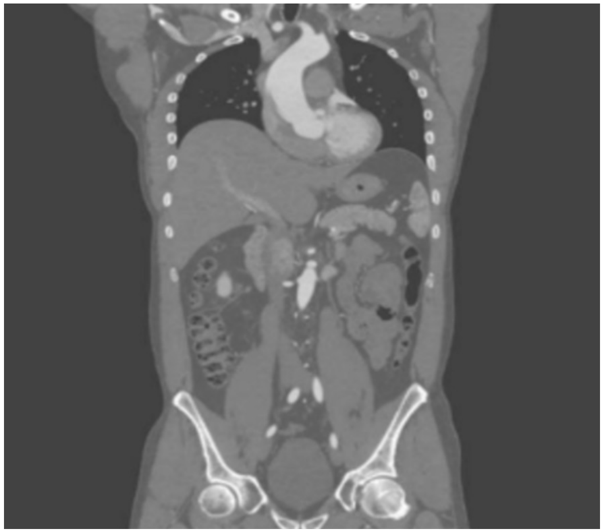

Input

0	-2	0
-2	9	-2
0	-2	0

Filter

Sharpen

Output

Reference: https://setosa.io/ev/image-kernels/

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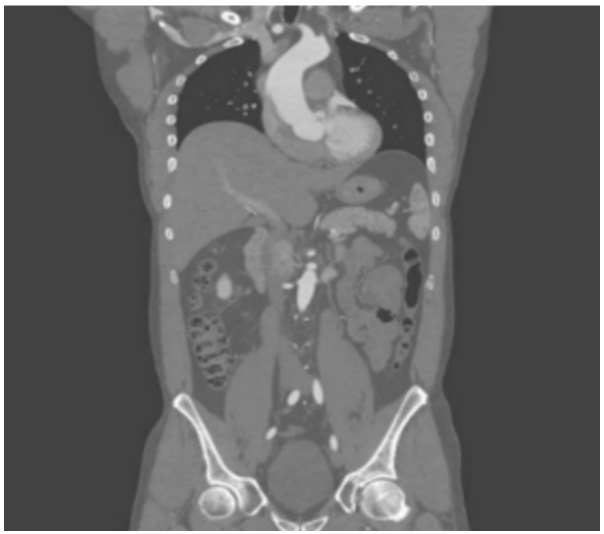
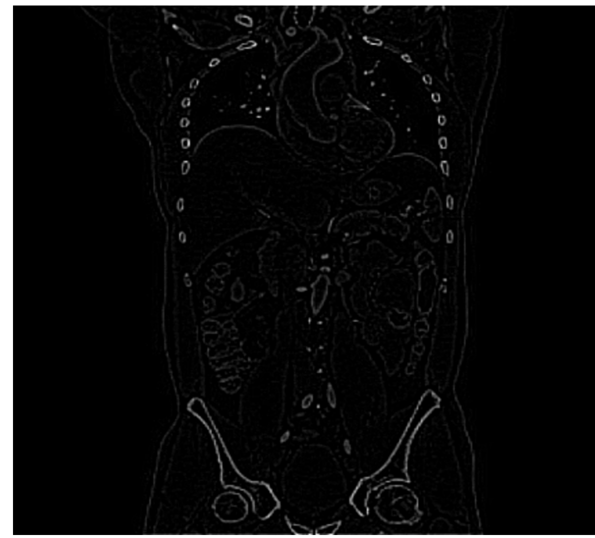


Input

-1	-1	-1
-1	8	-1
-1	-1	-1

Filter

Outline



Output

Reference: https://setosa.io/ev/image-kernels/

Convolutions

Convolution filters with different parameters could have different functions.

Composition of convolutions could achieve more complex functions

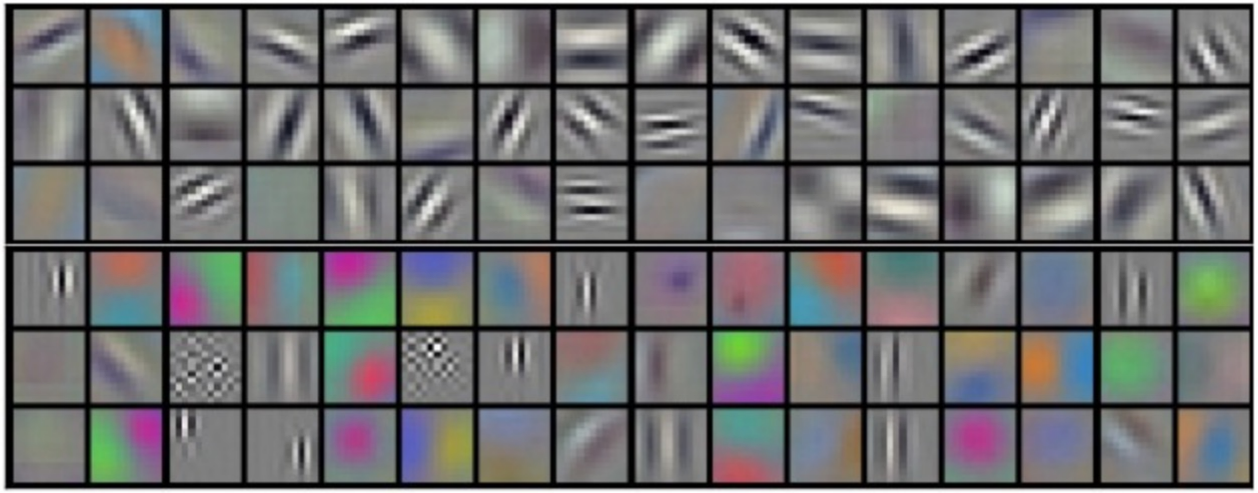
Reference: https://cs231n.github.io/convolutional-networks/

Convolutions

Convolution filters with different parameters could have different functions.

Composition of convolutions could achieve more complex functions

In convolutional neural networks, the convolution filters are learned by training on the dataset with backpropagation and gradient descent.

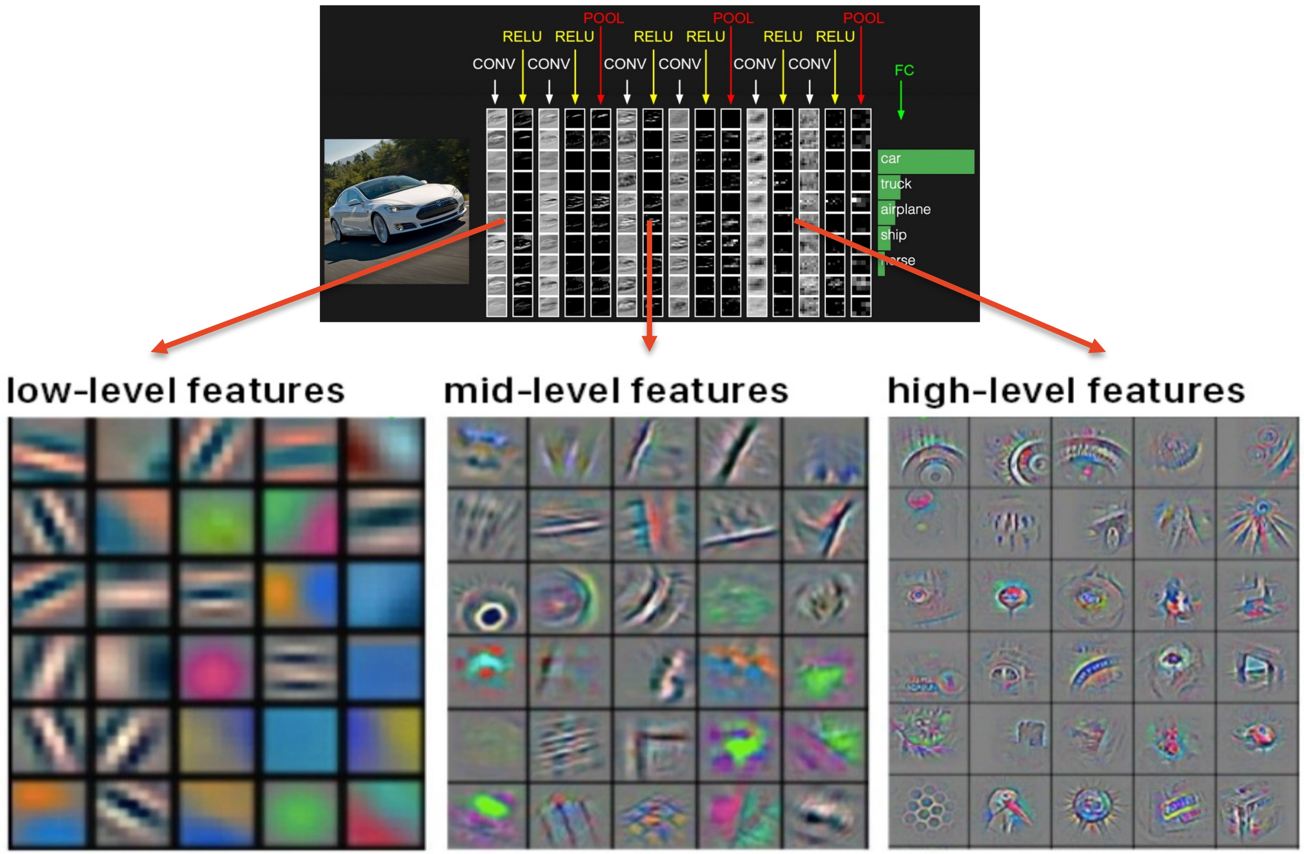


Example learned filters (Size 11x11)

Reference: https://cs231n.github.io/convolutional-networks/

Convolutional Neural Networks

Convolutional neural networks could build a hierarchical feature representation, from simple low-level features (e.g., edges and corners) at the first layers to complex high-level features (e.g., patterns and objects) at the last layers.



Reference: https://cs231n.github.io/convolutional-networks/
Reference: https://tvirdi.github.io/2017-10-29/cnn/

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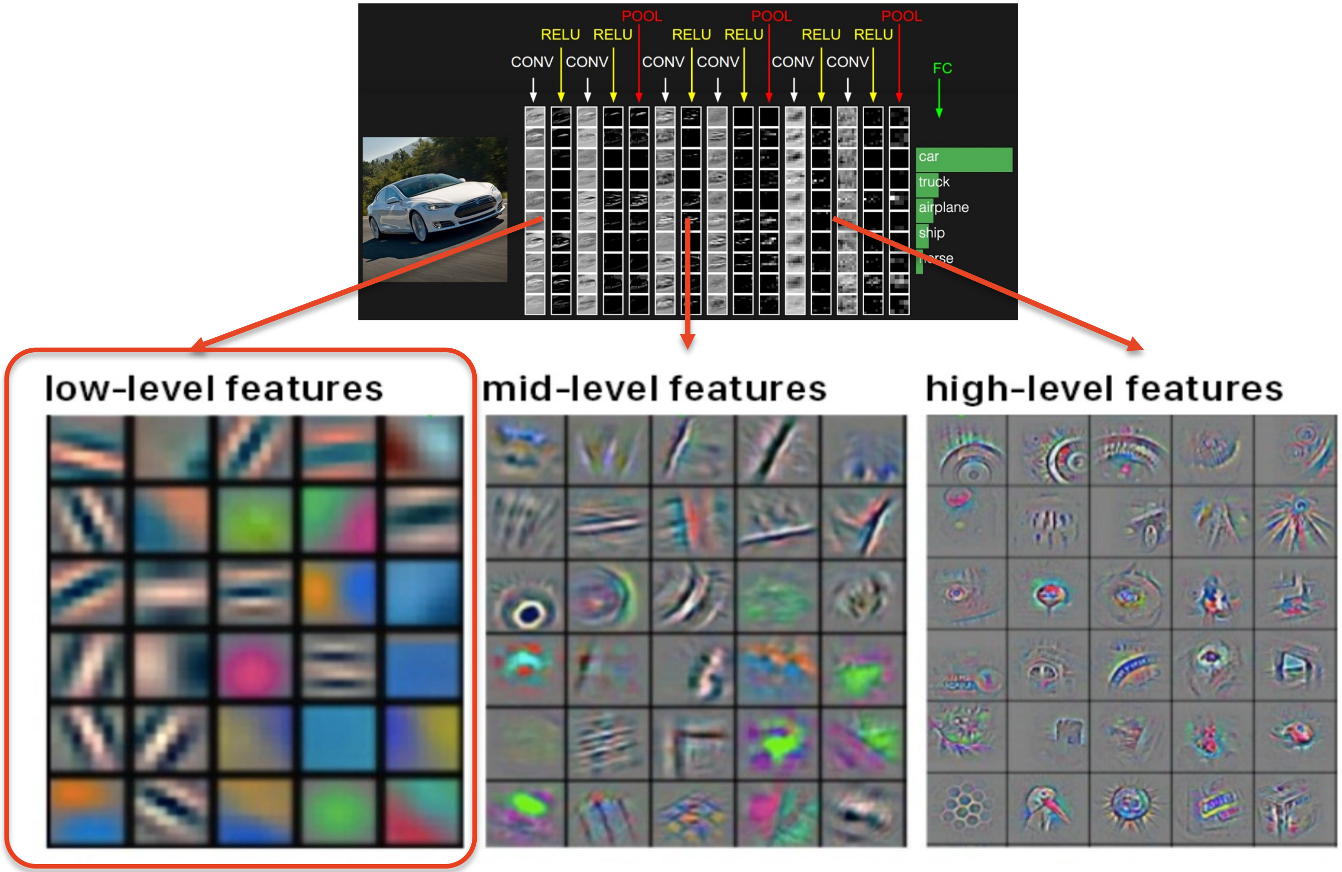

Reference: https://cs231n.github.io/convolutional-networks/
Reference: https://tvirdi.github.io/2017-10-29/cnn/

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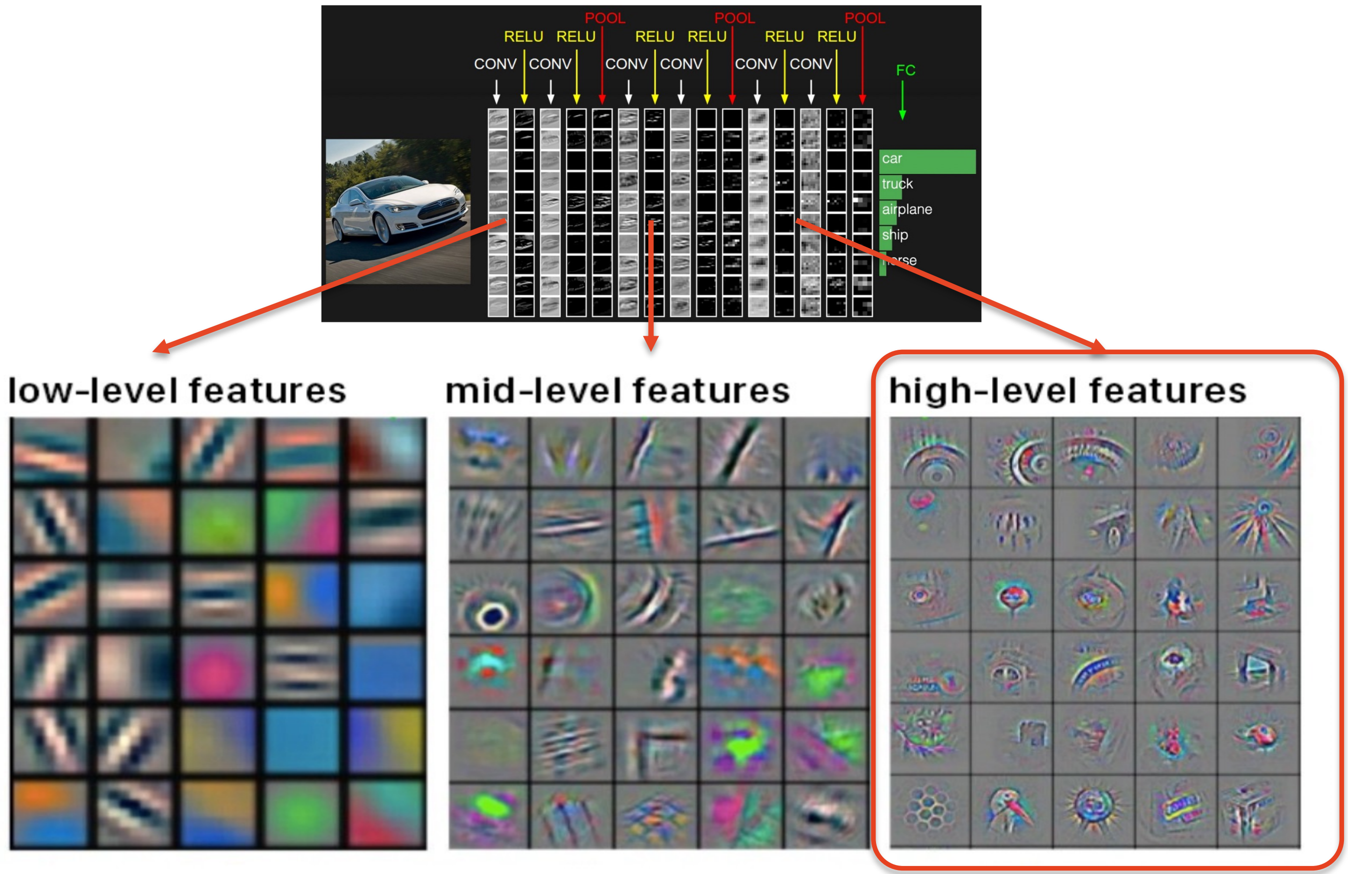
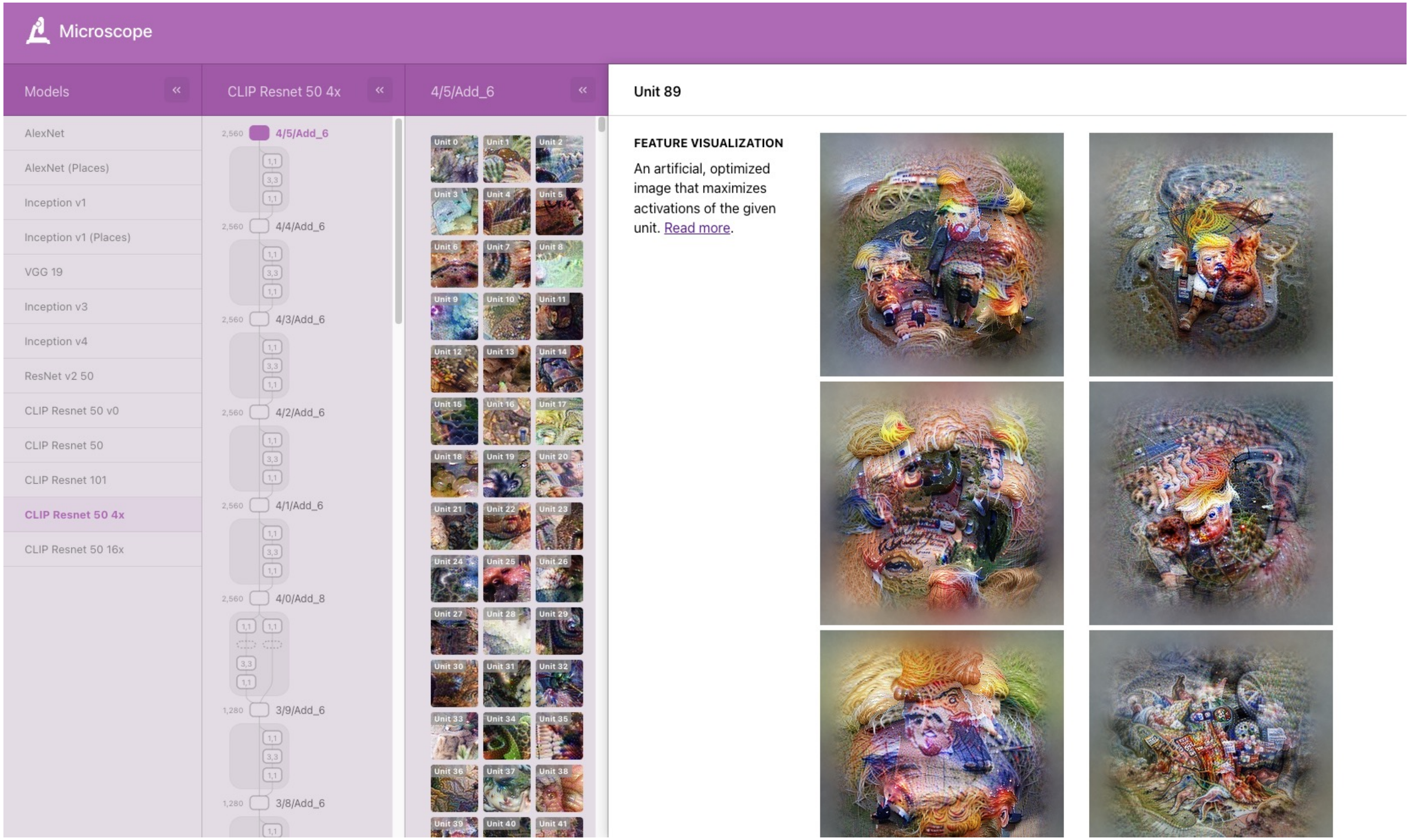


