SIMON FRASER UNIVERSITY
ENGAGING THE WORLD

TRIUMF SCIENCE WEEK

Deep Learning for Medical Imaging Applications

Ghassan Hamarneh

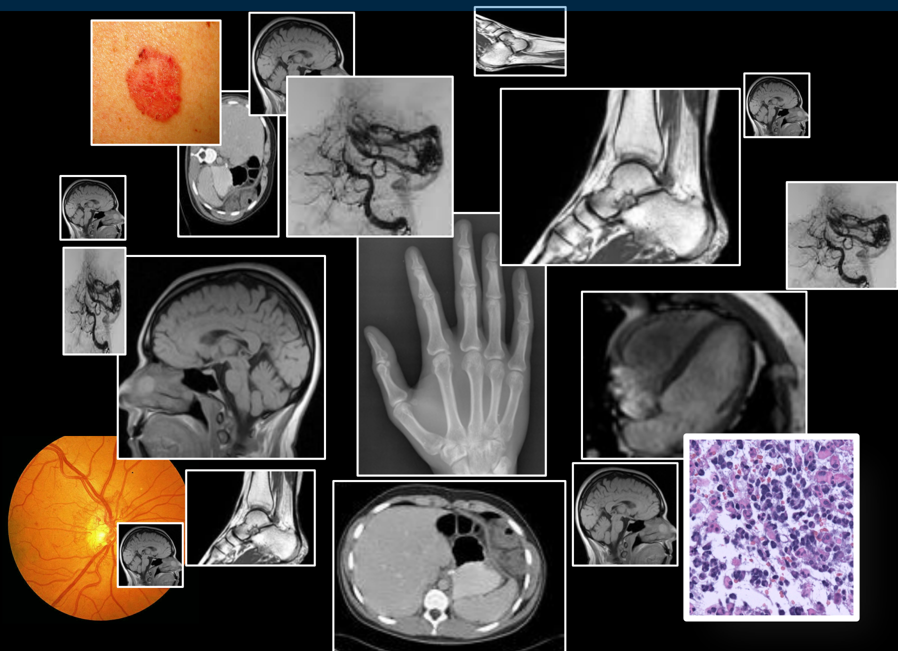
www. **Medical Image Analysis** .com

23 August 2019

TRIUMF Science Week

Data Science and Quantum Computing Workshop

www. Medical Image Analysis .com



Clinical & Patient Data

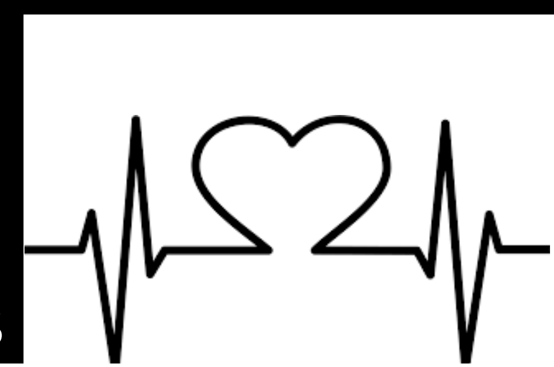
multi-modal medical imaging

Computational Techniques

biomedical computer vision

Improving Healthcare

understand, prevent, treat, and track diseases



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Funding Research and Treatment of Parkinson's Disease
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National Cancer Institute
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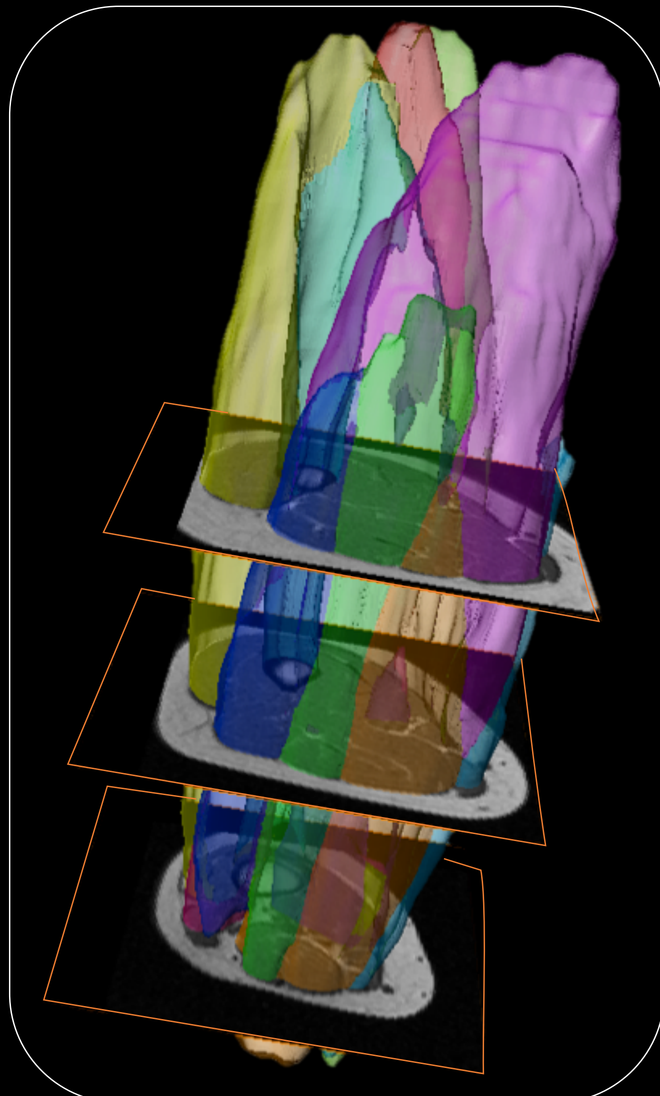
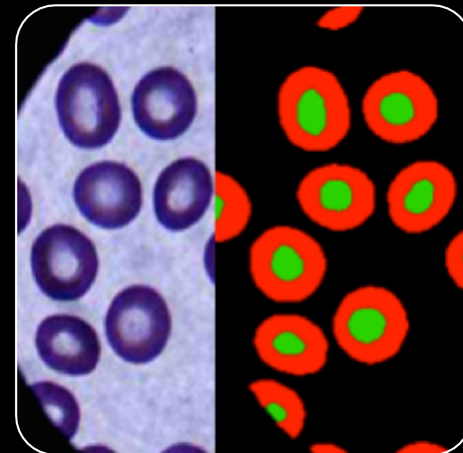
CARE + RESEARCH