Reference: https://cs231n.github.io/convolutional-networks/
Reference: https://tvirdi.github.io/2017-10-29/cnn/

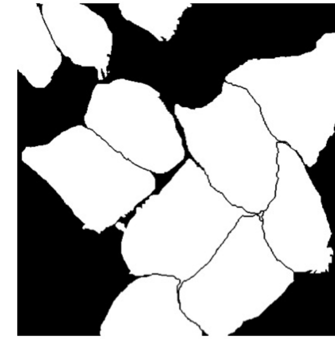
OpenAI Microscope



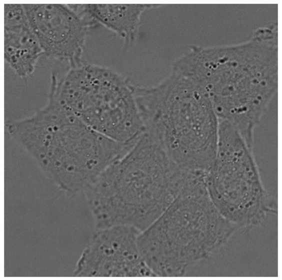
Reference: https://microscope.openai.com/models/contrastive_4x/image_block_4_5_Add_6_0/89
Reference: https://distill.pub/2021/multimodal-neurons/#person-neurons

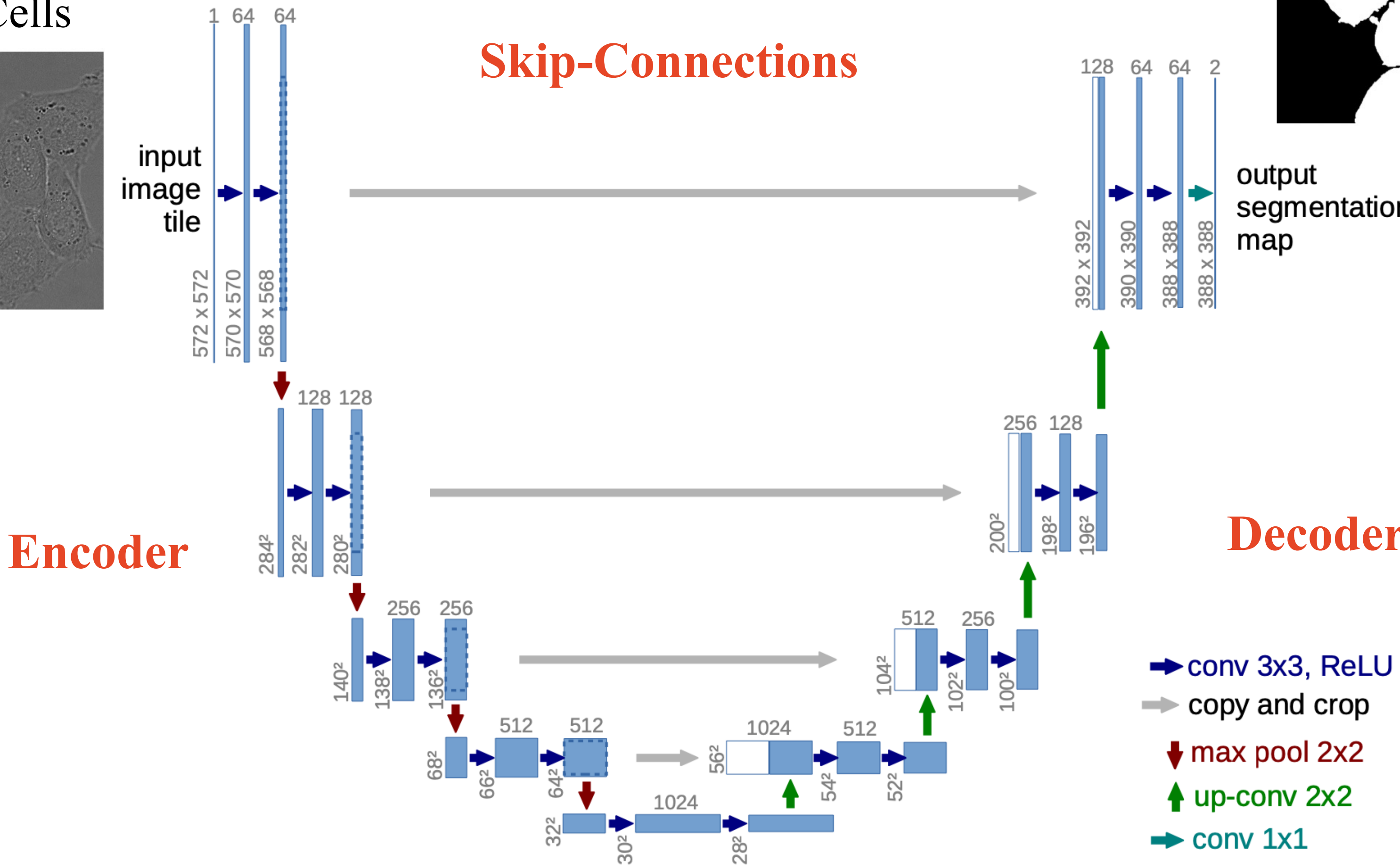
U-Net

Cell Masks



HeLa Cells

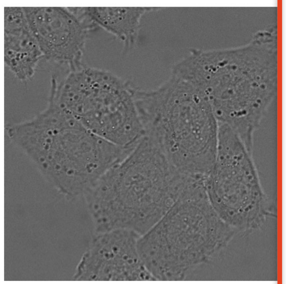




Reference: U-Net: Convolutional Networks for Biomedical Image Segmentation

U-Net

HeLa Cells



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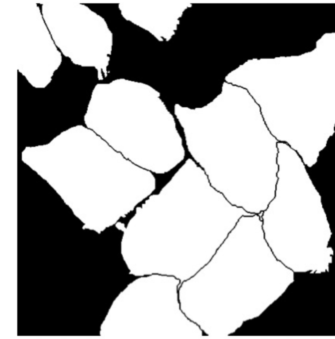

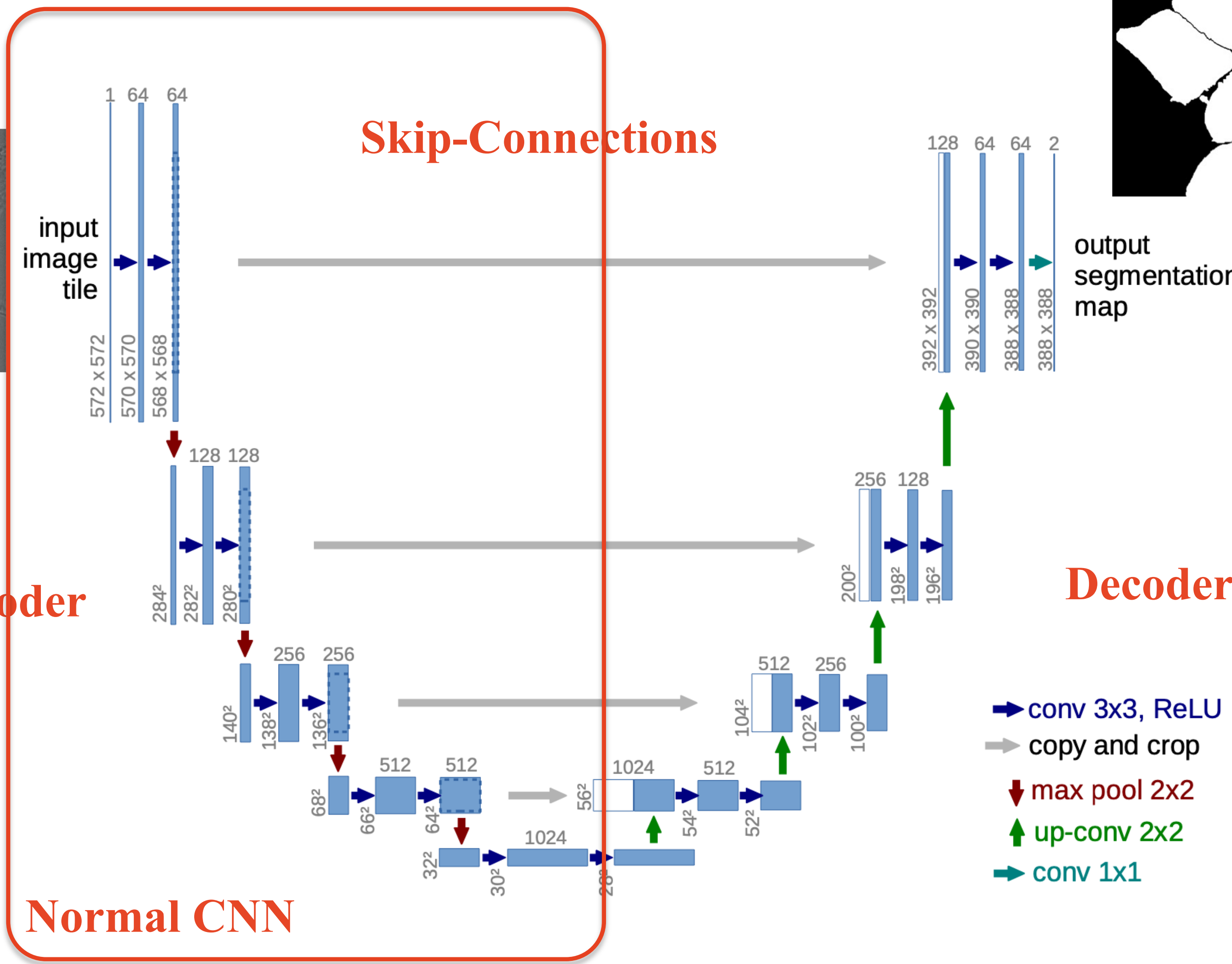

Reference: U-Net: Convolutional Networks for Biomedical Image Segmentation

U-Net

(Recall the hierarchical feature representation in CNNs)

The encoder down-samples the image to extract high-level semantics

The decoder up-samples the image to restore low-level details

The skip connections enable information passing between the two

Encoder: Convolutions + Down-sampling + Activations

- Increasing number of convolution filters
- Decreasing spatial size

Decoder: Convolutions + Up-sampling + Activations

- Decreasing number of convolution filters
- Increasing spatial size

Biomedical Image Segmentation

Classical Methods:
only use single image
- Watershed Algorithm

Learning-based Methods:
require a separate training step with many images
- Convolutional Neural Networks and U-Net
- Segment Anything Model (SAM)

Biomedical Image Segmentation

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only use single image
- Watershed Algorithm

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require a separate training step with many images
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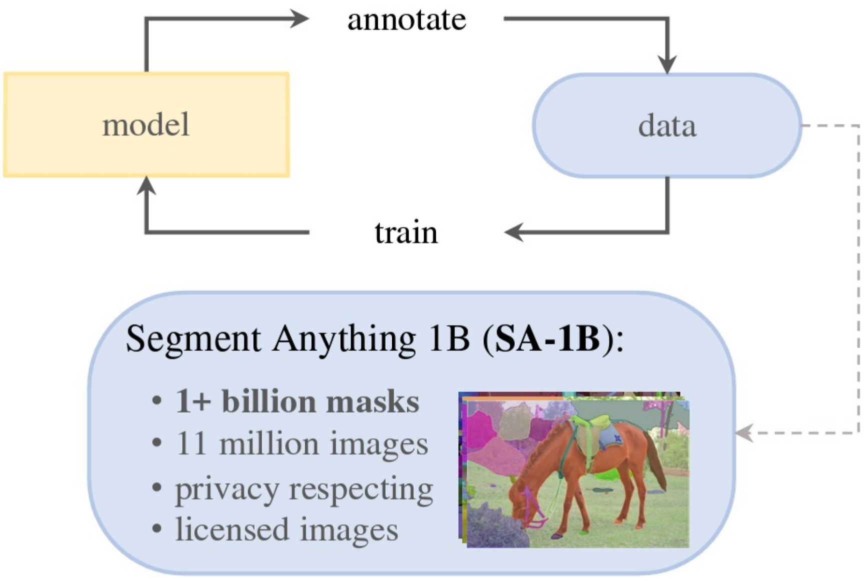
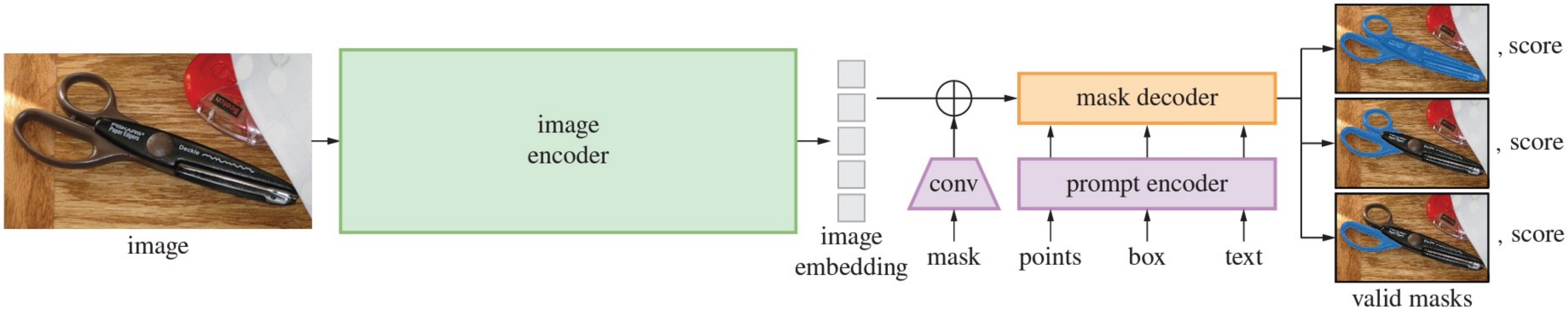
- **Segment Anything Model (SAM)**

Segment Anything Model (SAM)

A large visual foundation model for image segmentation:

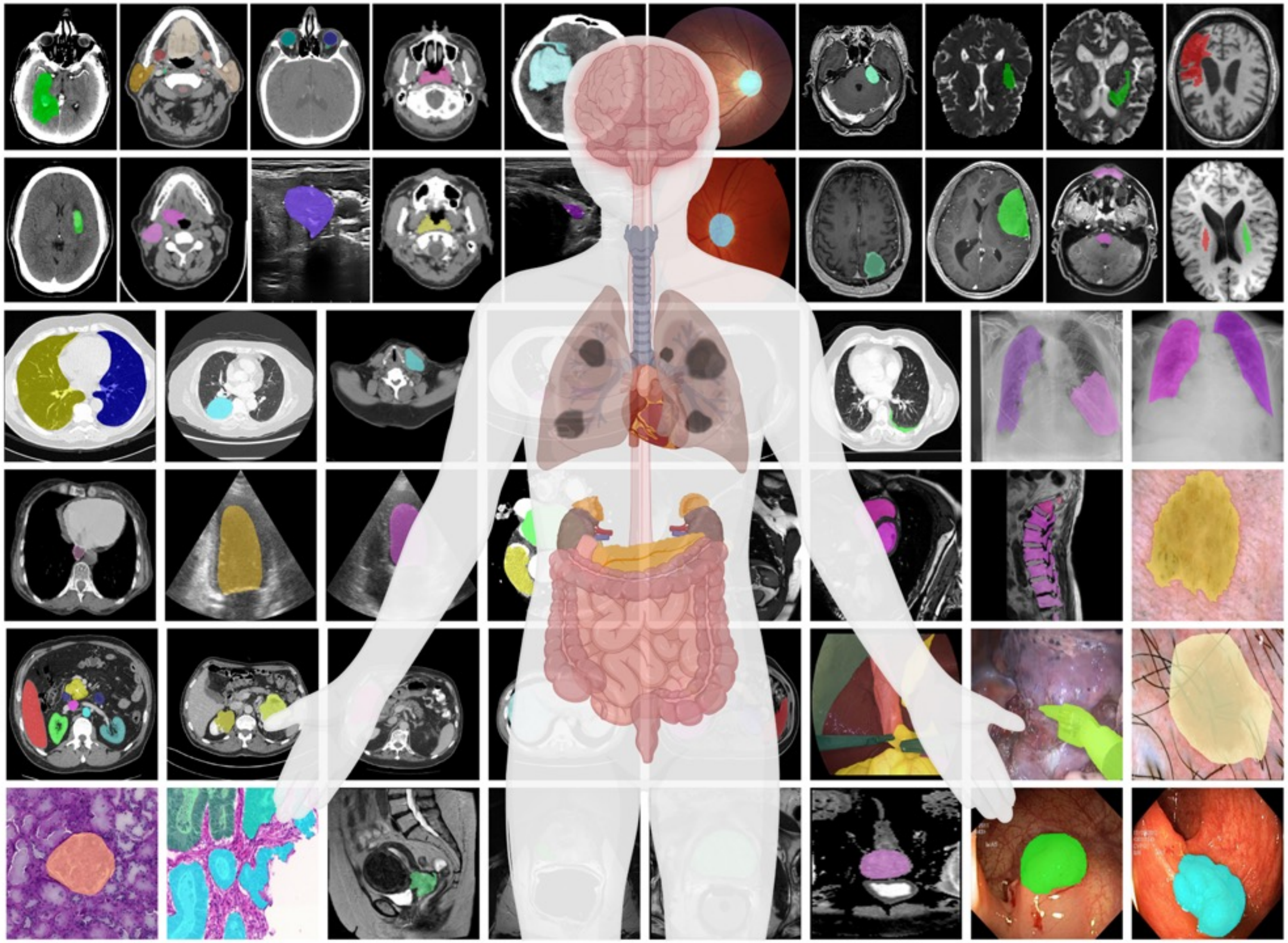
- Interactive (point, box, text)
- Zero-shot generalization
- Trained on large scale datasets





https://arxiv.org/abs/2304.02643

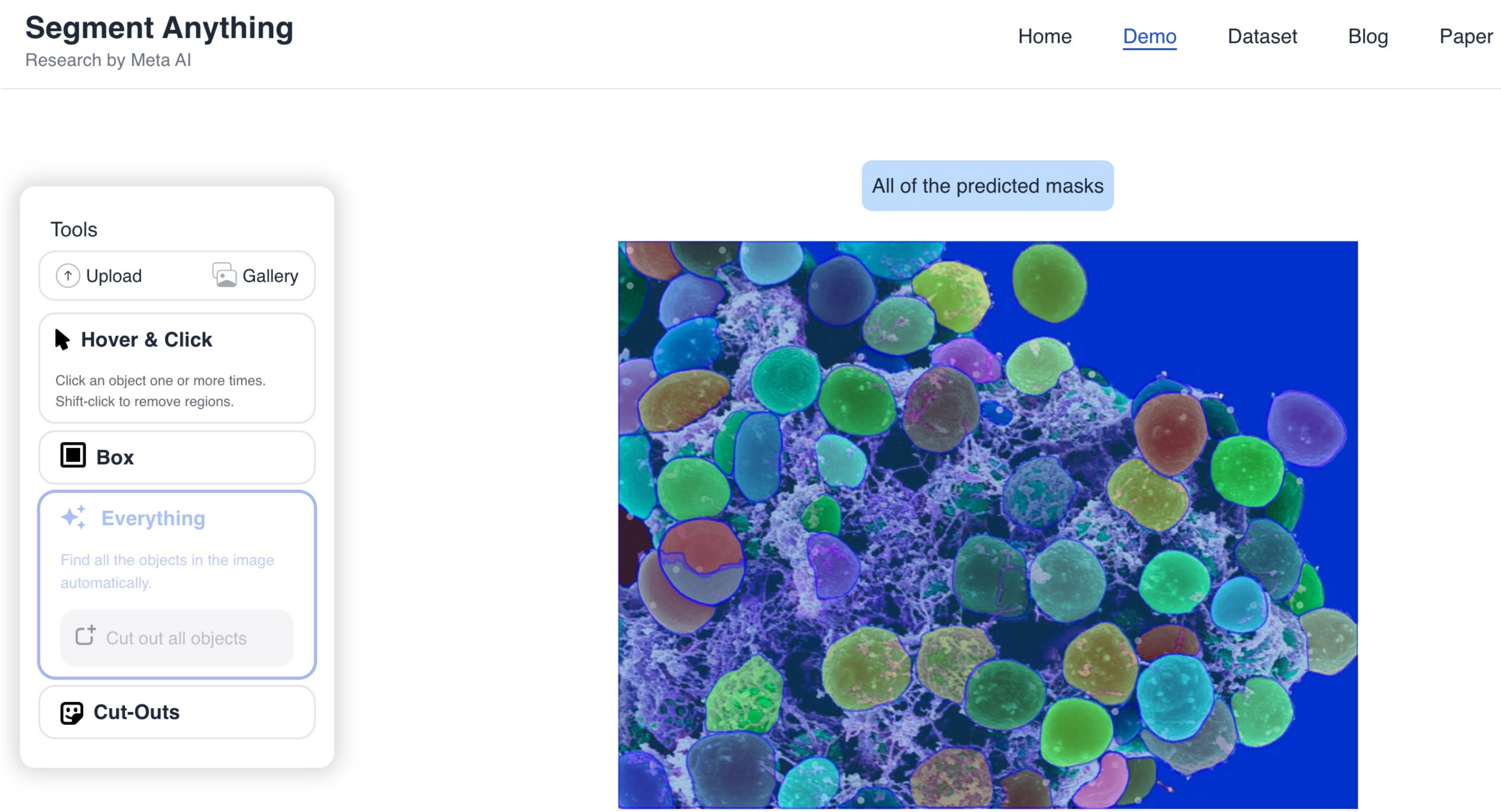
Segment Anything Model (SAM)



Widely used in recent medical image analysis research

https://arxiv.org/abs/2304.12306

Segment Anything Model (SAM)



https://segment-anything.com/demo

Task-specific topics:

- Biomedical image segmentation
- Biomedical image registration

Task-agnostic topics:

- Interpretability
- Uncertainty

Task-specific topics:

Biomedical image segmentation

Biomedical image registration

Task-agnostic topics:

Interpretability

Uncertainty

Biomedical Image Registration

The task of aligning or bringing into spatial correspondence two different images or volumes.

Applications include - but are not limited to:

- ***Multi-modal registration for image-guided surgery***: aligning real-time ultrasound scans to pre-operative CT or MRI scans to real-time achieve guidance (ultrasound to CT / MRI)
- ***Atlas-based image segmentation***: aligning new images to those carefully segmented, such that the reference segmentations can be propagated to new images (new images to atlas)
- ***Longitudinal comparison of images for a patient***: for example, comparing the outcome of given cancer treatment in a patient's scans over time (registration to the same subject)
- ***Inter-subject comparison***: for example a population study of organ shapes (registration to a different subject)

Reference: https://github.com/DeepRegNet/DeepReg

Biomedical Image Registration

Registration is treated as an optimization problem where we wish to find a transform that maps the moving image to the fixed image, yielding a transformed image that maximizes some similarity metric with respect to the original true fixed image.

Reference: Deformable Registration of Brain MR Images via a Hybrid Loss

Biomedical Image Registration

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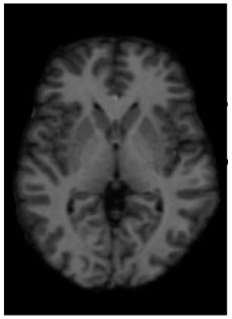
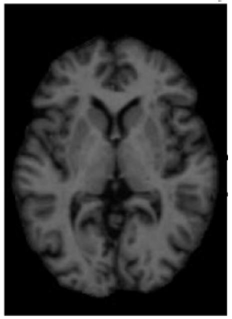
Fixed Image



Moving Image



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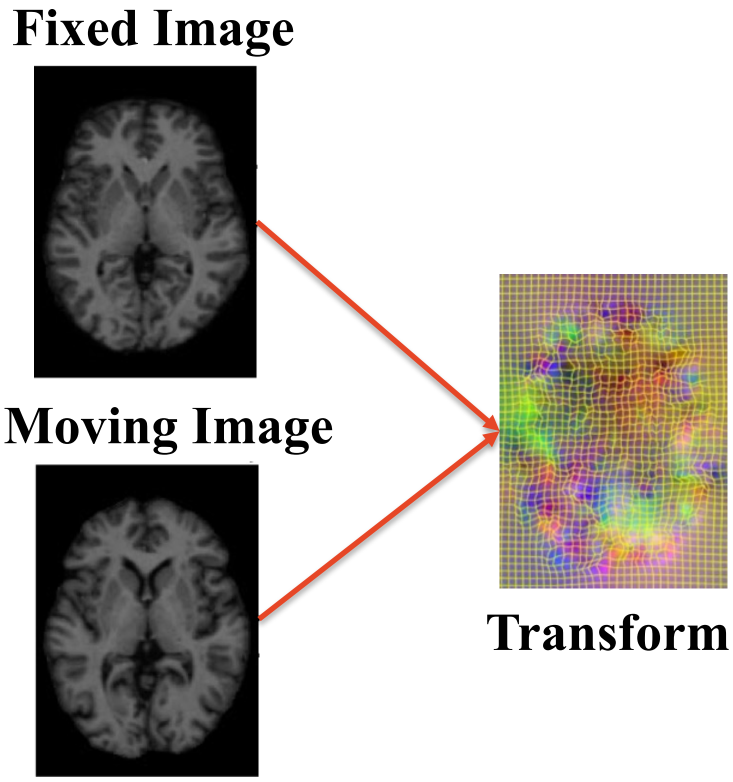

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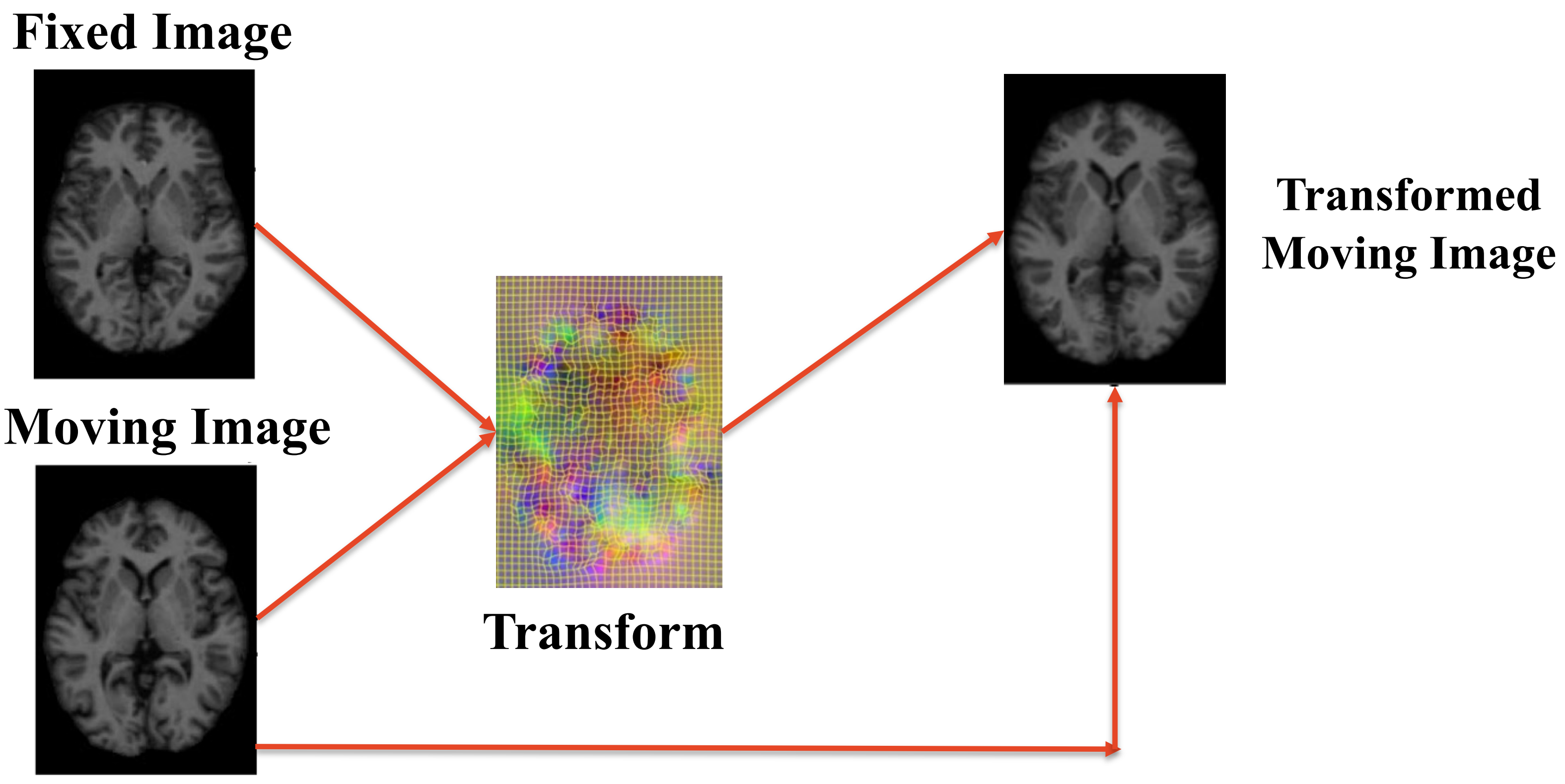

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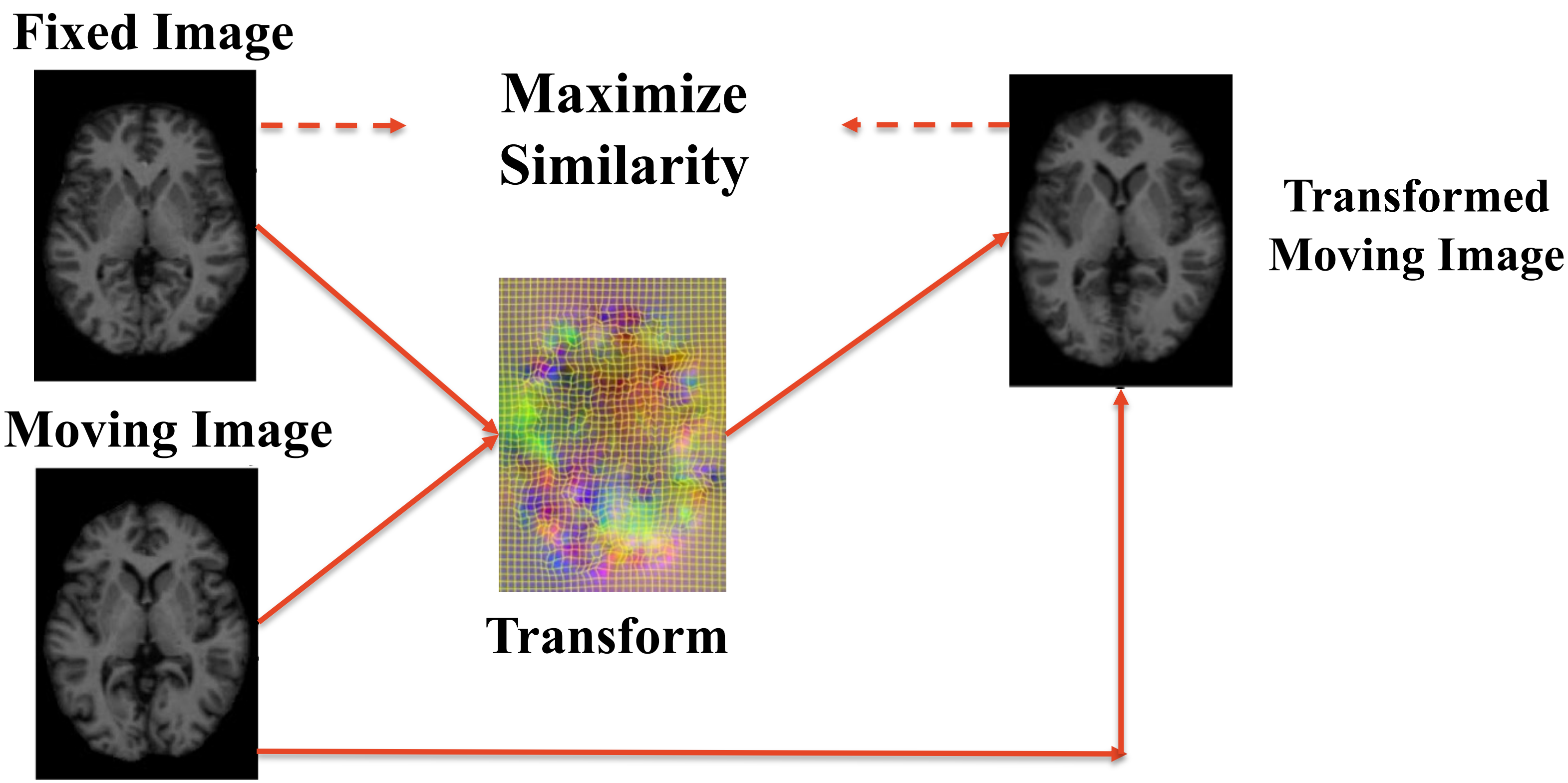