biomedical image segmentation

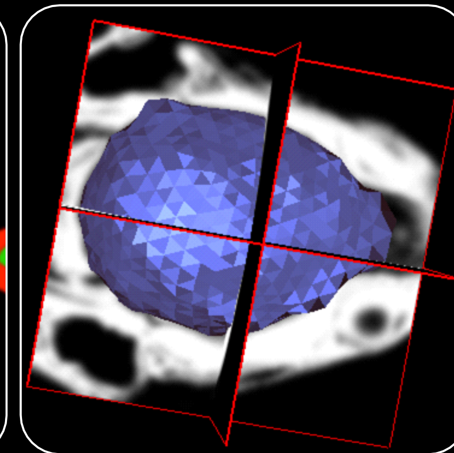
input: image



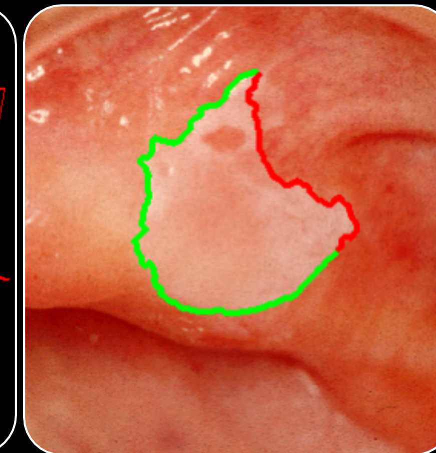
thigh muscles



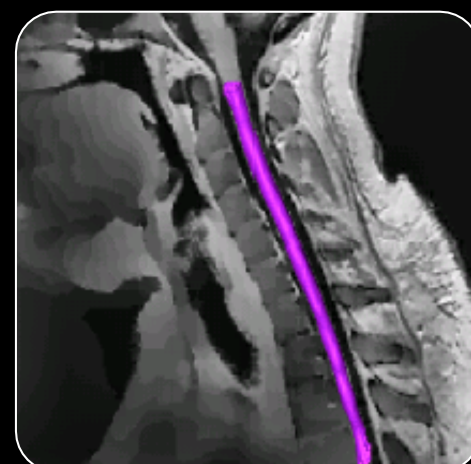
cells



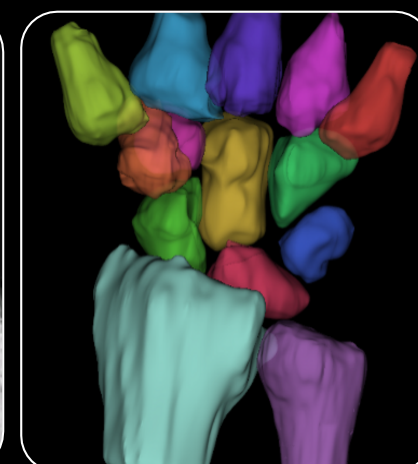
mice



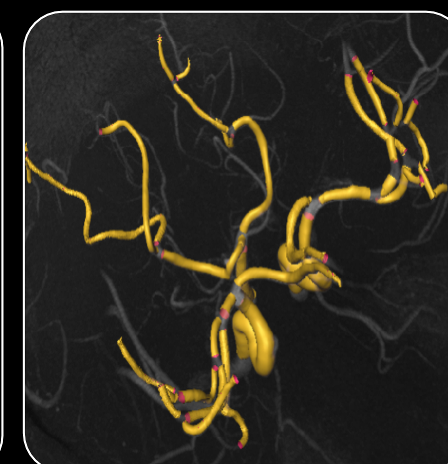
lesions



spinal cord

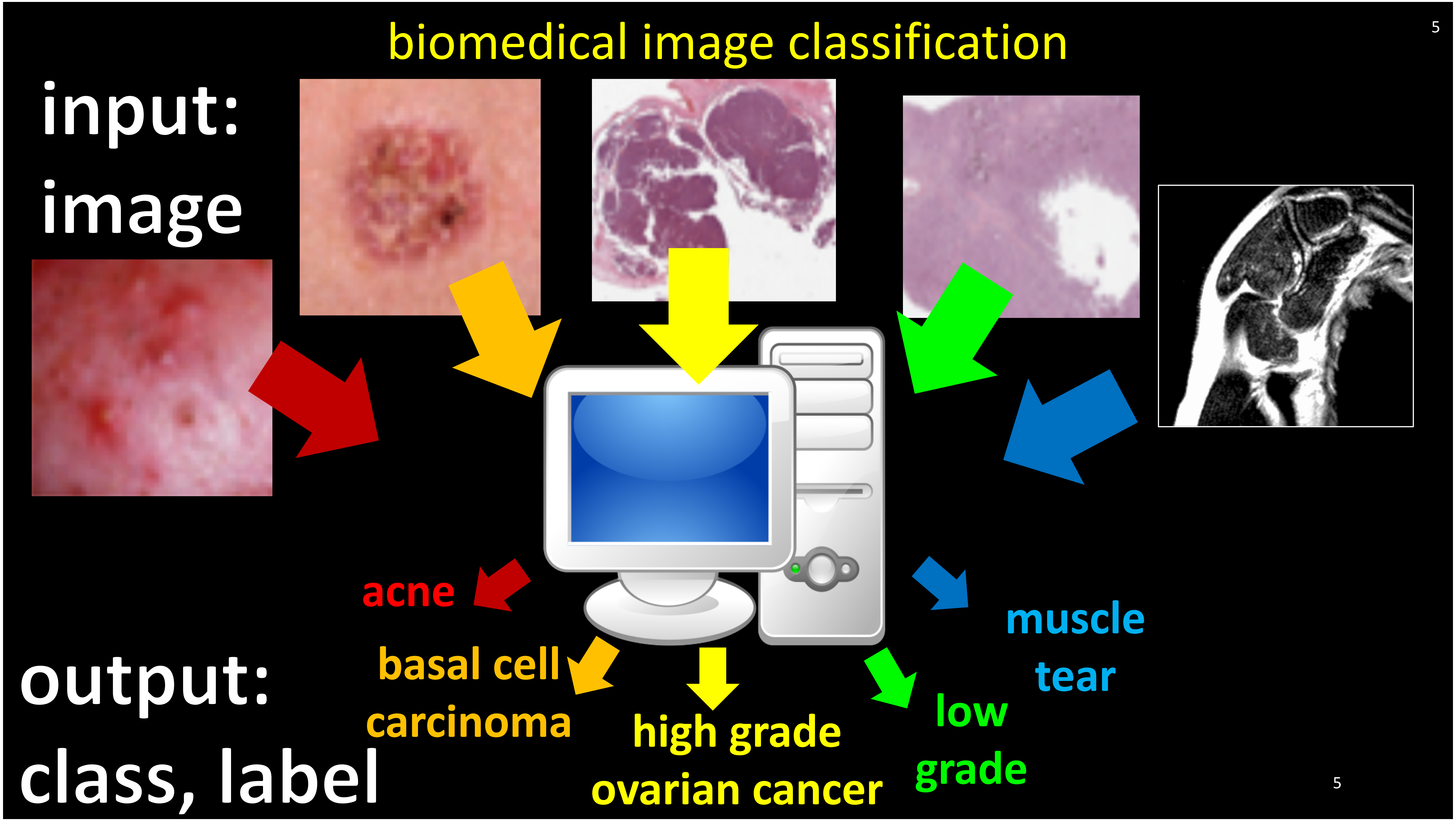


bones



vessels

output: localization, delineation



biomedical image classification
input:
image
acne
basal cell
carcinoma
high grade
ovarian cancer
low
grade
muscle
tear
output:
class, label
5

Stanford ML Group

CheXNet: Radiologist-Level Pneumonia Detection on Chest X-Rays with Deep Learning

Pranav Rajpurkar*, Jeremy Irvin*, Kaylie Zhu, Brandon Yang, Hershel Mehta, Tony Duan, Daisy Ding, Aarti Bagul, Curtis Langlotz, Katie Shpanskaya, Matthew P. Lungren, Andrew Y. Ng

https://stanfordmlgroup.github.io/projects/chexnet/ https://arxiv.org/abs/1711.05225

COVER STORY

AI applications in ophthalmology achieve human expert-level performance

Ocular Surgery News U.S. Edition, June 10, 2018

https://www.healio.com/ophthalmology/technology/news/print/ocular-surgery-news/%7B373d8cf8-f72b-43fe-b362-29ba35c416ba%7D/ai-applications-in-ophthalmology-achieve-human-expert-level-performance

nature machine intelligence

Article | Published: 13 May 2019

Pathologist-level interpretable whole-slide cancer diagnosis with deep learning

Zizhao Zhang, Pingjun Chen, Mason McGough, Fuyong Xing, Chunbao Wang, Marilyn Bui, Yuanpu Xie, Manish Sapkota, Lei Cui, Jasreman Dhillon, Nazeel Ahmad, Farah K. Khalil, Shohreh I. Dickinson, Xiaoshuang Shi, Fujun Liu, Hai Su, Jinzheng Cai & Lin Yang

https://www.nature.com/articles/s42256-019-0052-1

nature
International journal of science

Letter | Published: 25 January 2017

Jan. 2017

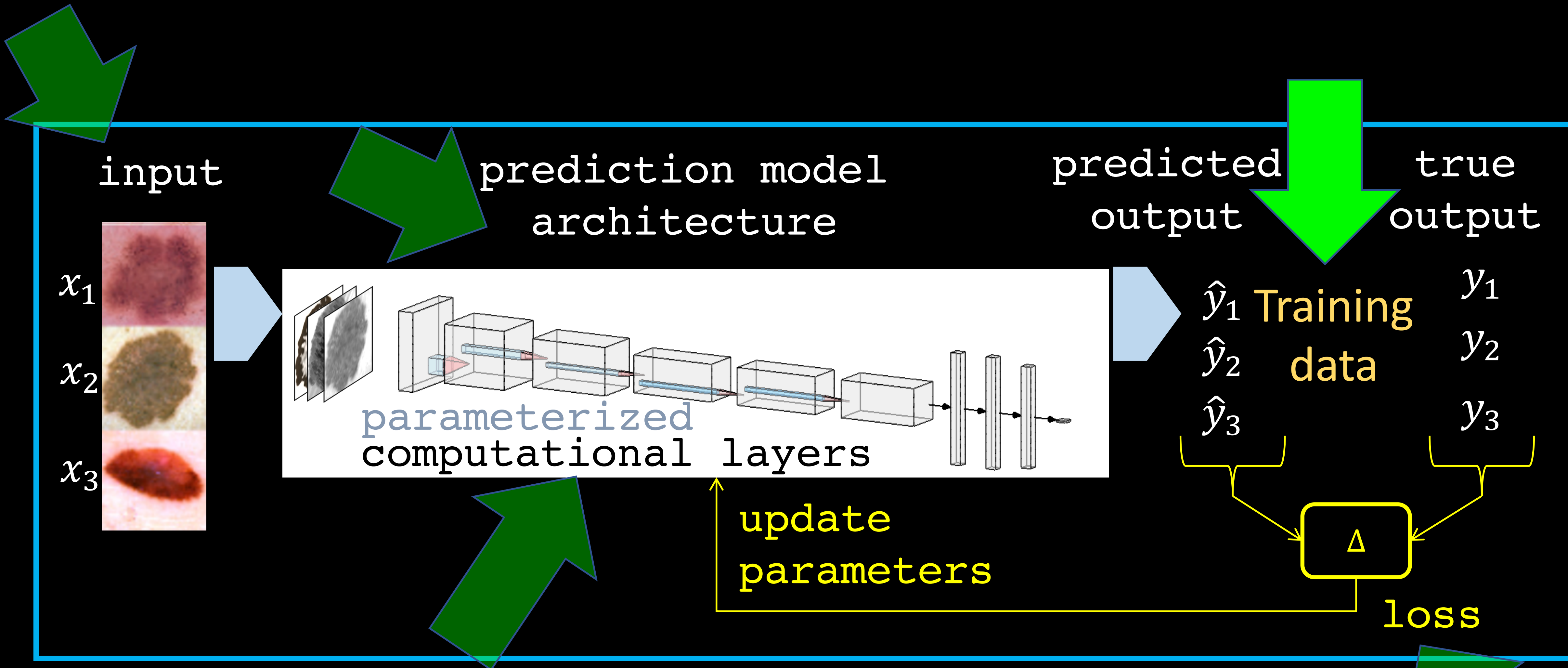
Dermatologist-level classification of skin cancer with deep neural networks

Andre Esteva, Brett Kuprel, Roberto A. Novoa, Justin Ko, Susan M. Swetter, Helen M. Blau & Sebastian Thrun