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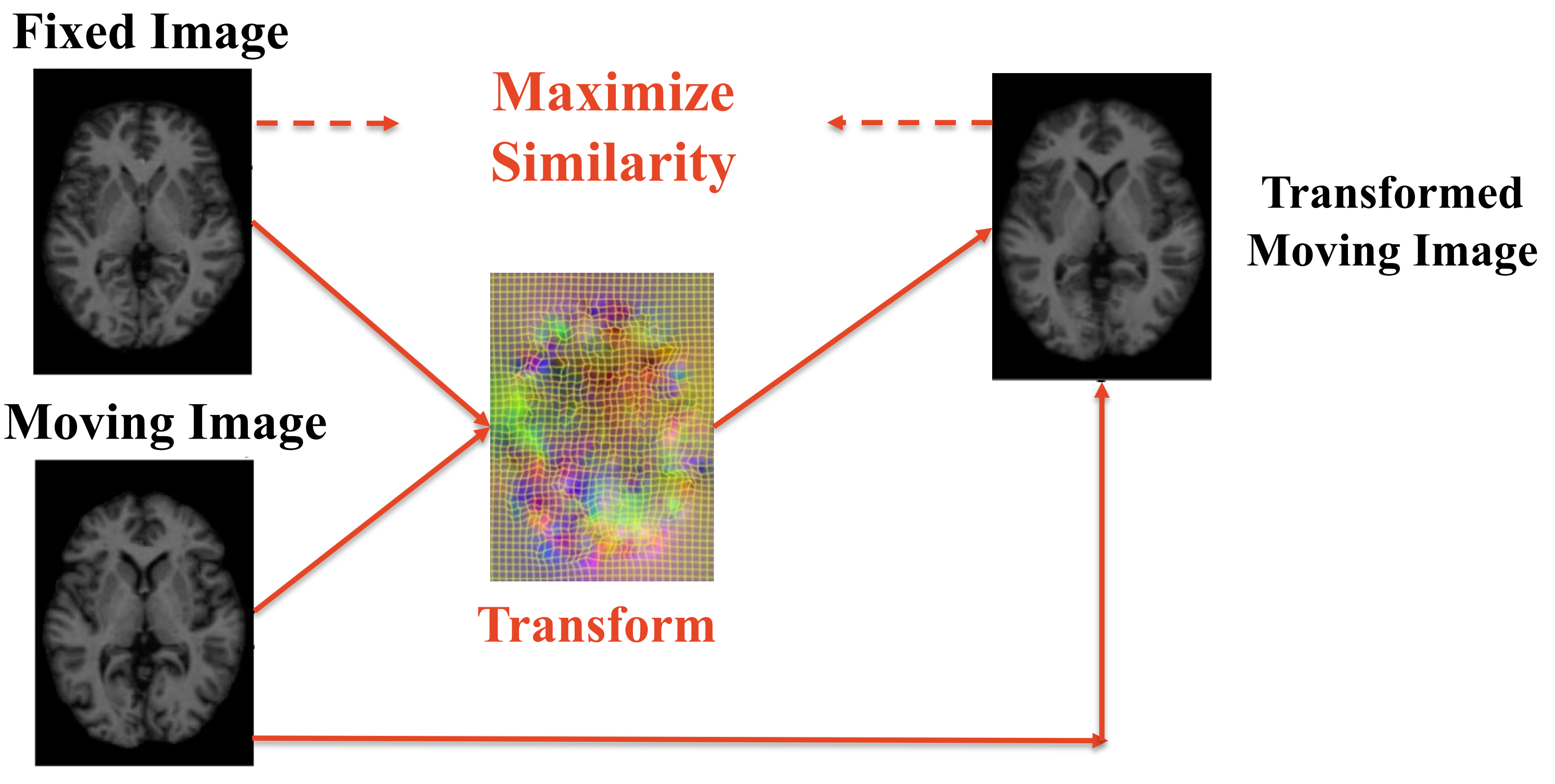


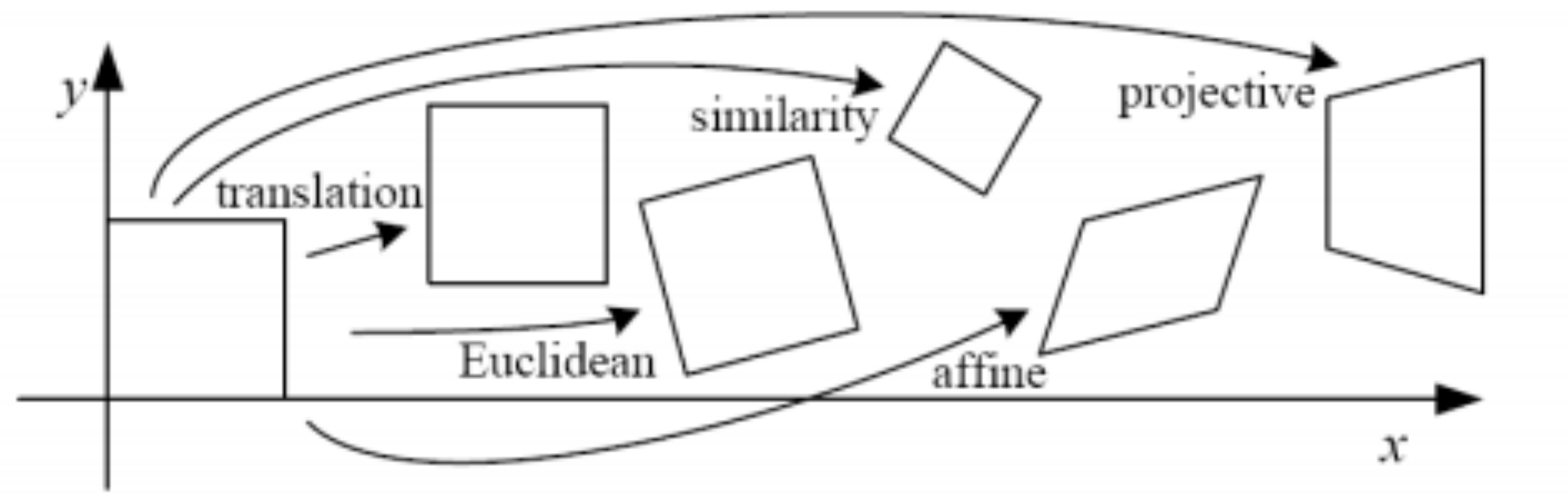
Reference: Deformable Registration of Brain MR Images via a Hybrid Loss

Biomedical Image Registration

- Classical Transforms, Similarity Metrics, Optimizers
- Deep Learning for Registration

Transforms

- Euclidean Transform: Translation + Rotation
- Similarity Transform: Euclidean + Uniform Scaling
- Affine Transform: Similarity + Nonuniform Scaling + Shear
- Projective Transform: Affine + Perspective Distortion

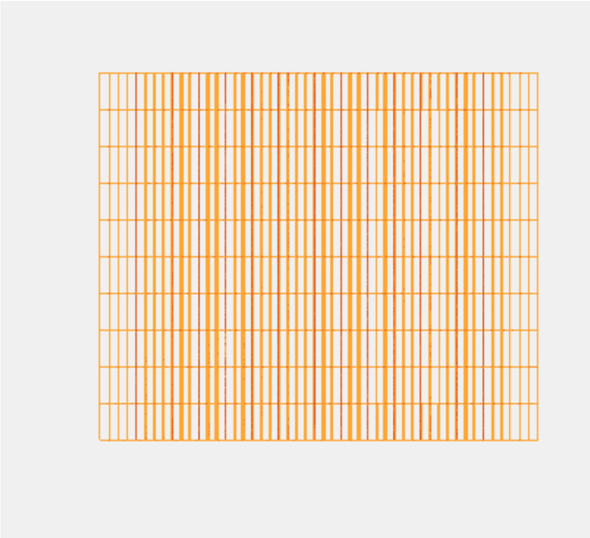


Reference: https://www.chegg.com

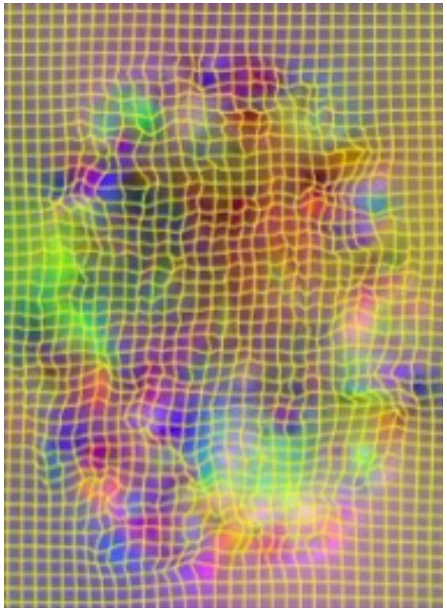
Transforms

Deformable transform is important when modeling higher-dimensional tissue deformations, which is usually represented as Dense Displacement Field (DDF)

3D DDF



2D DDF



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Similarity Metrics

Mean Squares: Naïve pixel-wise distance

$$d(A,B) = \frac{1}{N}\sum_{i=1}^{N}(A_i - B_i)^2$$

Normalized Cross-Correlation: Pixel-wise cross correlation

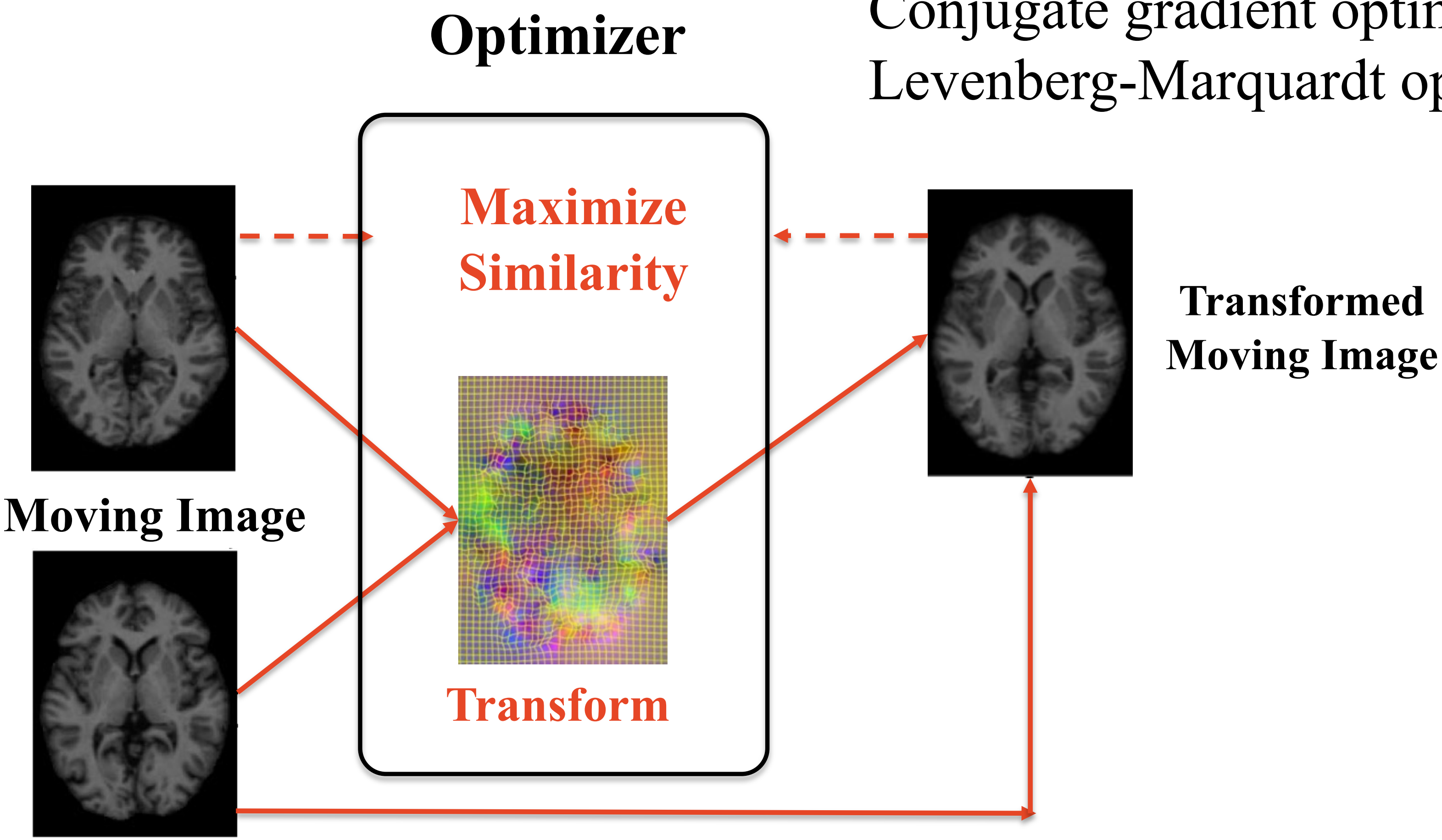
$$s(A,B) = \frac{\sum_i [A_i - \mu_A][B_i - \mu_B]}{\sqrt{\sum_i [A_i - \mu_A]^2 \sum_i [B_i - \mu_B]^2}}$$

Mutual Information: Similarity in an information theoretic sense

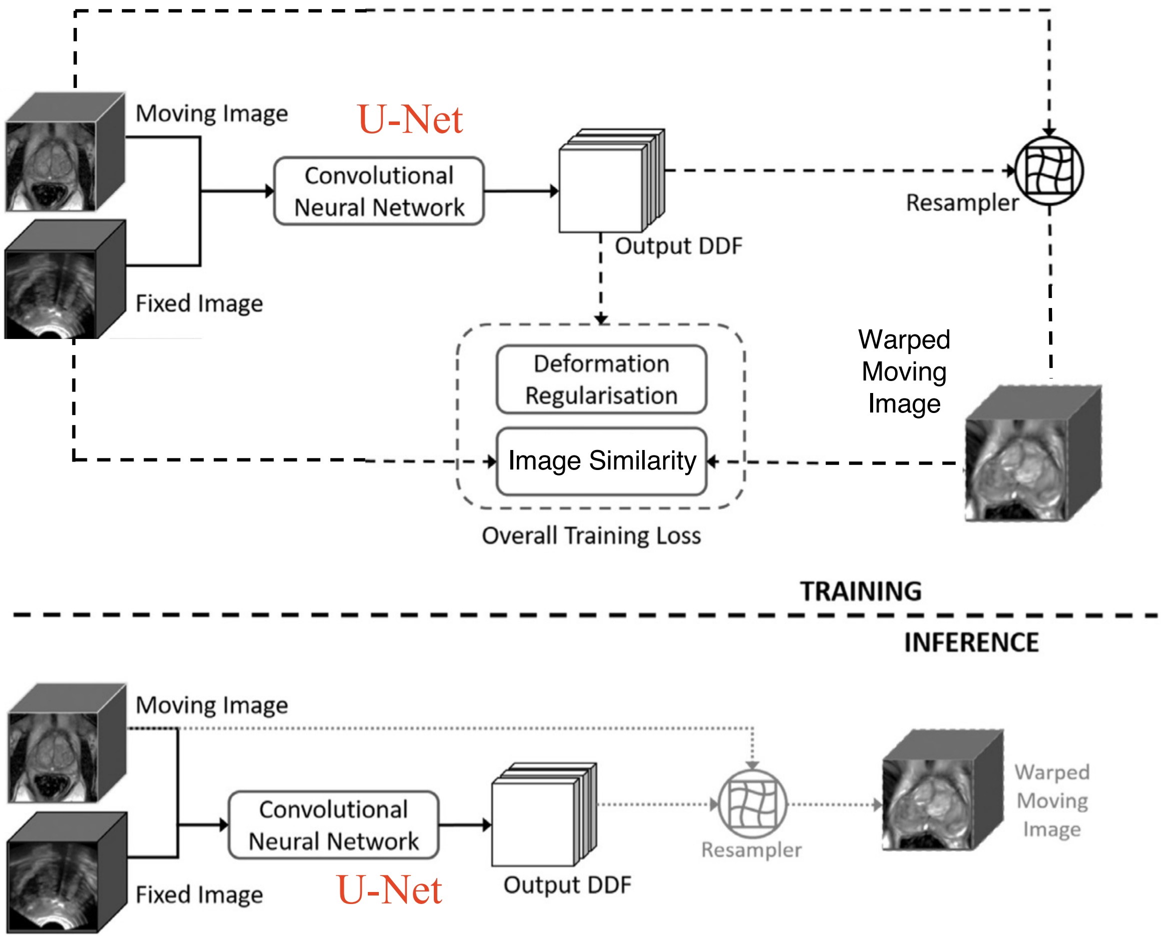
$$I(A,B) = \sum_{a,b} p_{AB}(a,b) log \frac{p_{AB}(a,b)}{p_A(a)p_B(b)}$$