Nature **542**, 115–118 (02 February 2017) | Download Citation

https://www.nature.com/articles/nature21056

Deep learning for medical image interpretation



$y = f(x)$

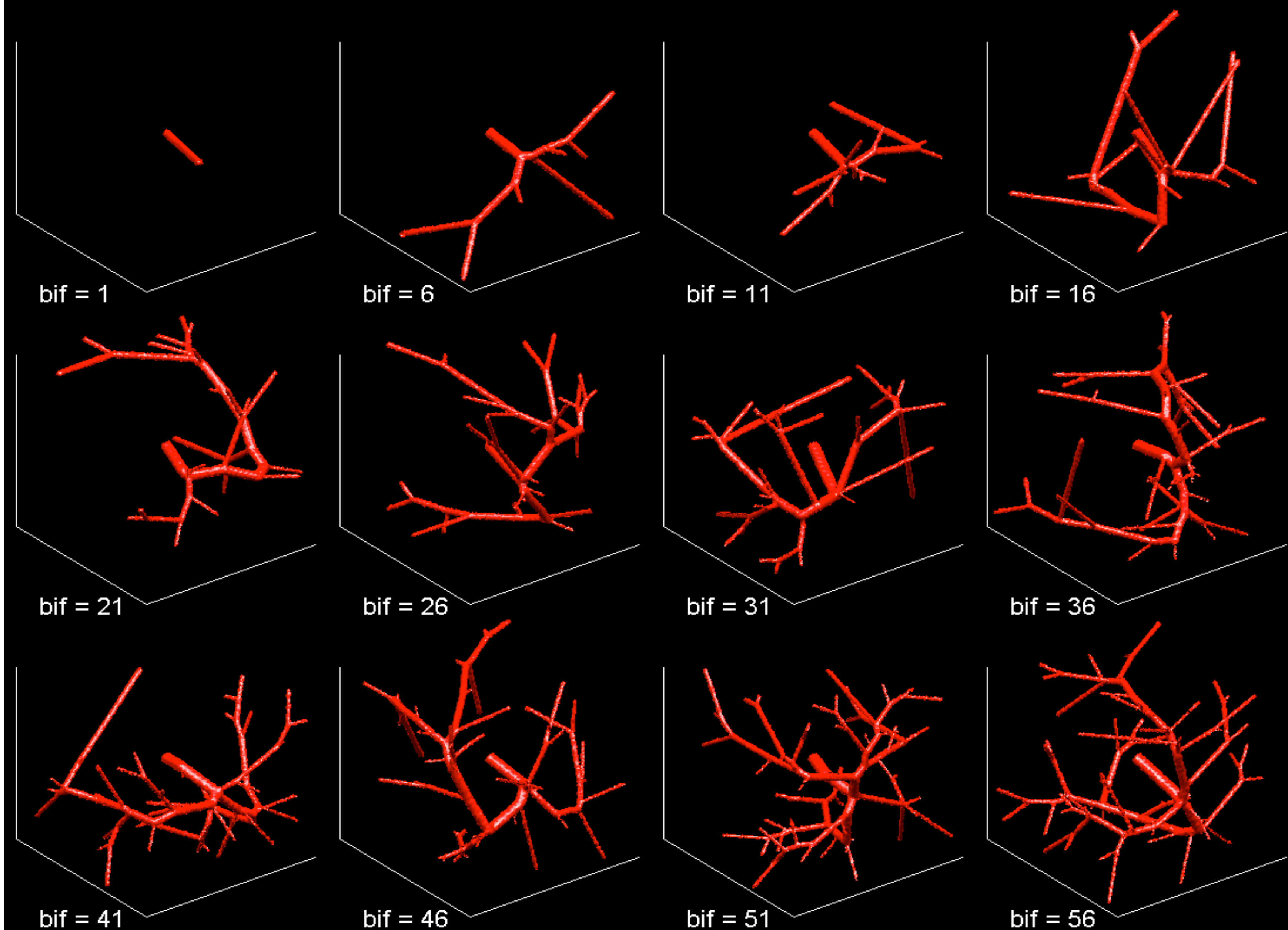
1. Training: Learn f from $\{(x_i, y_i)\}$
2. Inference: Use f on new x

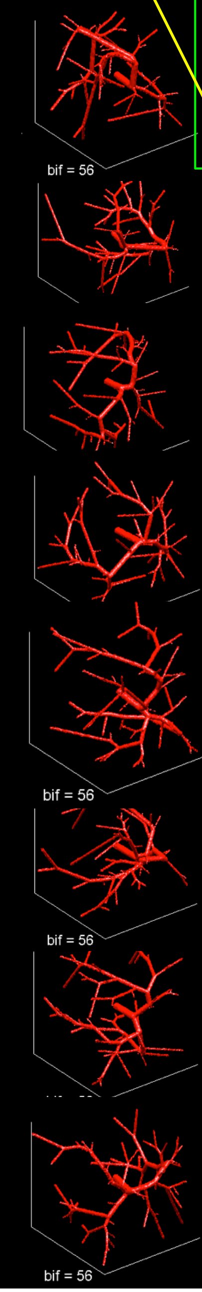
Data synthesis

click link to download PDF
bibliography at end of presentation

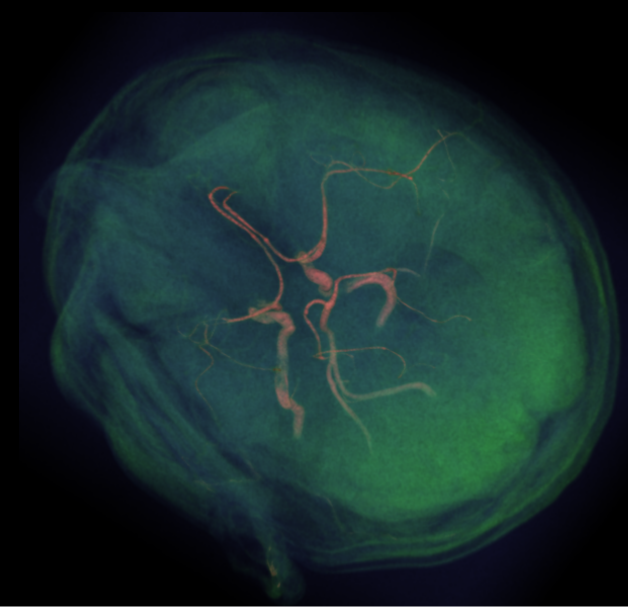
VascuSynth.cs.sfu.ca

Hamarneh, Jassi
CMIG 2010, IJ2011
http://www.cs.sfu.ca/~hamarneh/ecopy/cmig2010.pdf
http://www.cs.sfu.ca/~hamarneh/ecopy/ij2011.pdf





Synthesize 3D images of vasculature by optimizing branch locations, lengths, and radii to maximize supply of nutrients



Data augmentation

Simulation via Physically- and Statistically-based Warps

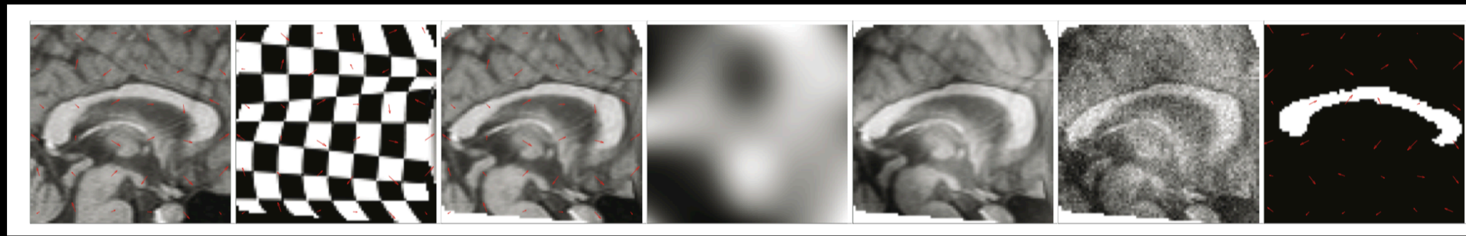
DeformIt

Hamarneh, Jassi, Tang, Booth
MICCAI 2008
http://www.cs.sfu.ca/~hamarneh/ecopy/isbi2014b.pdf
http://www.cs.sfu.ca/~hamarneh/ecopy/miccai2008b.pdf

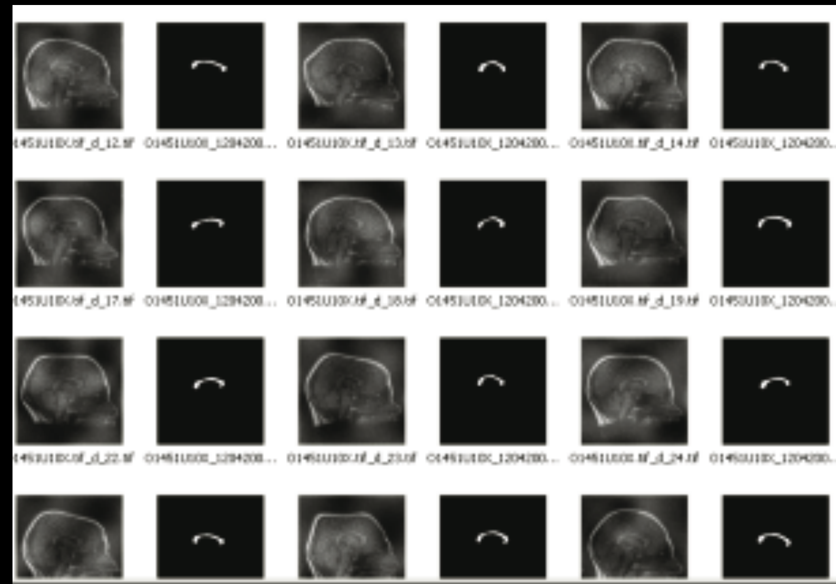
$$I = \bar{I} + \alpha \mathbf{Pb} + (1-\alpha)\Phi \mathrm{u}$$