Classical Registration Optimizers

Gradient descent optimizer
Conjugate gradient optimizer
Levenberg-Marquardt optimizer



Deep Learning for Registration (DeepReg)



Trained with image similarity

Reference: Weakly-supervised convolutional neural networks for multimodal image registration

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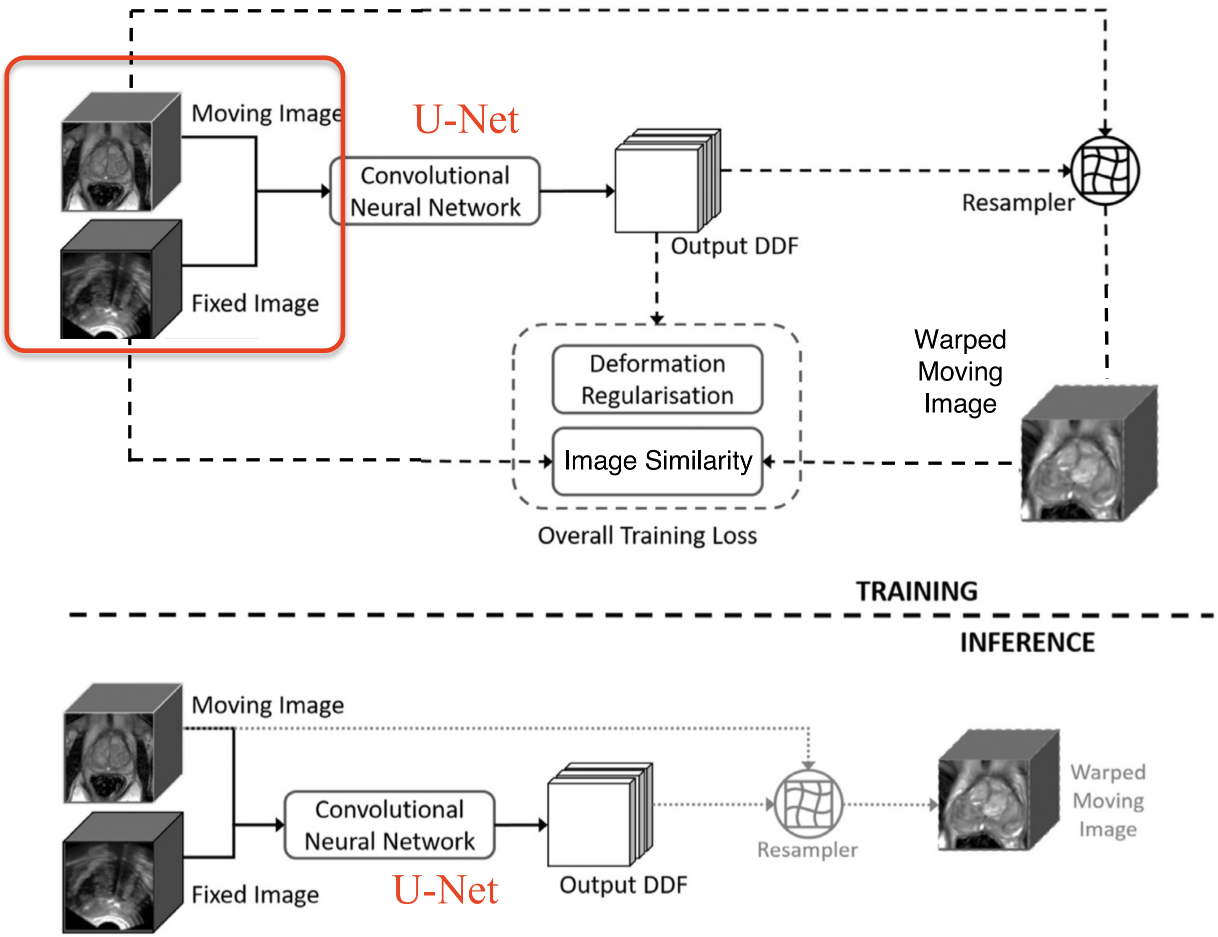

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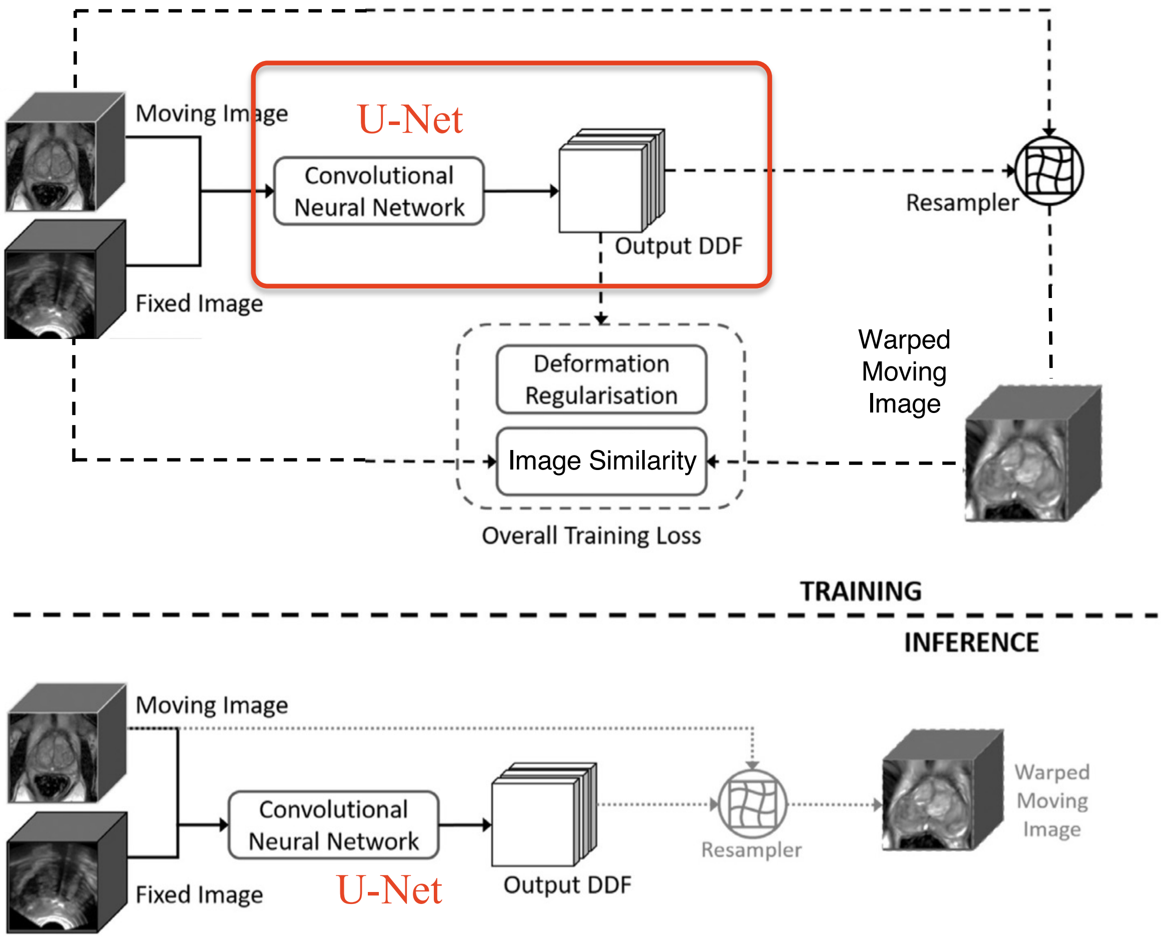

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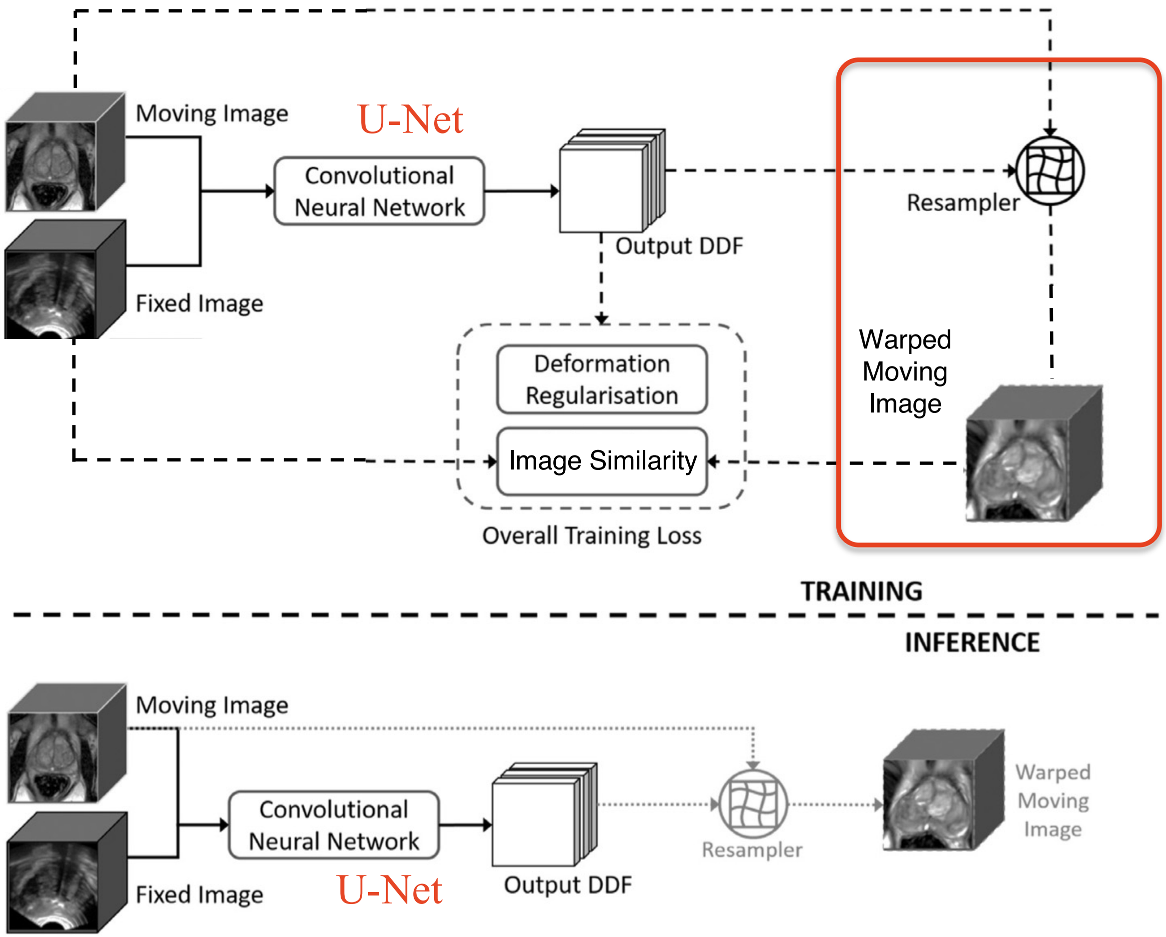

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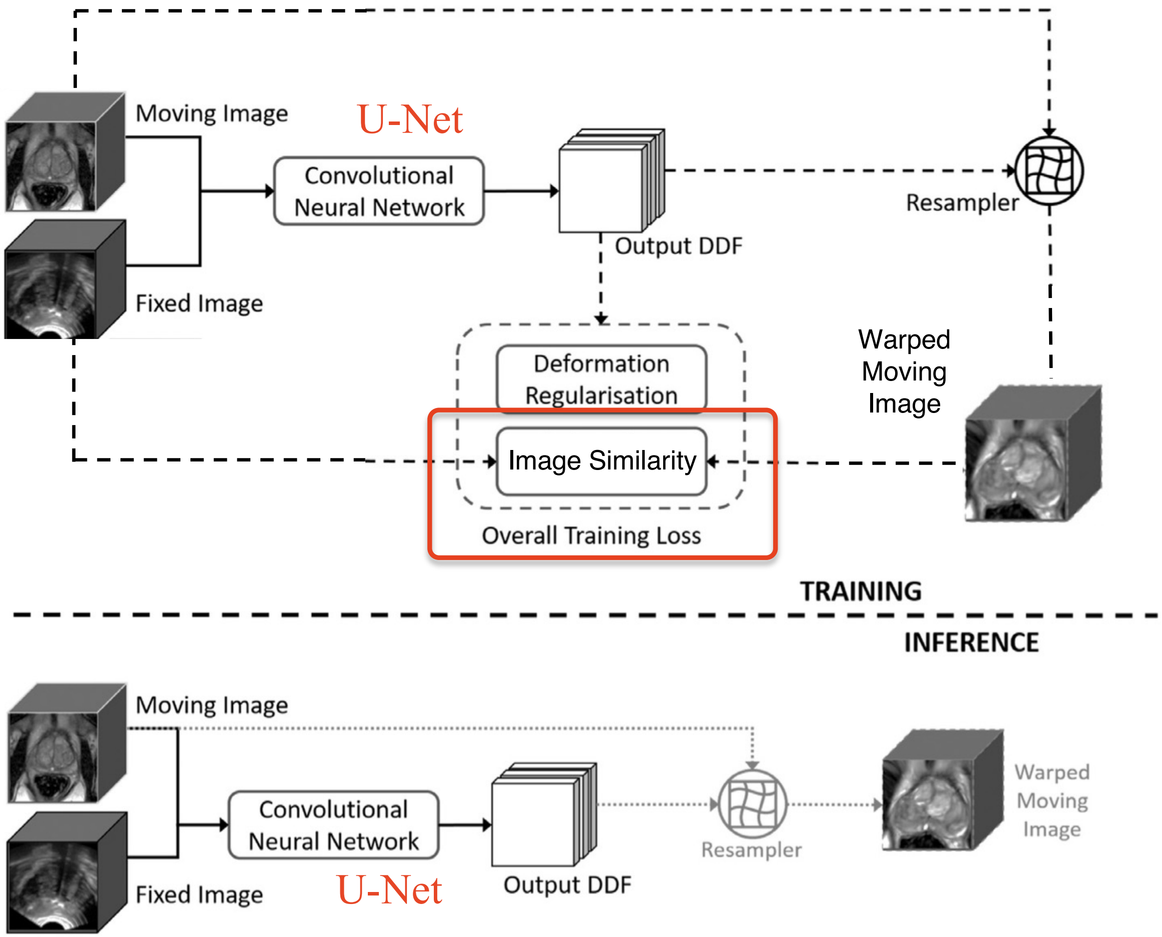

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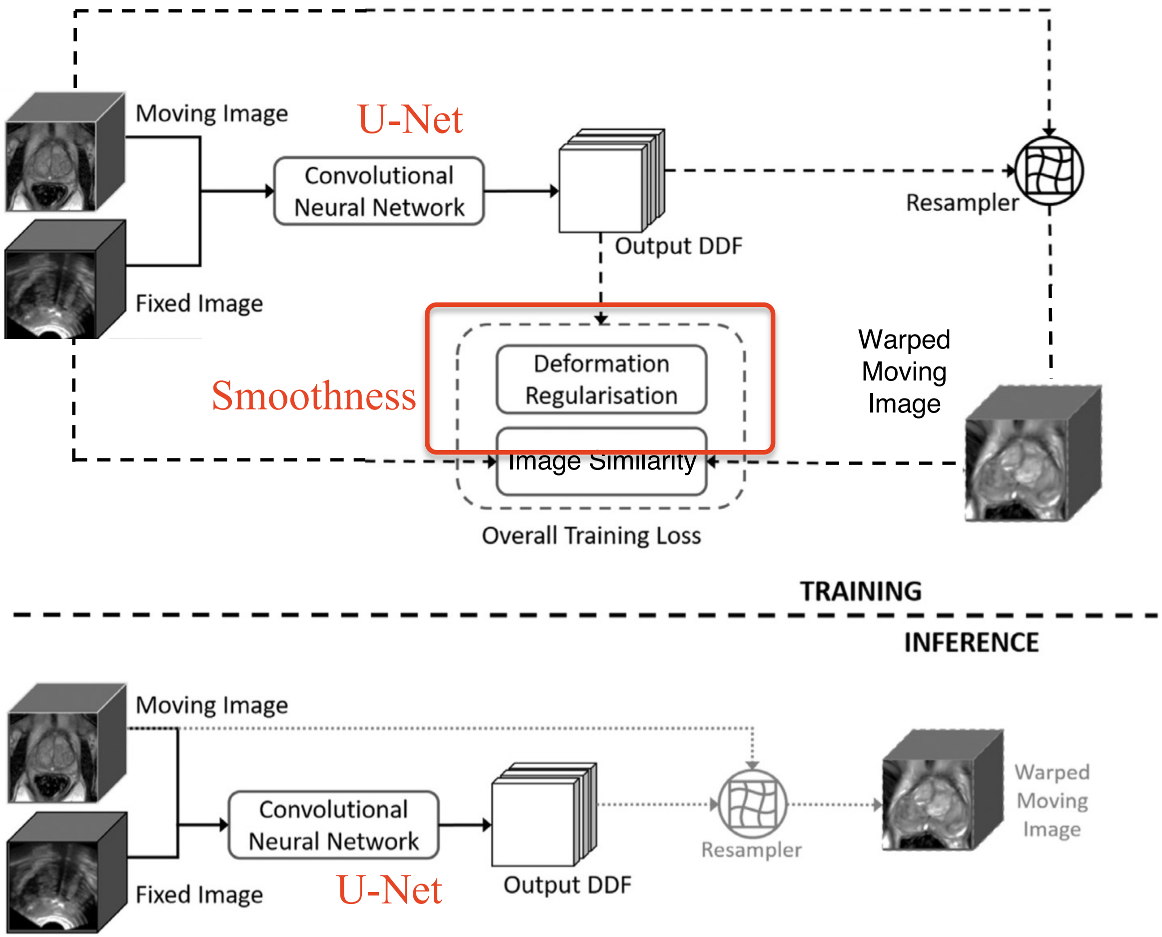