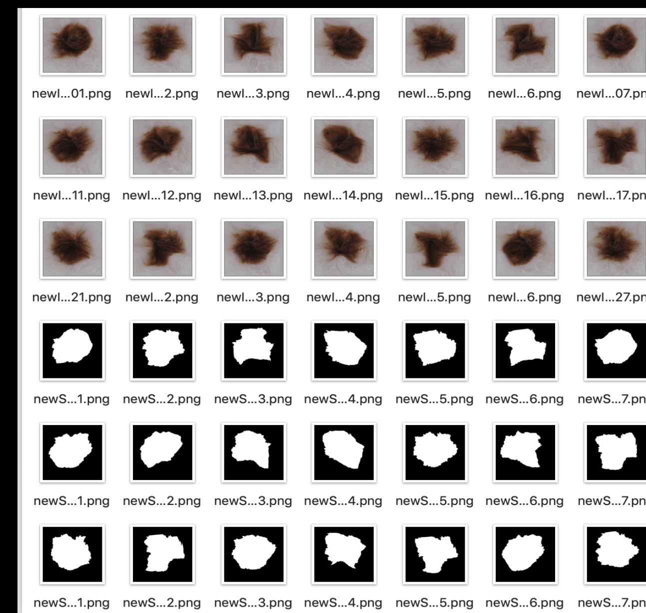
variational PCA

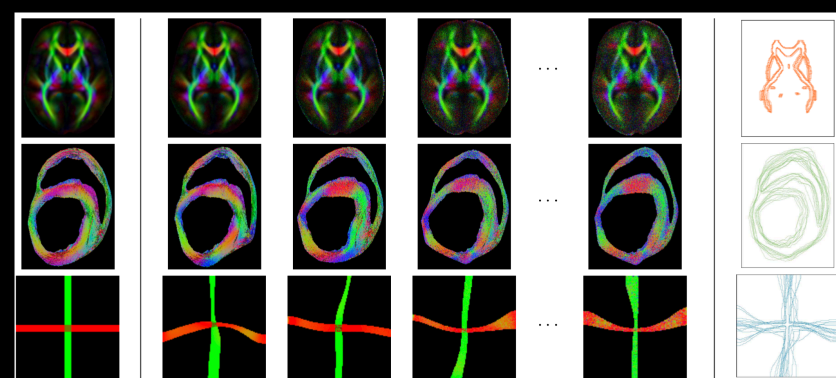
Vibrational FEM



From a single training sample, we obtain....



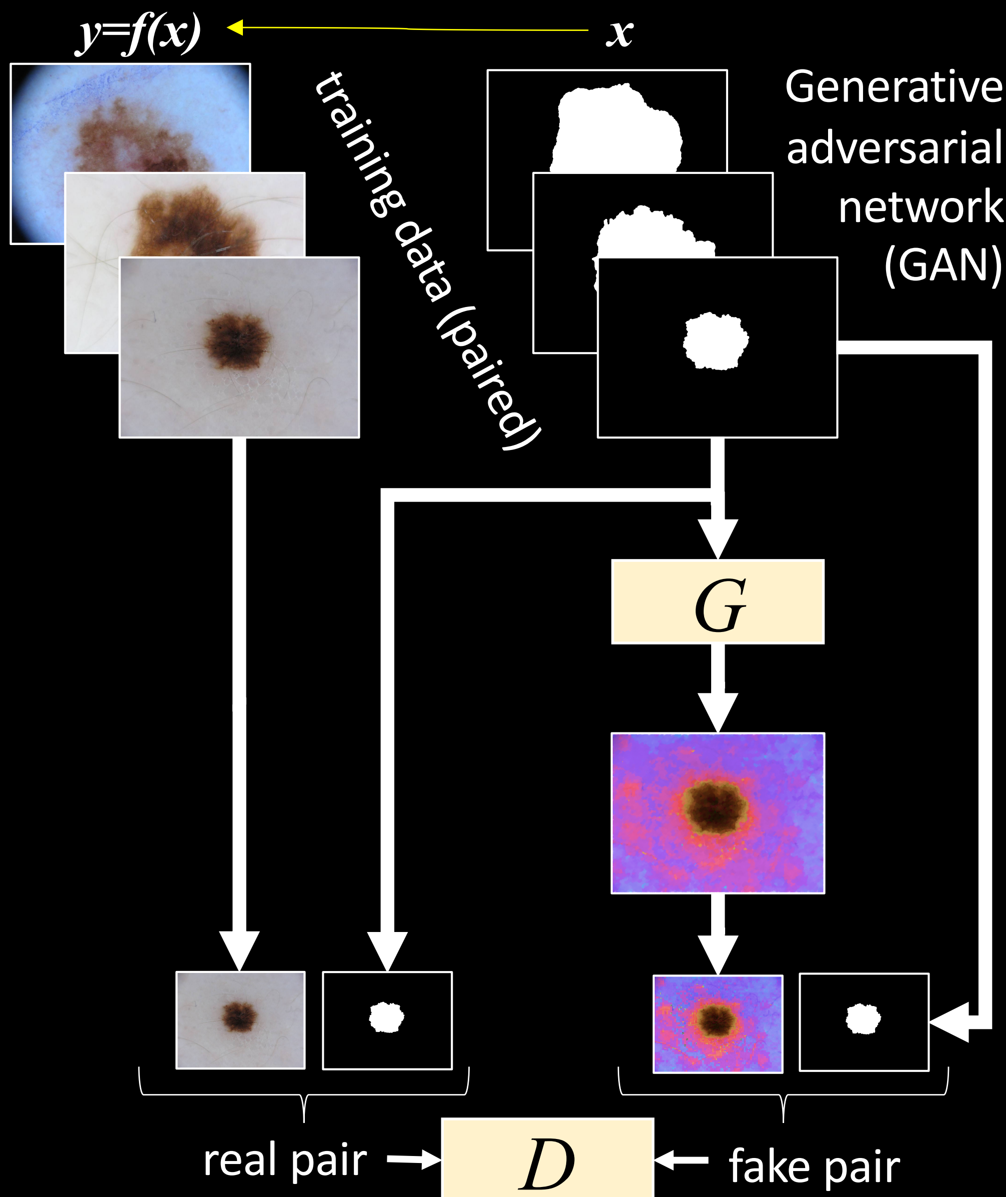




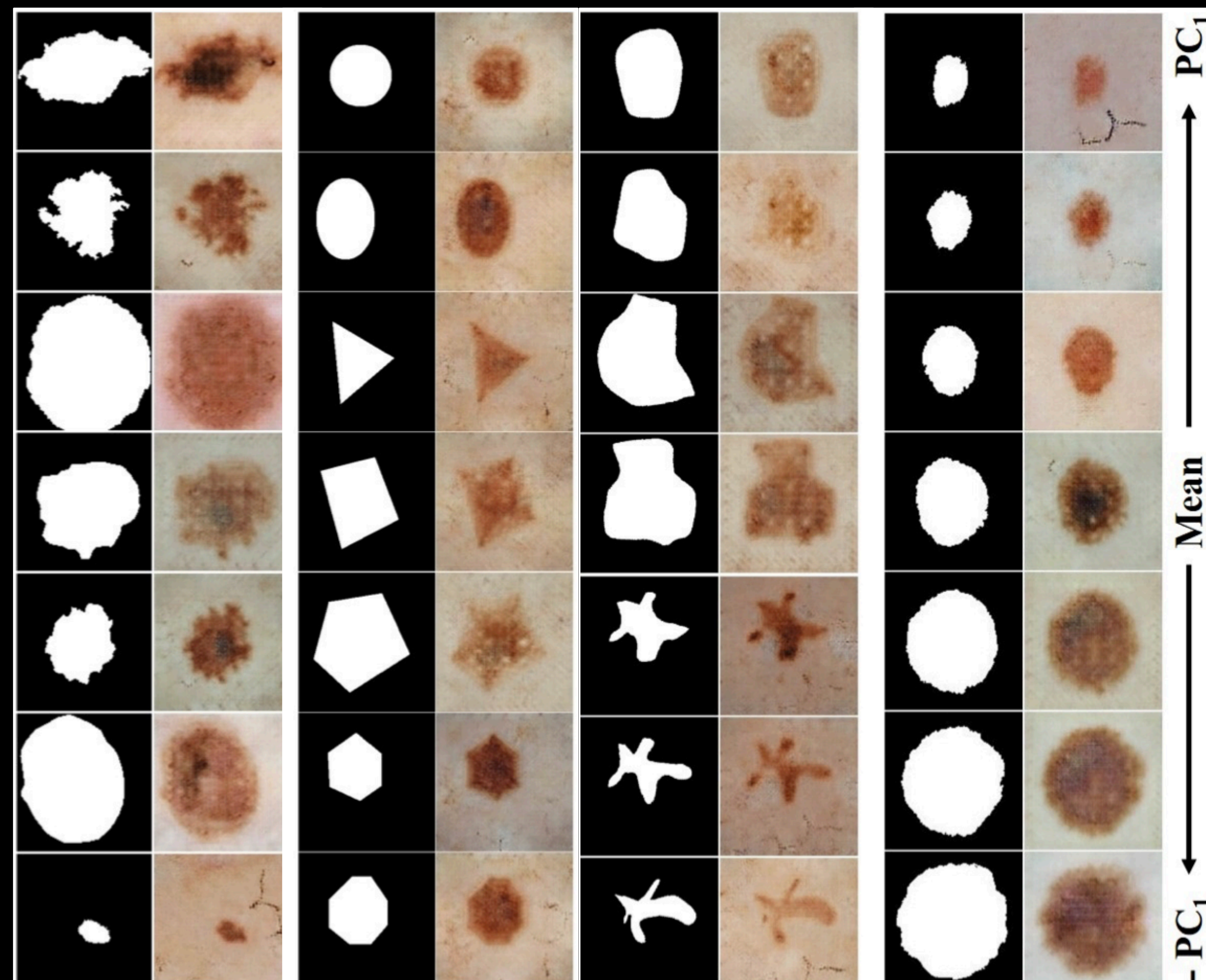
↑data ➔ ↑α
rely more on statistical model and less on knowledge-based models

Data augmentation

GAN-based **Mask2Lesion** translation

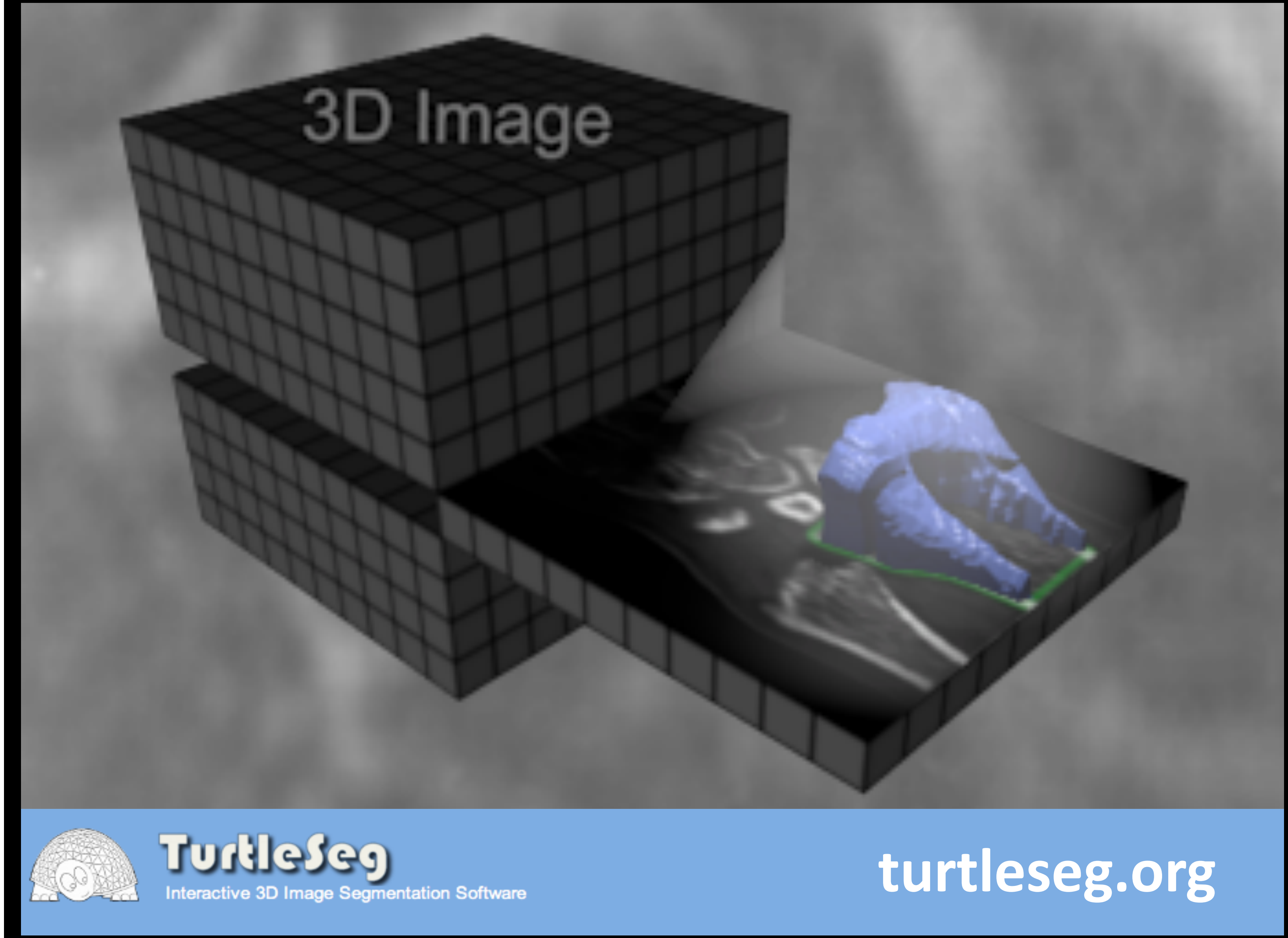


Abhishek, Hamarneh. MICCAI SASHIMI 2019
https://www.cs.sfu.ca/~hamarneh/ecopy/miccai_sashimi2019.pdf



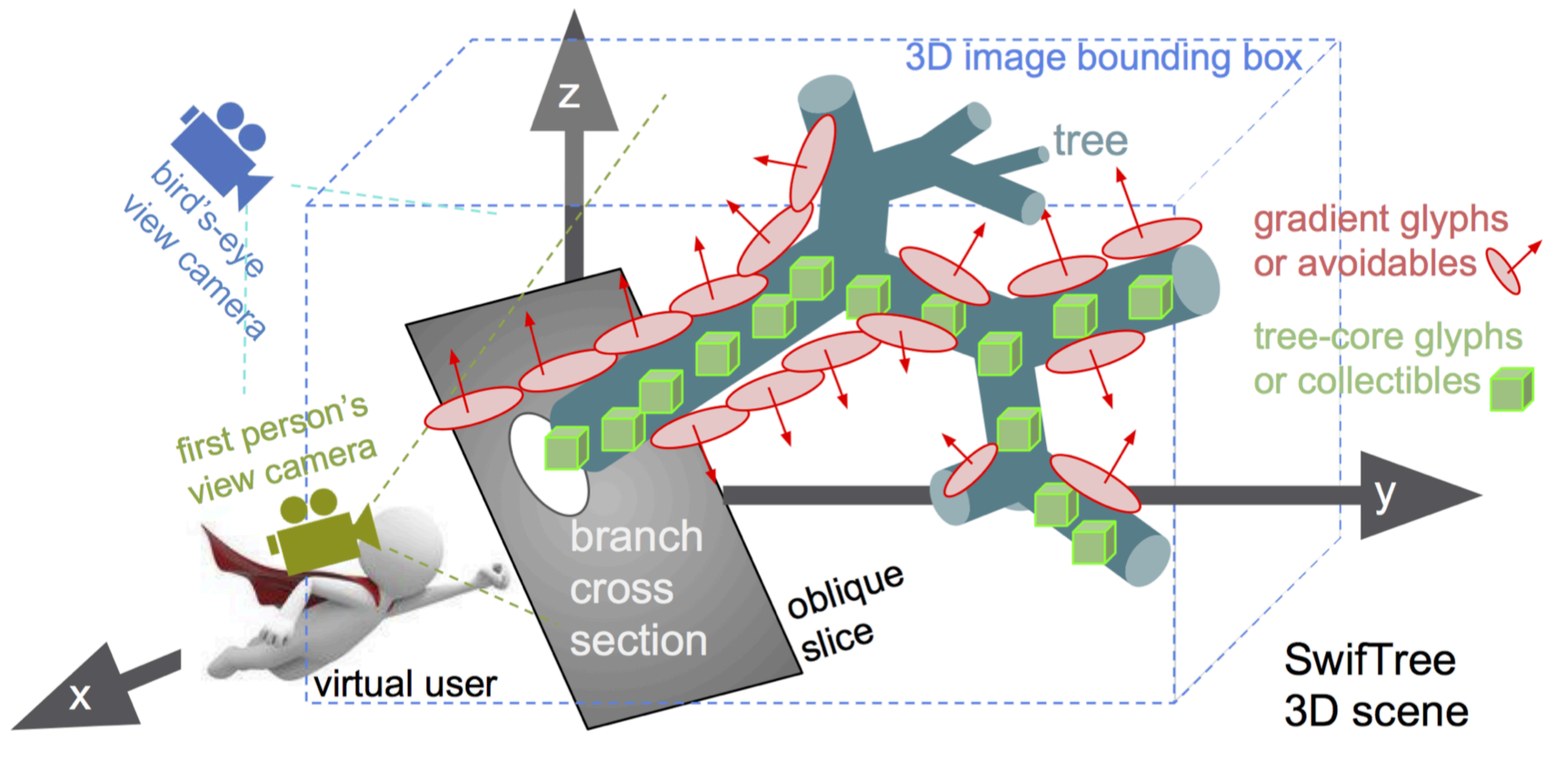
Targeted annotation

Top, Hamarneh, Abugharbieh, MICCAI MCV 2010, MICCAI 2011
https://www.cs.sfu.ca/~hamarneh/ecopy/miccai2011b.pdf
http://www.cs.sfu.ca/~hamarneh/ecopy/miccai_mcv2010.pdf



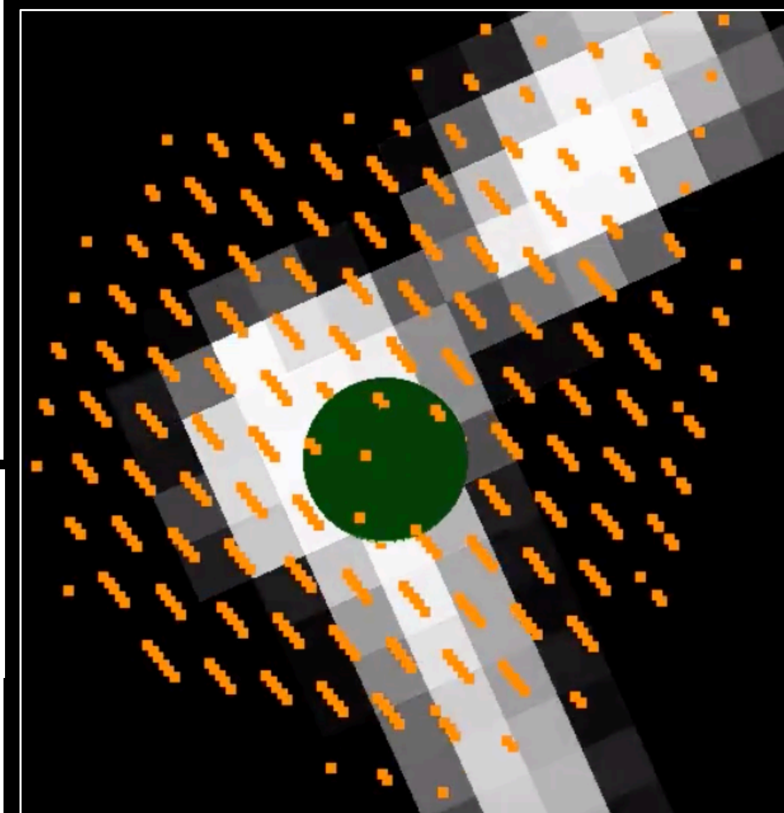
Active Learning based **Spotlight** highlights slice with maximal uncertainty for user to label