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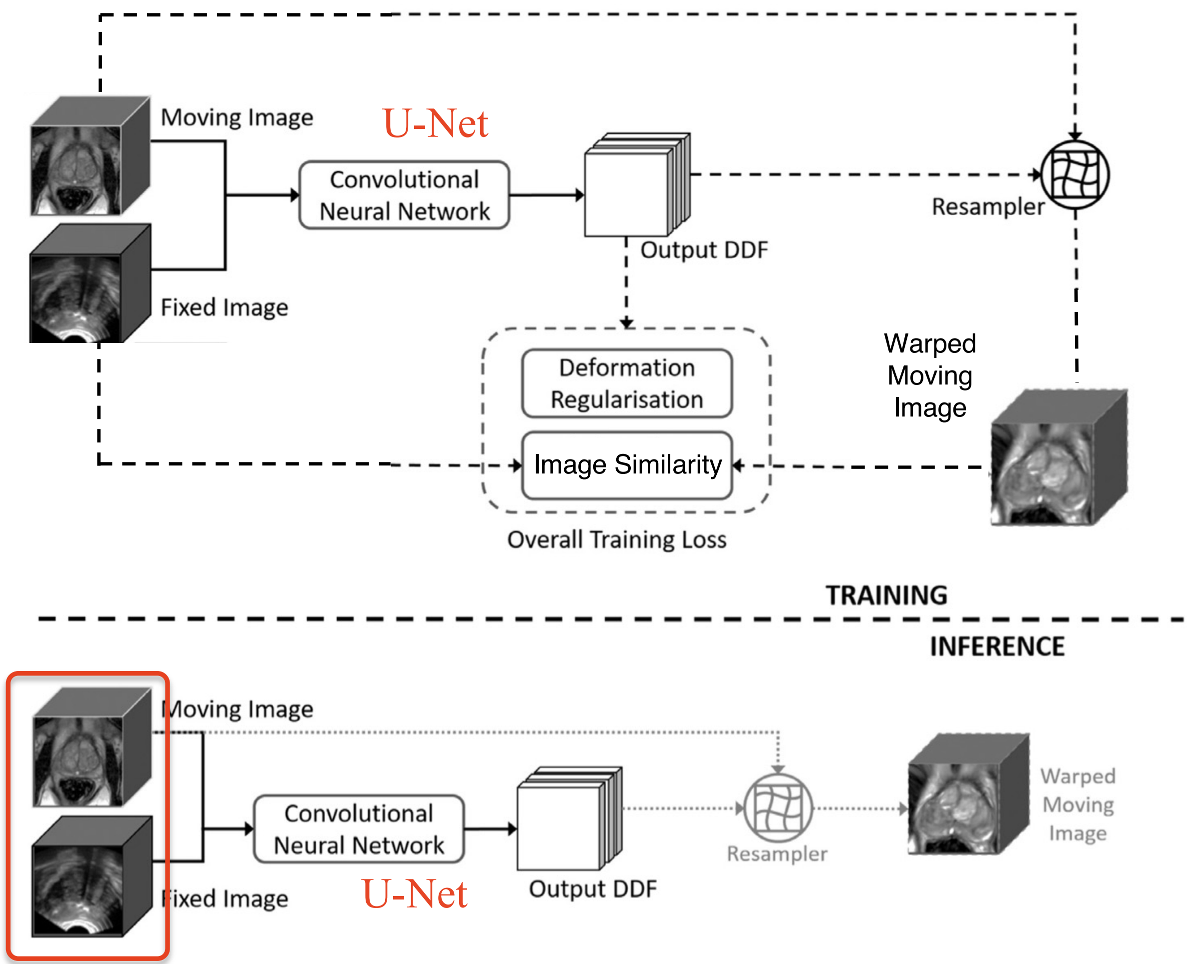

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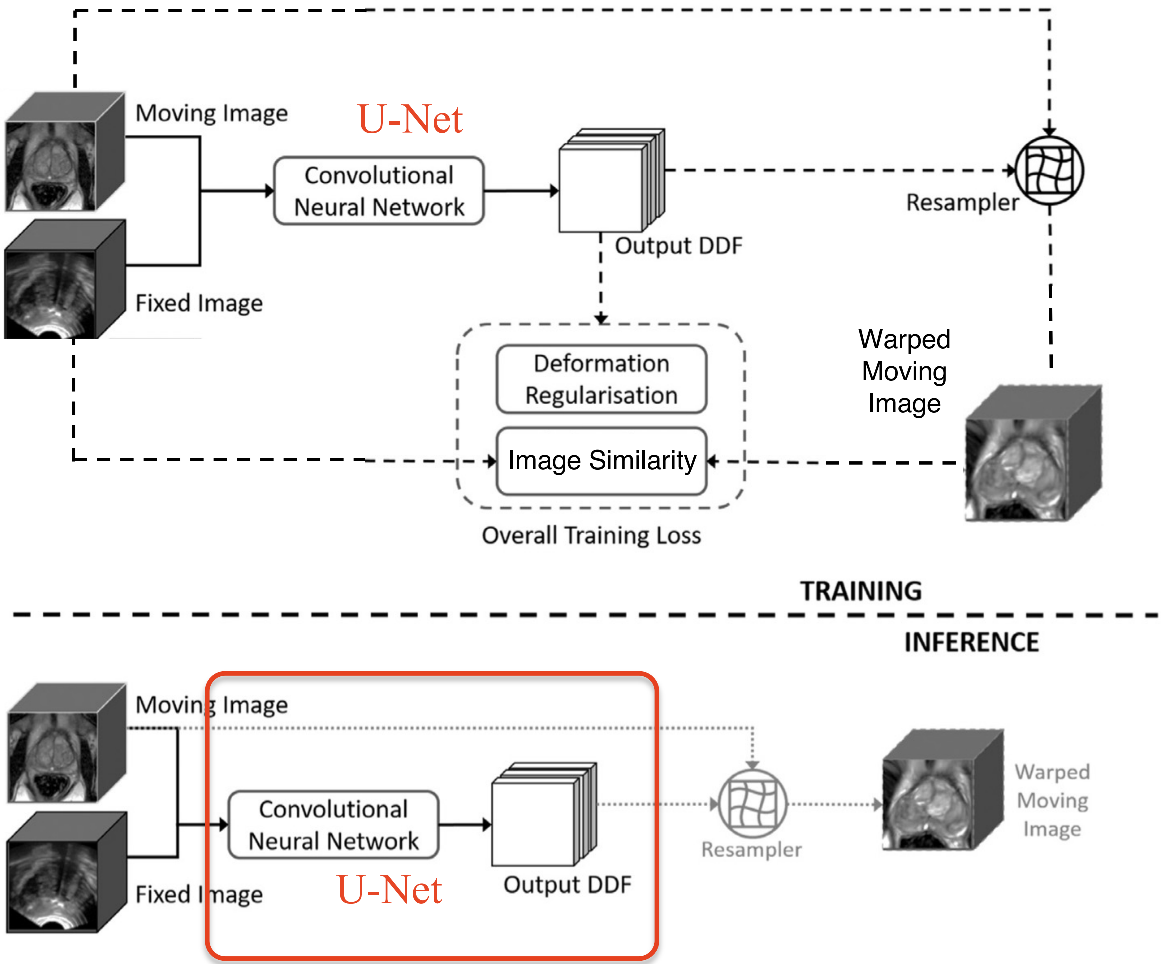

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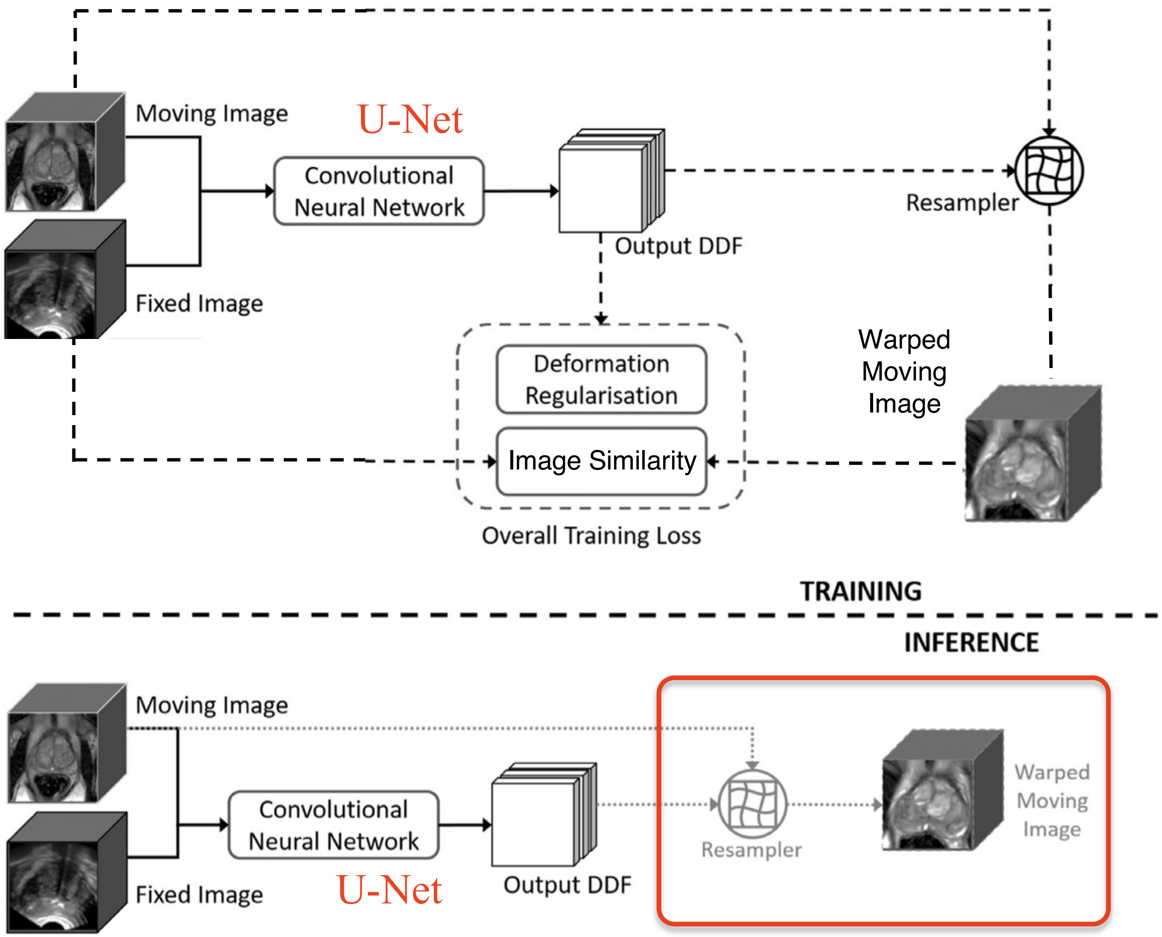

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Task-specific topics:

Biomedical image segmentation

Biomedical image registration

Task-agnostic topics:

Interpretability

Uncertainty

Task-specific topics:

Biomedical image segmentation

Biomedical image registration

Task-agnostic topics:

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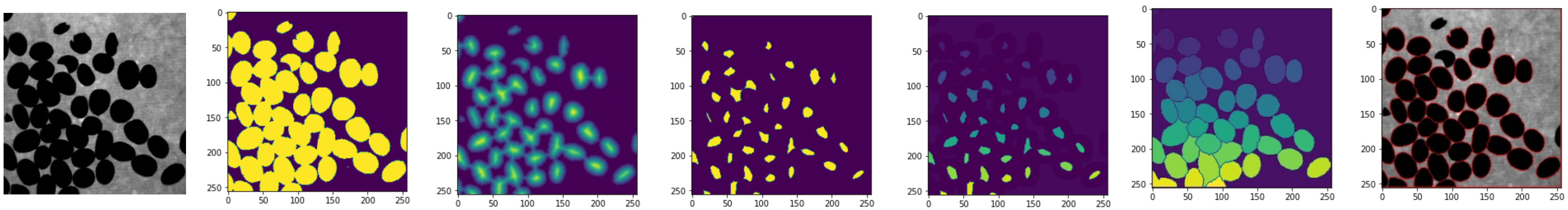
Uncertainty

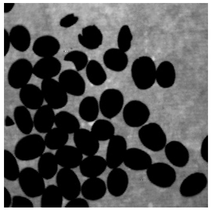
Interpretable AI

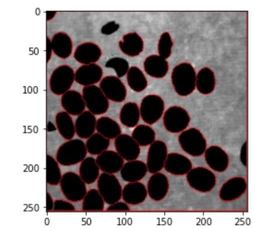
- Classic algorithms are interpretable (e.g., Watershed)



Whitebox

- Deep learning algorithms are not (e.g., U-Net, SAM)