Annotation via Crowdsourcing & Serious Gaming



SwifTree

Huan , Hamarneh
MICCAI LABELS 2017
https://www.cs.sfu.ca/~hamarneh/ecopy/miccai_labels2017b.pdf
https://www.youtube.com/watch?v=AReIFQc47H4



Weak Annotations

data	
100	clean
1500	noisy

Miriharaji, Yan, Hamarneh, MICCAI MIL3ID 2019
https://www.cs.sfu.ca/~hamarneh/ecopy/miccai_mil3id2019.pd

100 images with clean labels

vs

1000 images with noisy labels?

Adaptively handle noisy annotations via modified deep model optimization

1. learn weight map W to control pixel contribution to loss
2. ↑W ⇔ ↑ agreement with clean data
   agreement in loss gradient

Dice %

original pretrain on noisy fine-tune on clean	modified
78.6	N/A
76.1	80.7
75.0	80.3
73.0	79.5
70.5	73.6

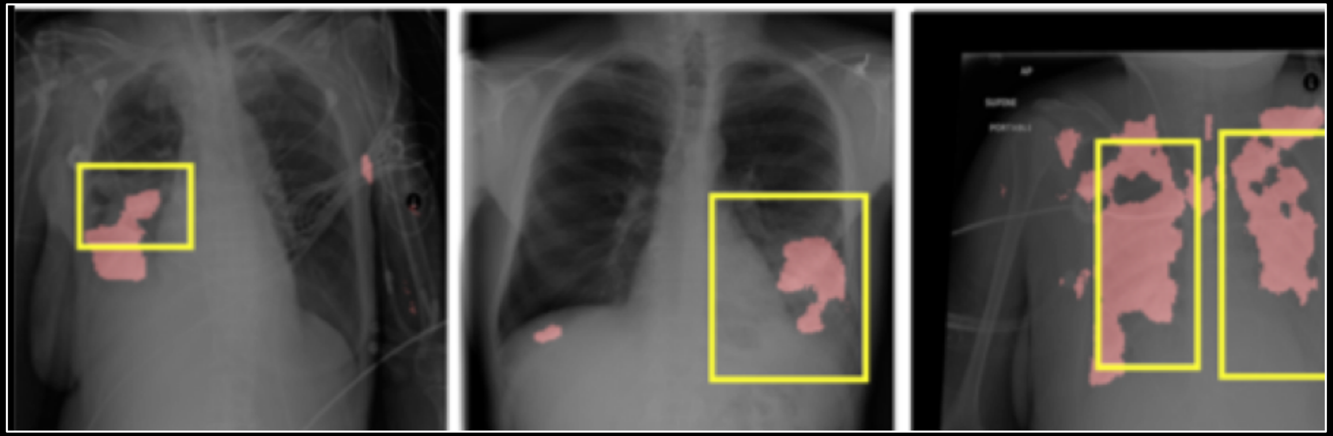
Learn to localize without segmentation labels

Goal: learn to localize disease from training data with image-level labels only

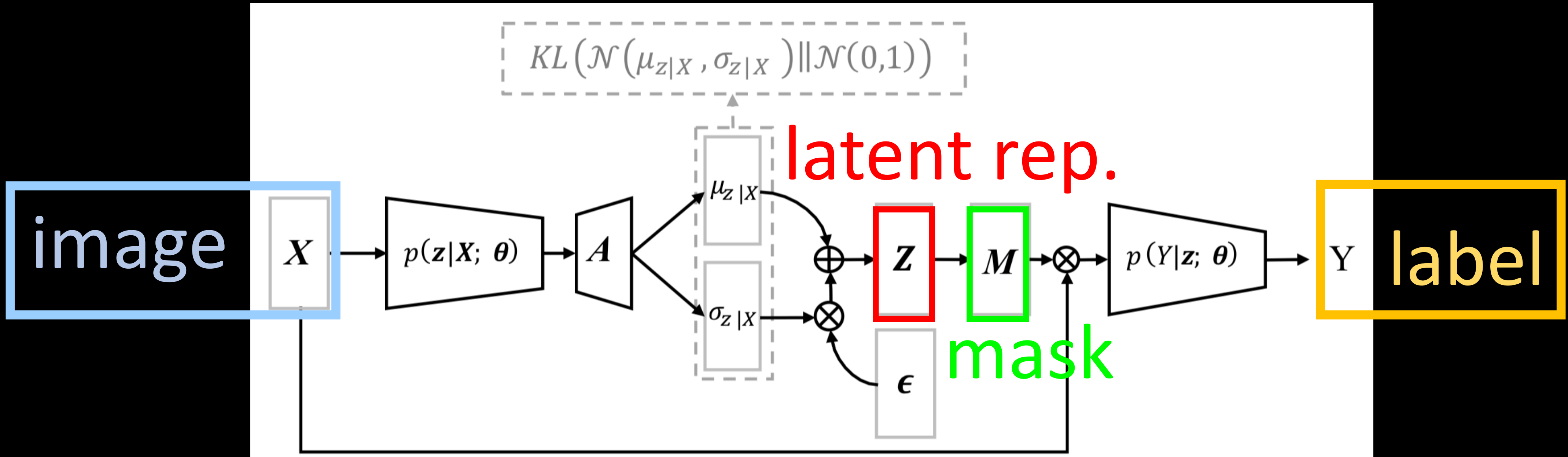
Asgari, Havaei, Berthier, Dutil, Di Jorio, Hamarneh, Bengio. MICCAI2019
http://www.cs.sfu.ca/~hamarneh/ecopy/miccai2019a.pdf

Using a variational autoencoder (VAE) with bottleneck masked latent representation that:

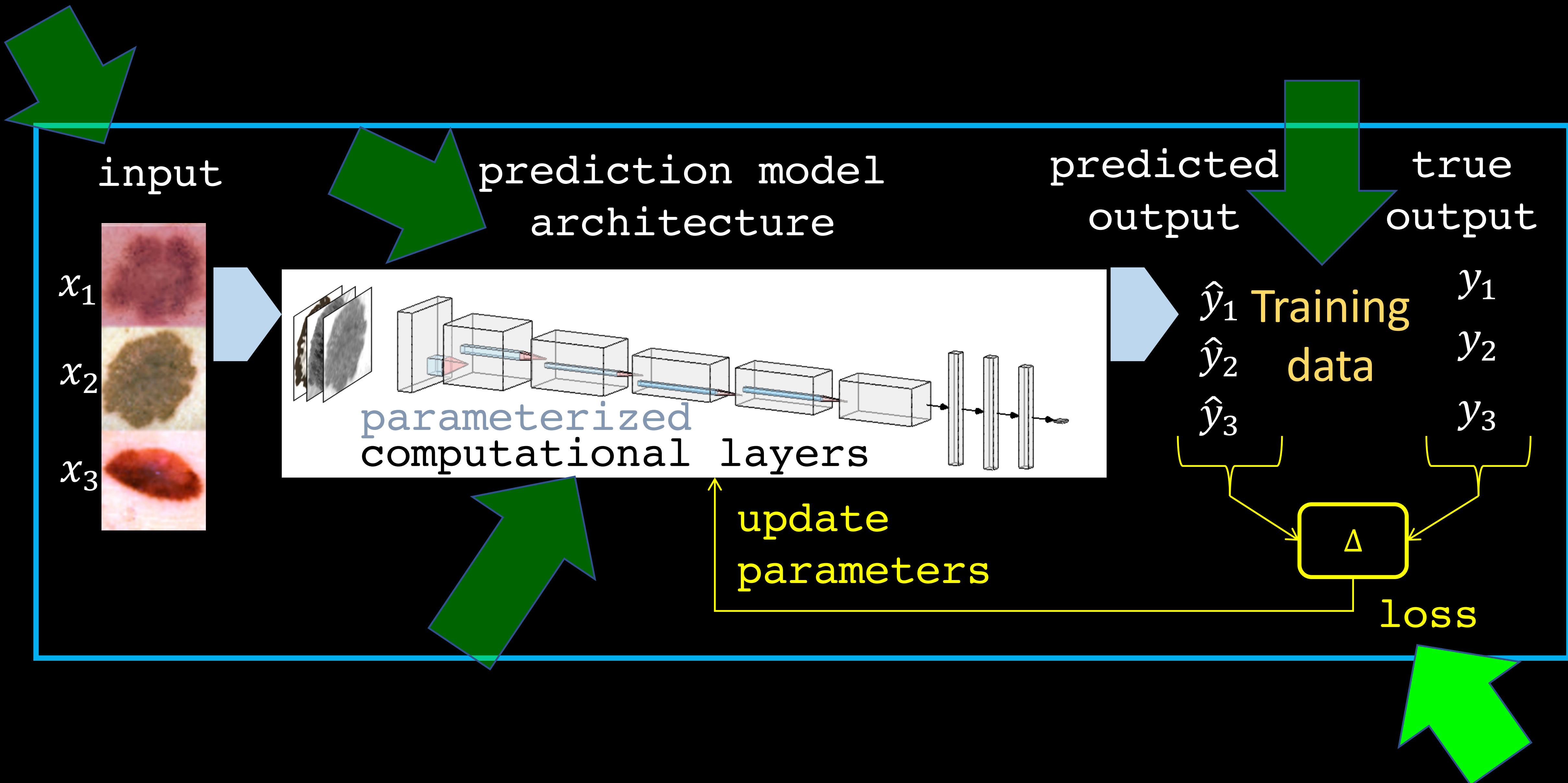
1) minimizes information about the input
   i.e. spatially-selective to disregard irrelevant input data
2) maximizes information about the target label



InfoMask



Loss function



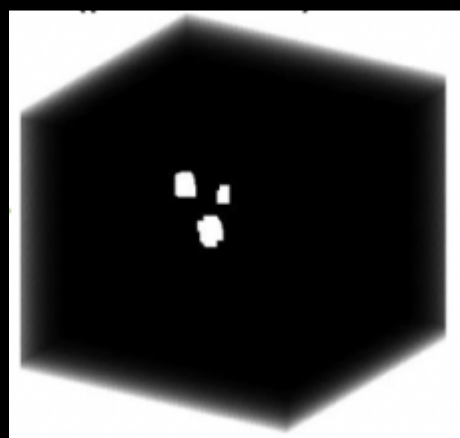
Weak Annotations

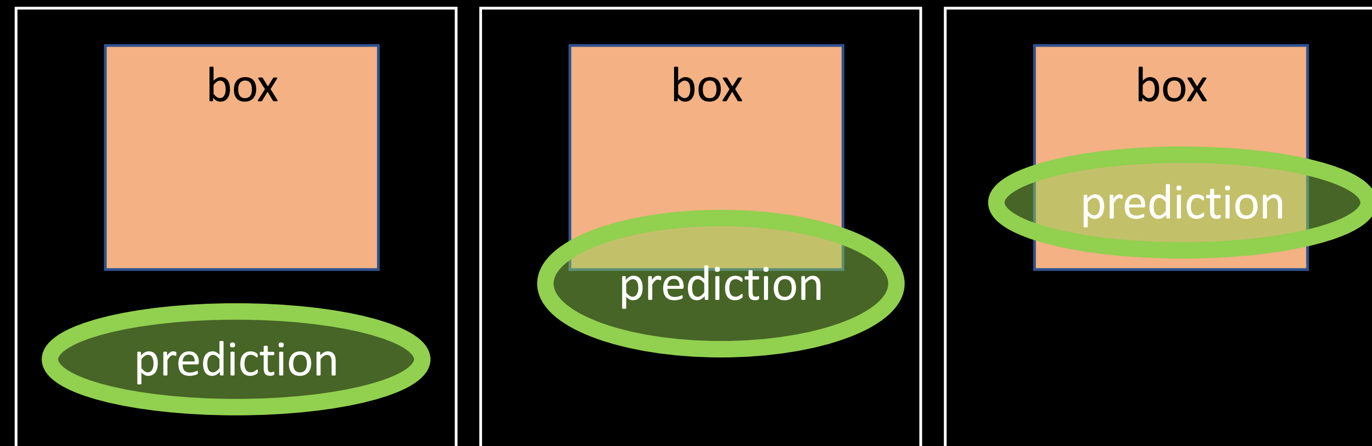
Afshari, Bentaieb, Hamarneh SPIE MI 2019
https://www.cs.sfu.ca/~hamarneh/ecopy/spiemi2019.pdf

New Loss = Modified Dice Loss + Classical Mumford Shah Energy

Manual delineation only provides a box

Network prediction

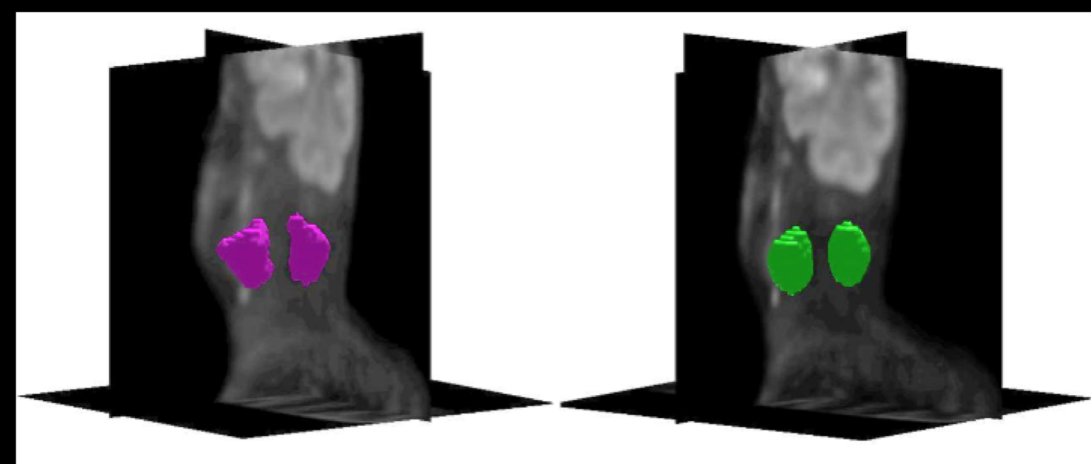




Dice

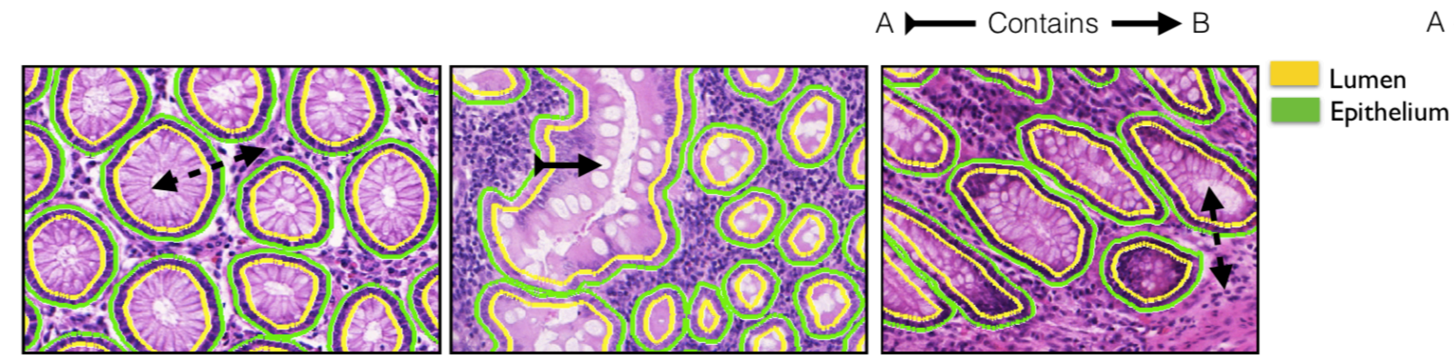
Weaken Dice's Loss

No Dice Loss Only MS

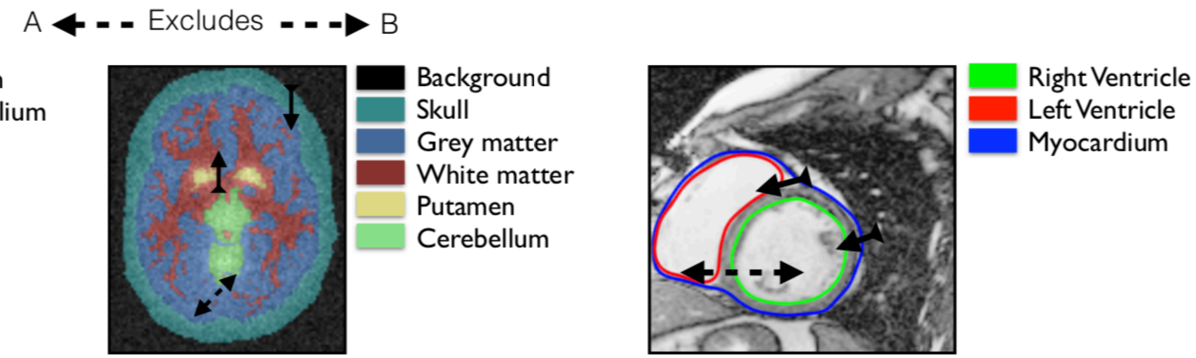


Topology Loss

BenTaieb, Hamarneh. MICCAI 2016
https://www.cs.sfu.ca/~hamarneh/ecopy/miccai2016a.pdf

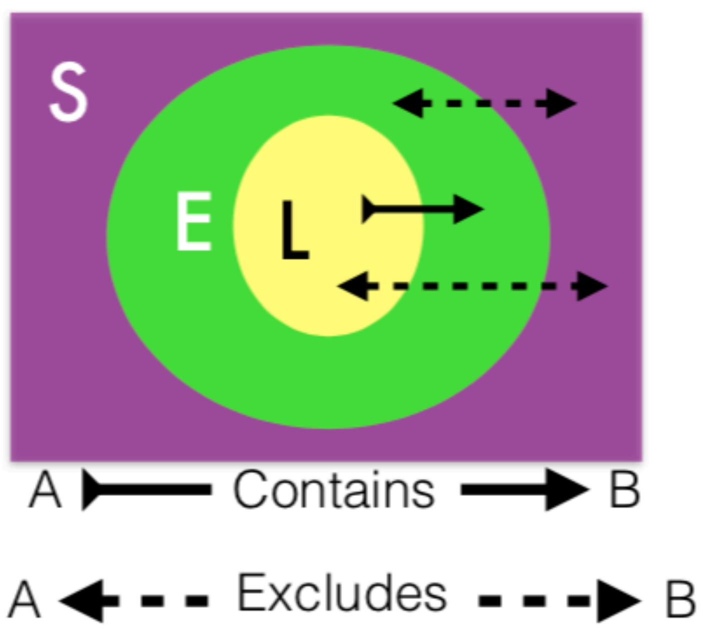


Colon Adenocarcinoma (Warwick-QU dataset) [1]