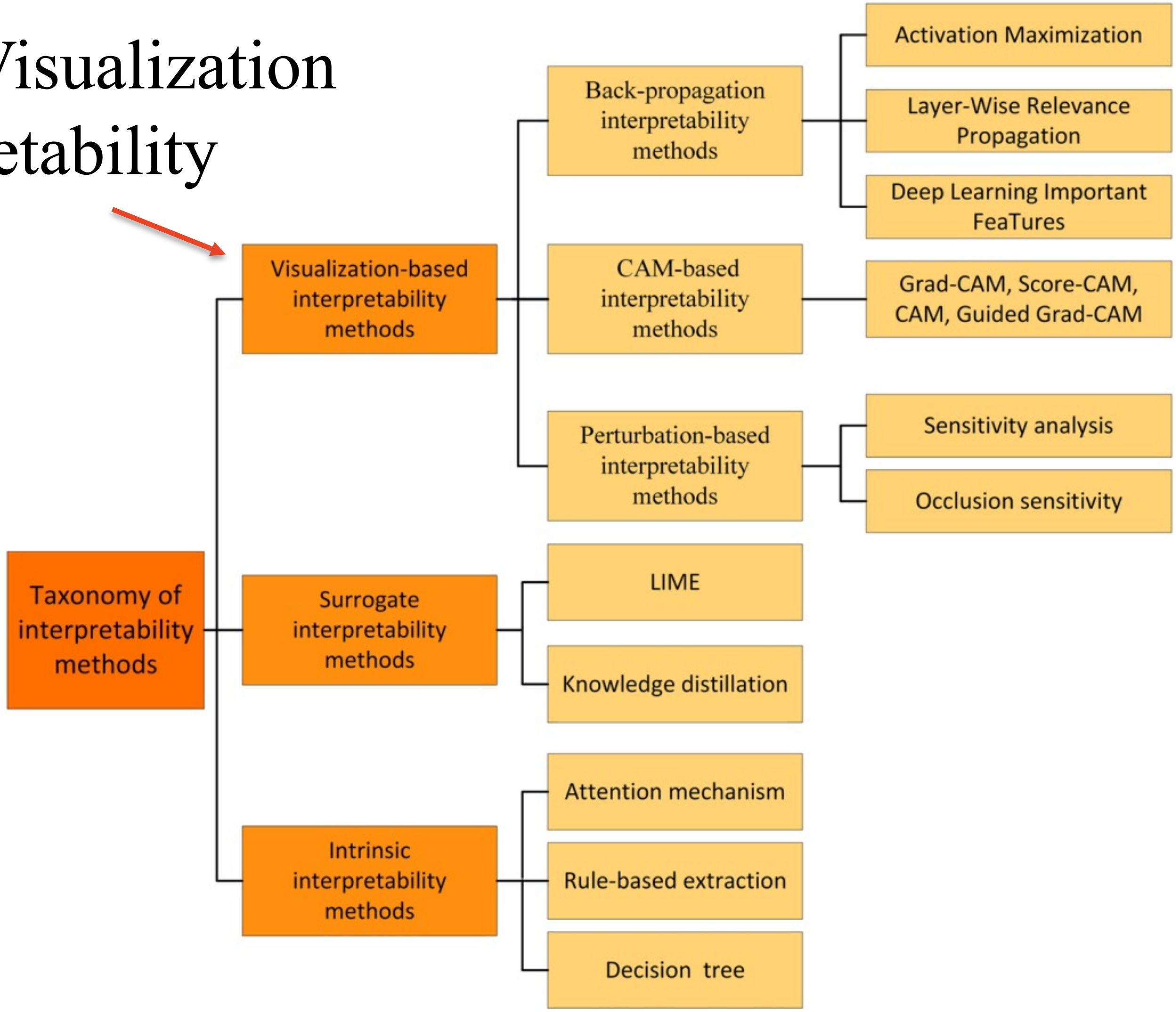




Blackbox

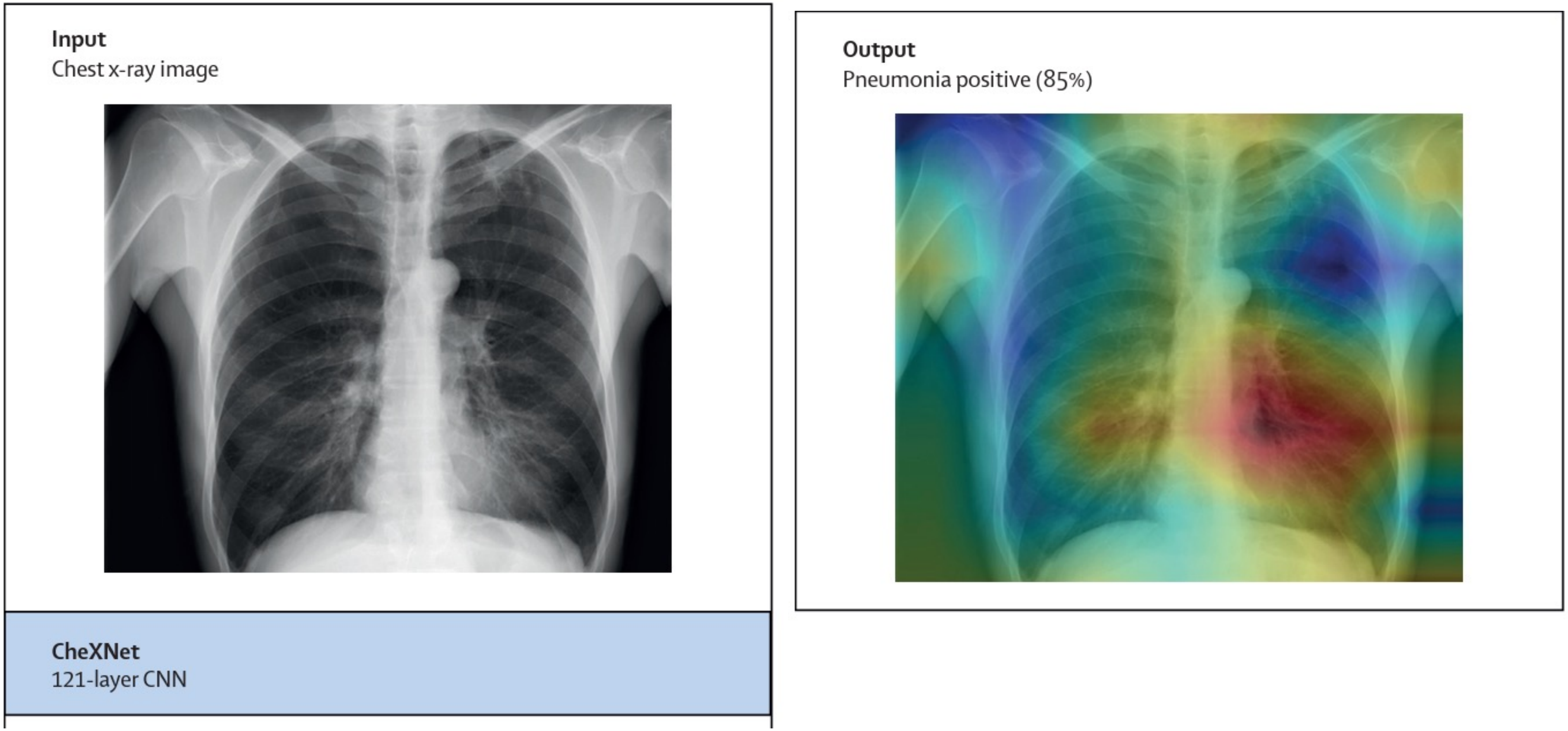
Interpretable AI

Heatmap Visualization for Interpretability



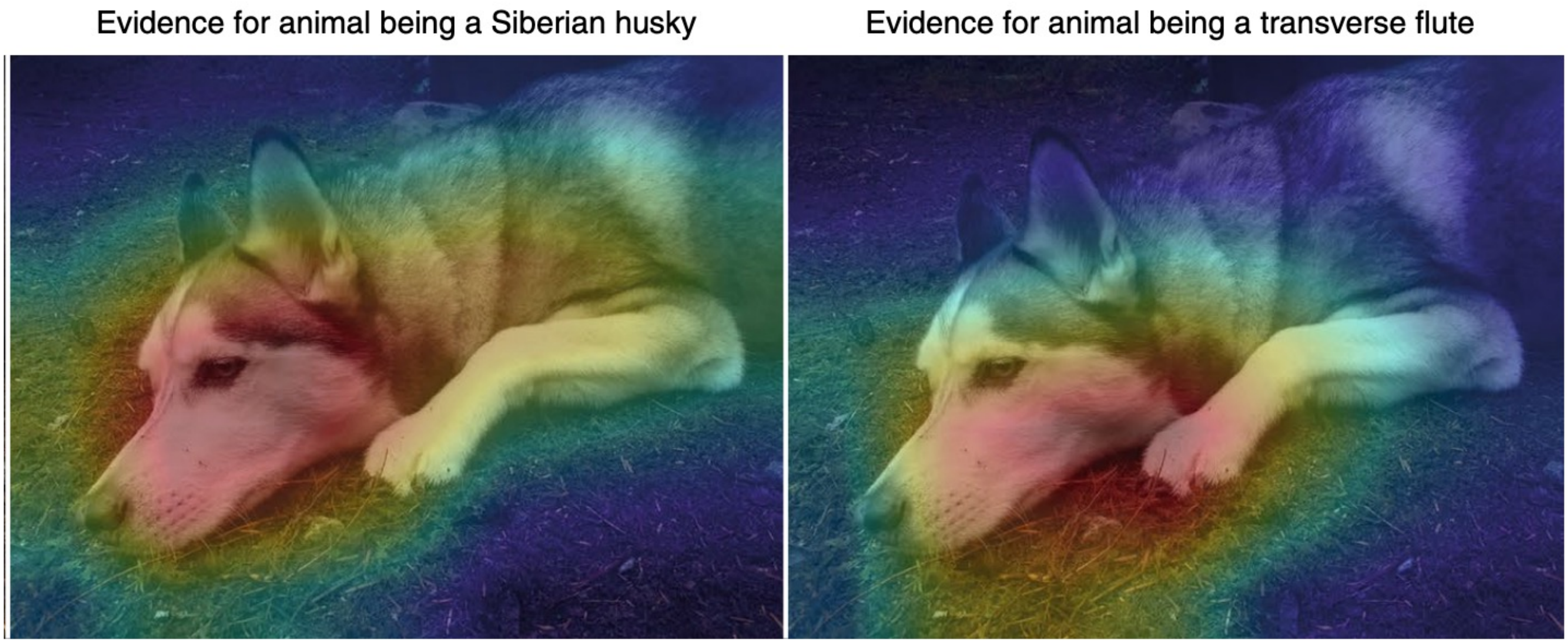
A survey on the interpretability of deep learning in medical diagnosis

Heatmap Visualization



The false hope of current approaches to explainable artificial intelligence in health care

The false hope of heatmap visualization

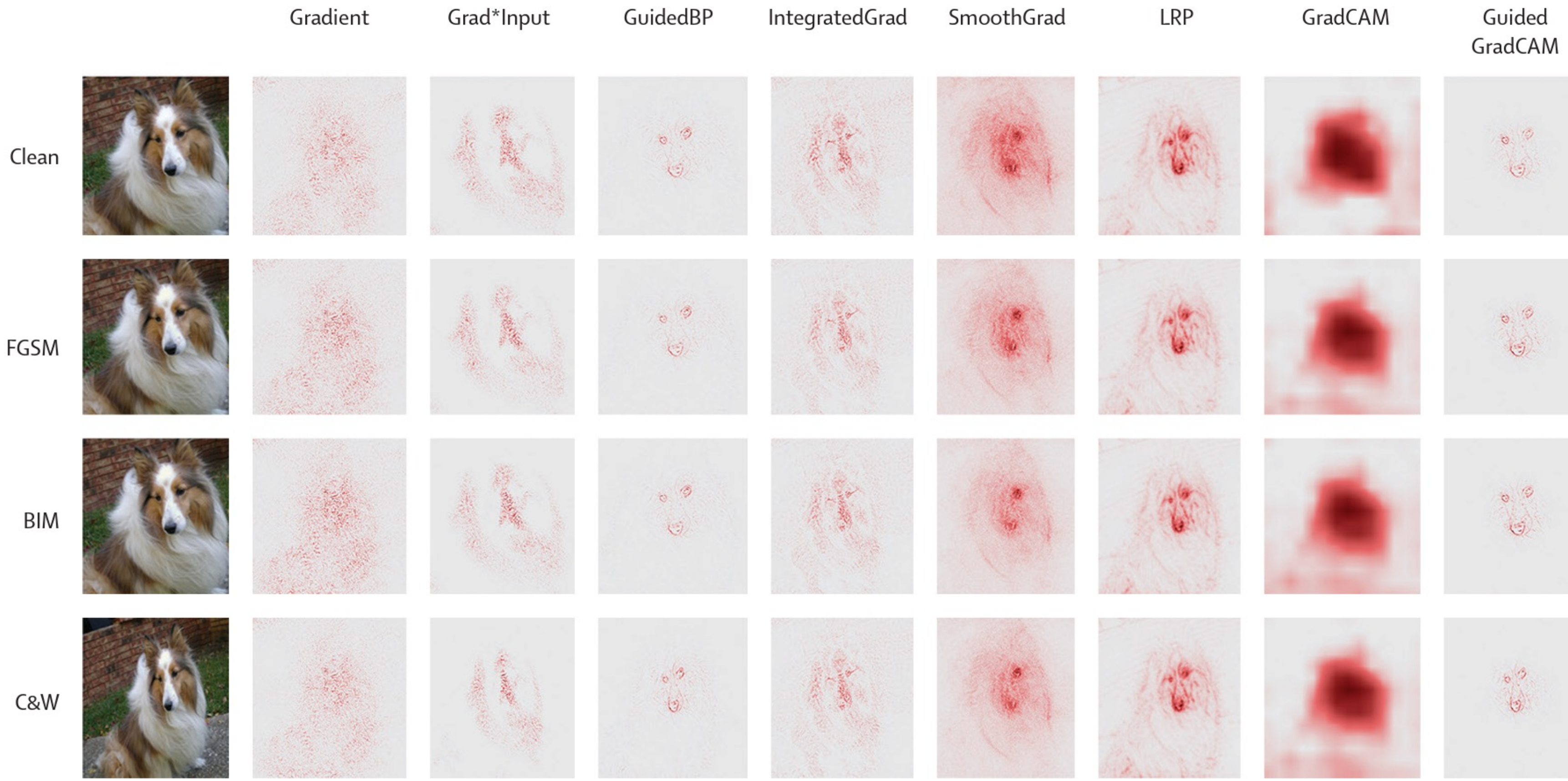


Husky *Flute*

Saliency does not explain anything except where the network is looking

Stop explaining black box machine learning models for high stakes decisions and use interpretable models instead

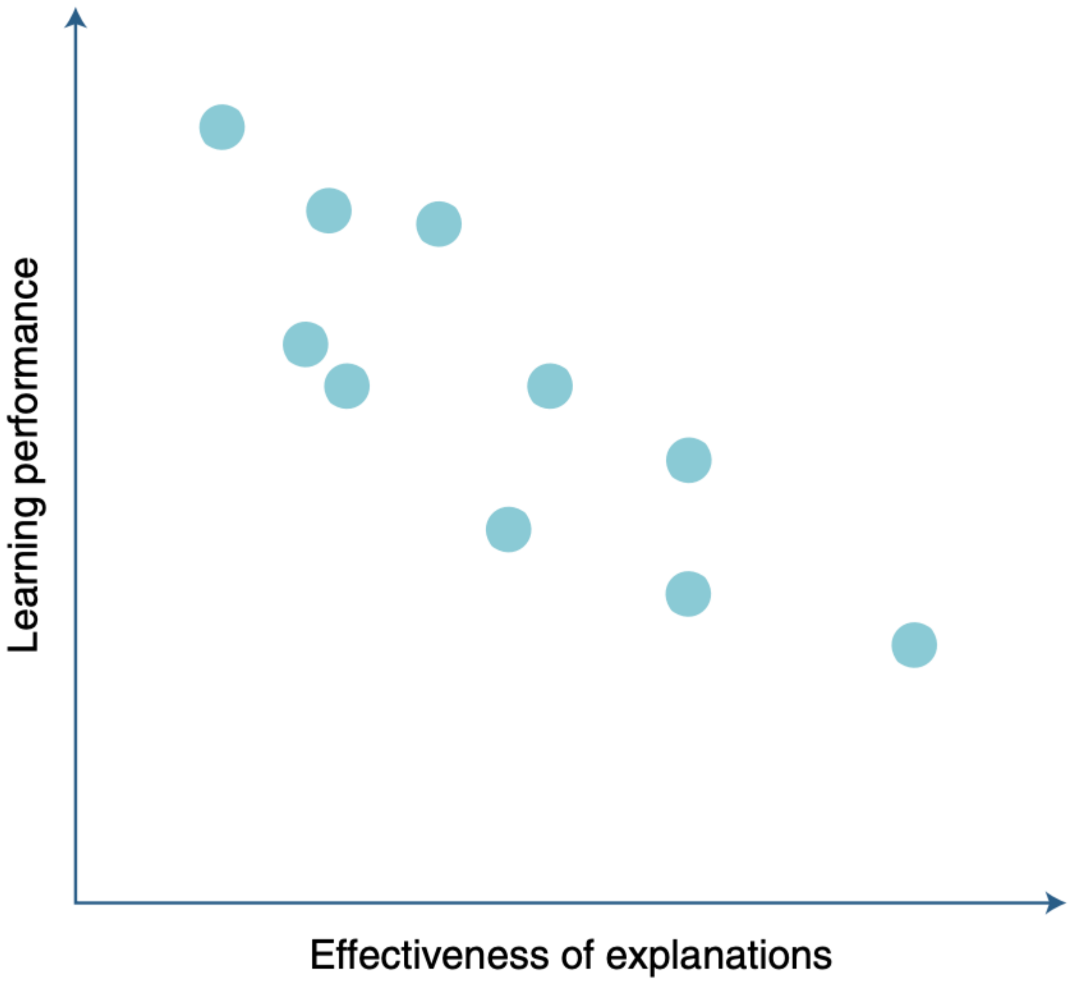
The false hope of heatmap visualization



The heatmaps keep unchanged when the model makes a different decision (being adversarially attacked)

The false hope of current approaches to explainable artificial intelligence in health care

Accuracy–interpretability trade-off



Stop explaining black box machine learning models for high stakes decisions and use interpretable models instead

Task-specific topics:

- Biomedical image segmentation
- Biomedical image registration

Task-agnostic topics:

- Interpretability
- Uncertainty

Task-specific topics:

Biomedical image segmentation

Biomedical image registration

Task-agnostic topics:

Interpretability

Uncertainty

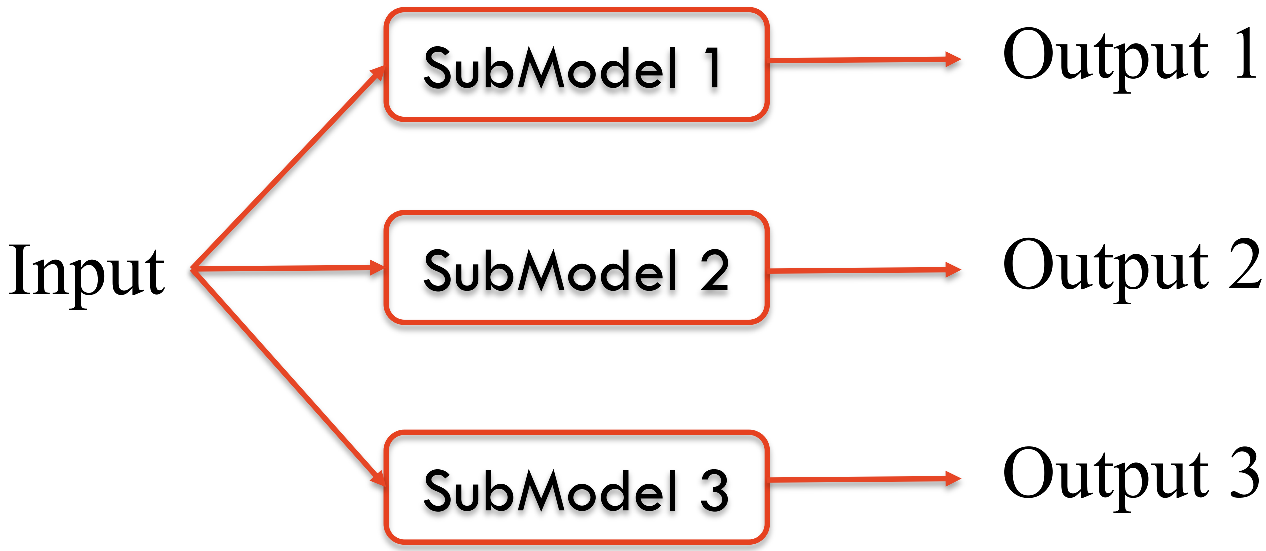
Uncertainty Measurement

When the model don't know the answer…

Current Model → *Make a guess*

Responsible Model → *"I don't know"*

Uncertainty Measurement

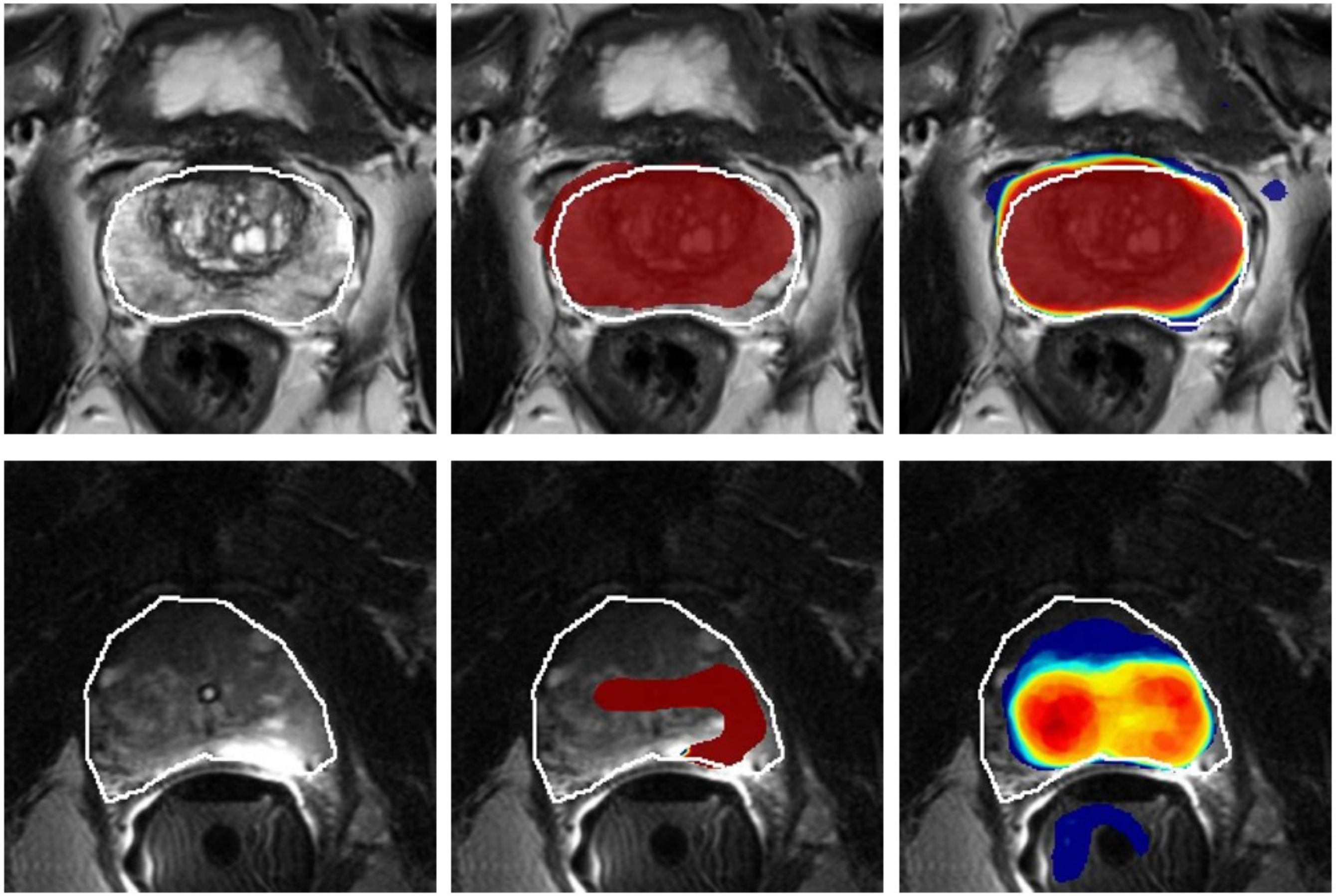


High variance: Uncertain

Low variance: Certain

Model Sampling
(e.g. Test-time Dropout)

Uncertainty Measurement



Input

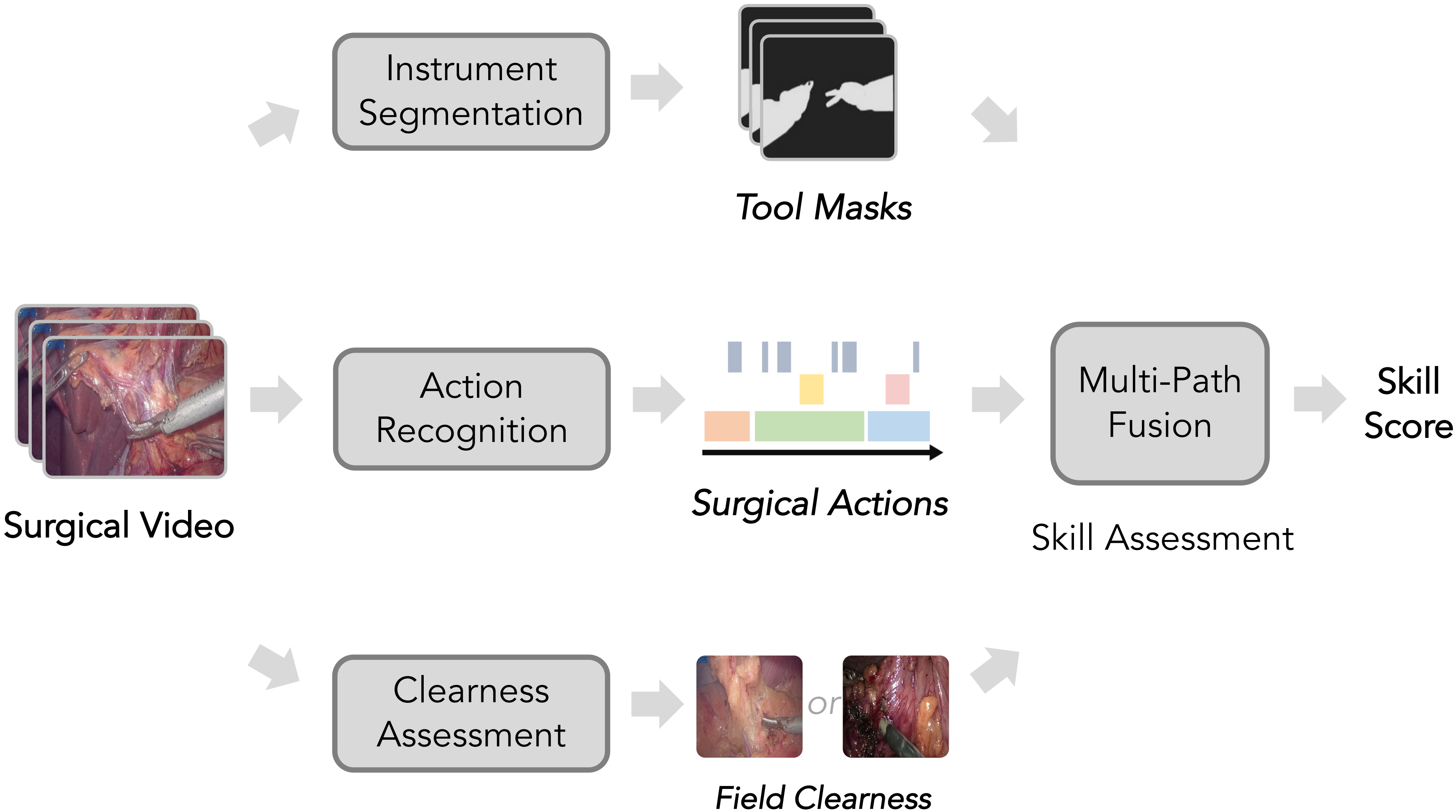
Output
No uncertainty measurement

Output
With uncertainty measurement

Confidence Calibrationand Predictive Uncertainty Estimation for Deep Medical Image Segmentation

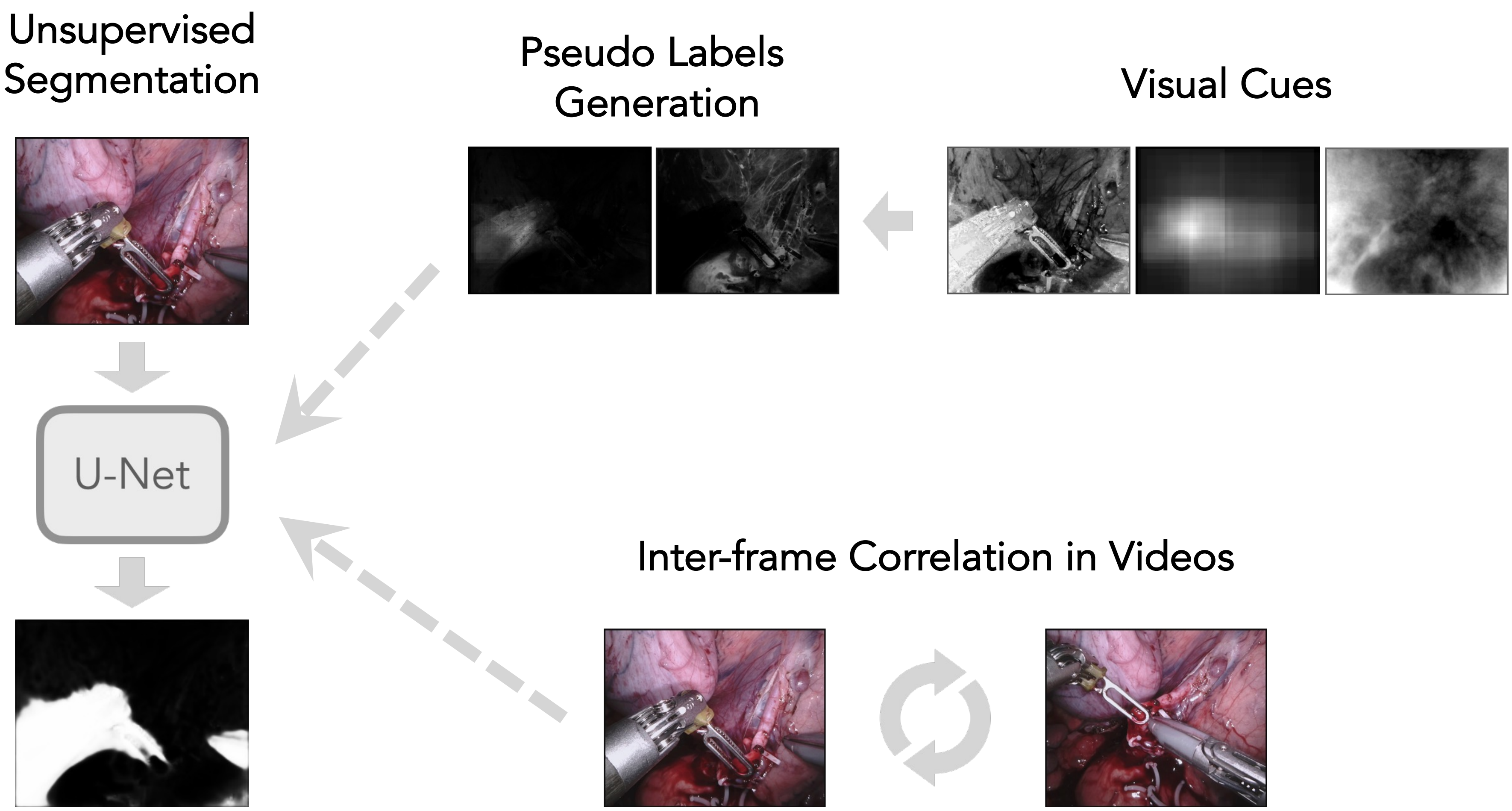
Side Story:
Surgical Video Analysis

Video-Based Surgical Skill Assessment



Reference: Towards Unified Surgical Skill Assessment

Surgical Instrument Segmentation



Reference: Unsupervised Surgical Instrument Segmentation via Anchor Generation and Semantic Diffusion

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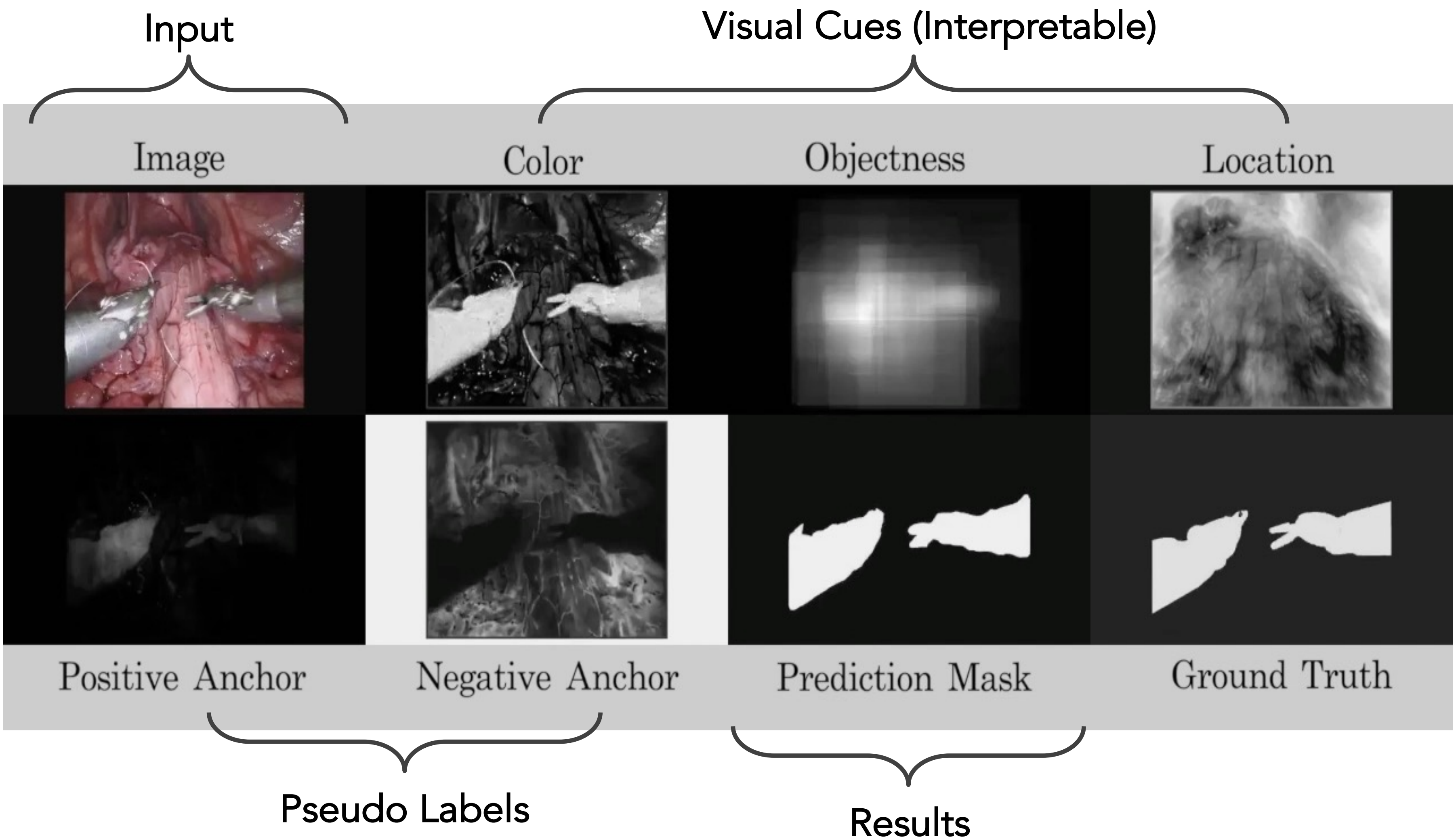

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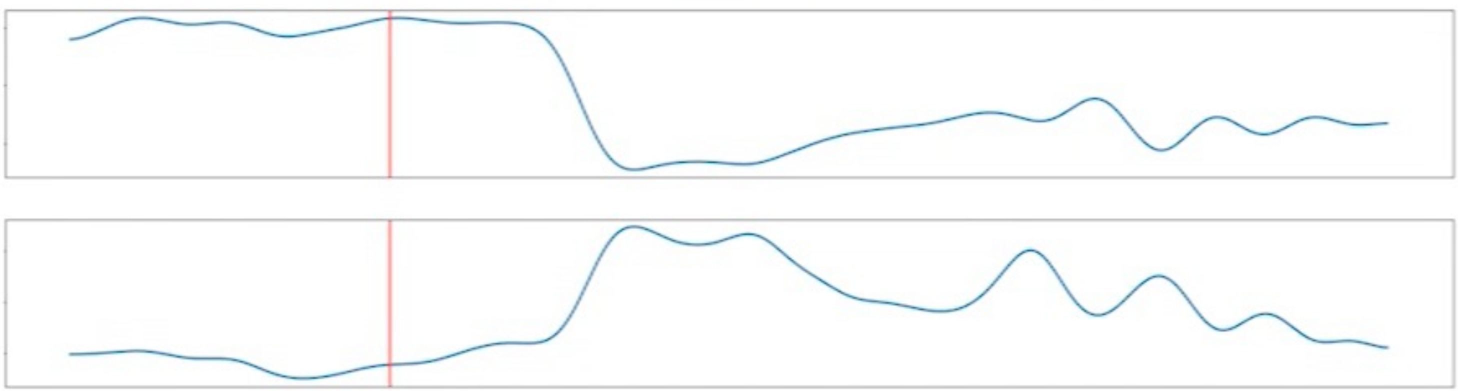
Surgical Skill Assessment

Skill
Score

Weight
(1D Heatmap)



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Thank You