Other Multi-Part Objects: Brain (PET), Heart (CT)

Multi-Region Interactions



Topological Validity Indicator

S	0	1	0	1	0	1	0	1
E	0	0	1	1	0	0	1	1
L	0	0	0	0	1	1	1	1
$V(y_p)$	0	1	1	0	0	0	1	0
y_p	-	S	E	-	-	-	L	-

$V = 1$ valid $V = 0$ invalid

$$\mathcal{L}_T(x;\theta) = \sum_{p\in\Omega} \sum_{r\in\{L,S,E\}} -y_p^r \log P(y_p^r = 1|x_p;\theta)$$

Marginalized probability

$$P(y_p|x_p;\theta) = \frac{1}{Z}\prod_r e^{f_r(x_p;\theta)y_p^r} \times V(y_p) \quad \forall y_p \in \{0,1\}^R \quad Z = \sum_{y_p} P(y_p|x_p;\theta)$$

Predicted joint probability

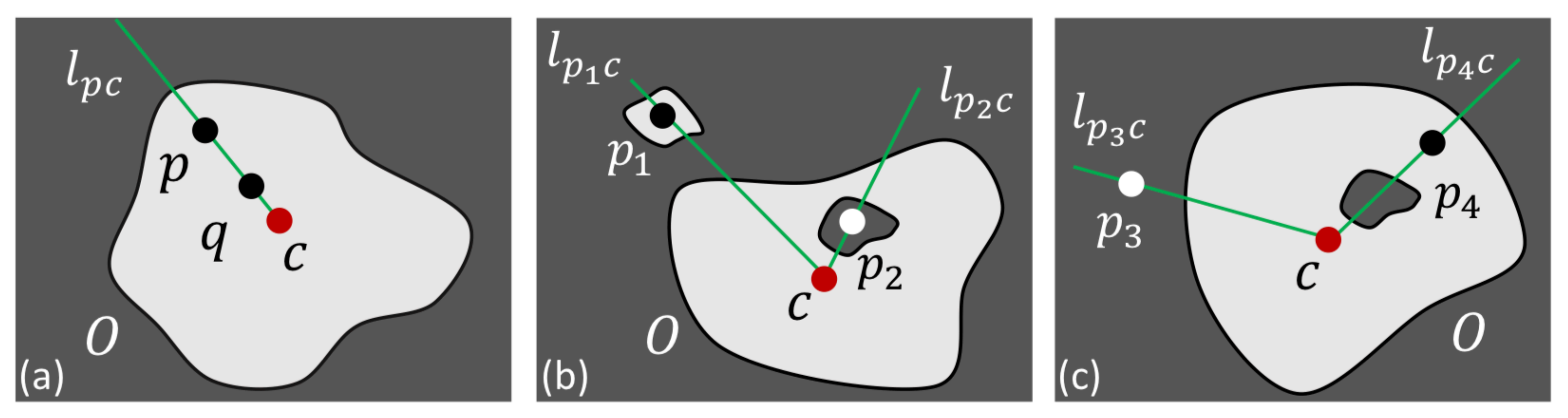
Validity indicator

All possible label vectors

Partition function

Star-Shape Loss

Mirikharaji, Hamarneh. MICCAI 2018
https://www.cs.sfu.ca/~hamarneh/ecopy/miccai2018a.pdf



Star shape

star shape violations

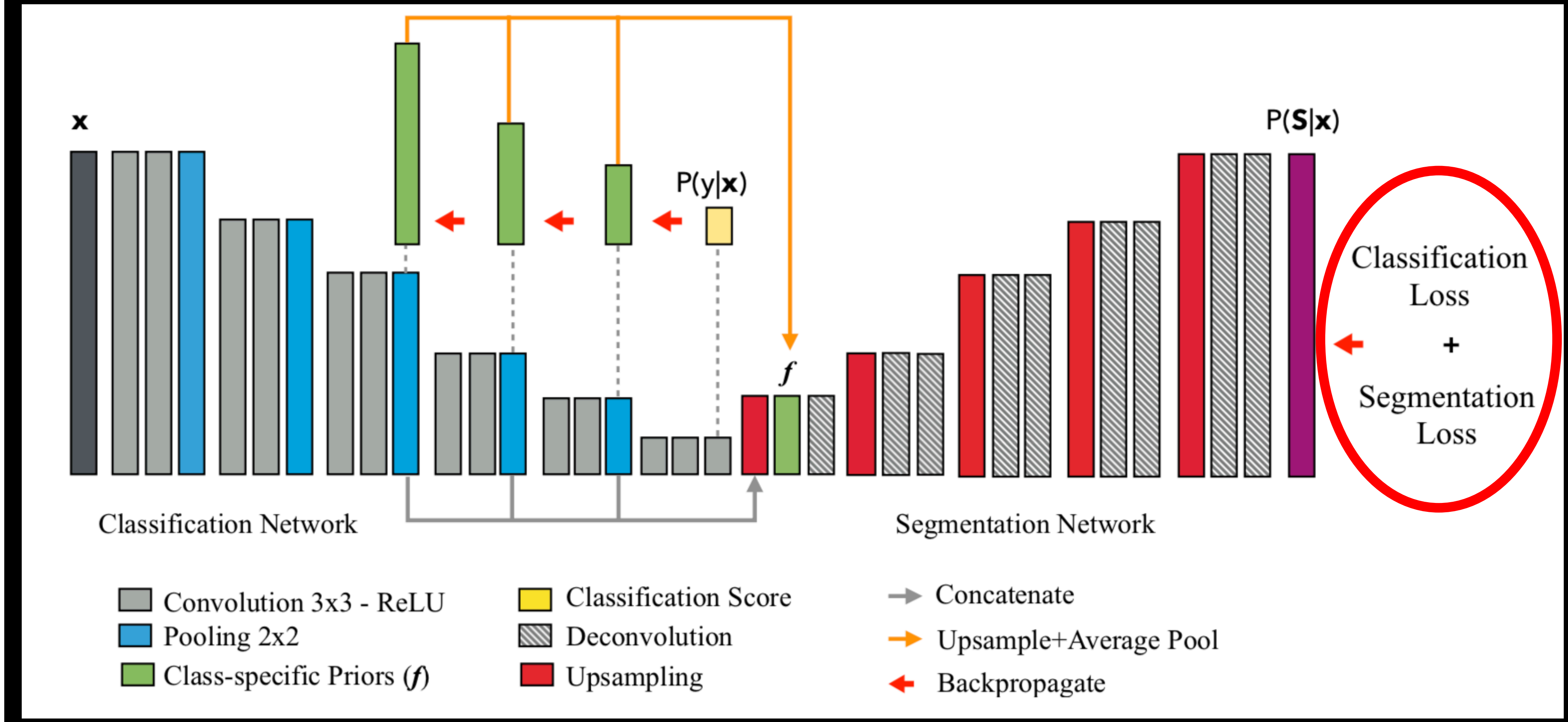
Loss penalizes segmentations violating star shape prior
reduce holes/islands

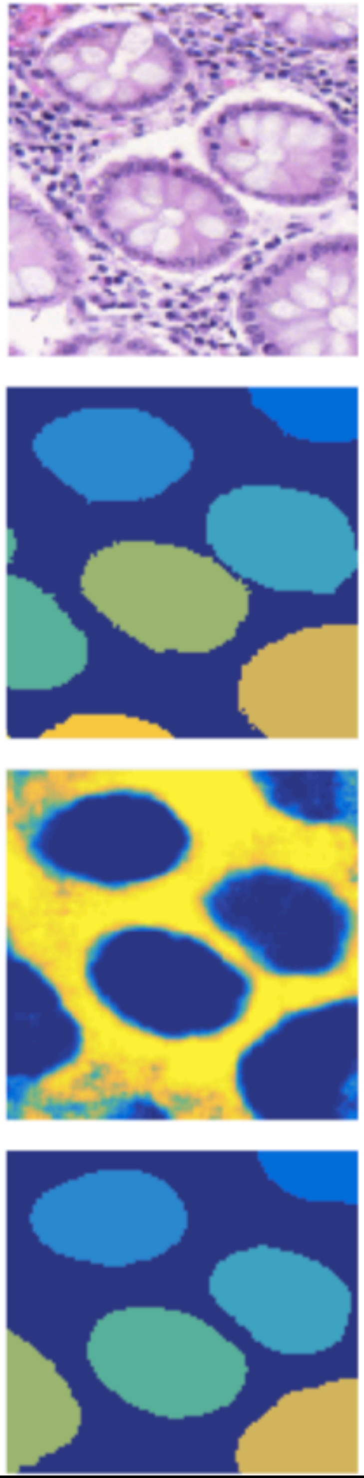
Joint Segmentation-Classification Loss

Bentaieb, Hamarneh. ISBI 2016
https://www.cs.sfu.ca/~hamarneh/ecopy/isbi2016a.pdf

- Classification depends on segmentation-based features
- Method and parameters of segmentation depend on class object

$$\mathcal{L}(x, y, S) = \lambda \, \mathcal{L}_c(x, y) + (1 - \lambda) \, \mathcal{L}_s(x, S, f)$$

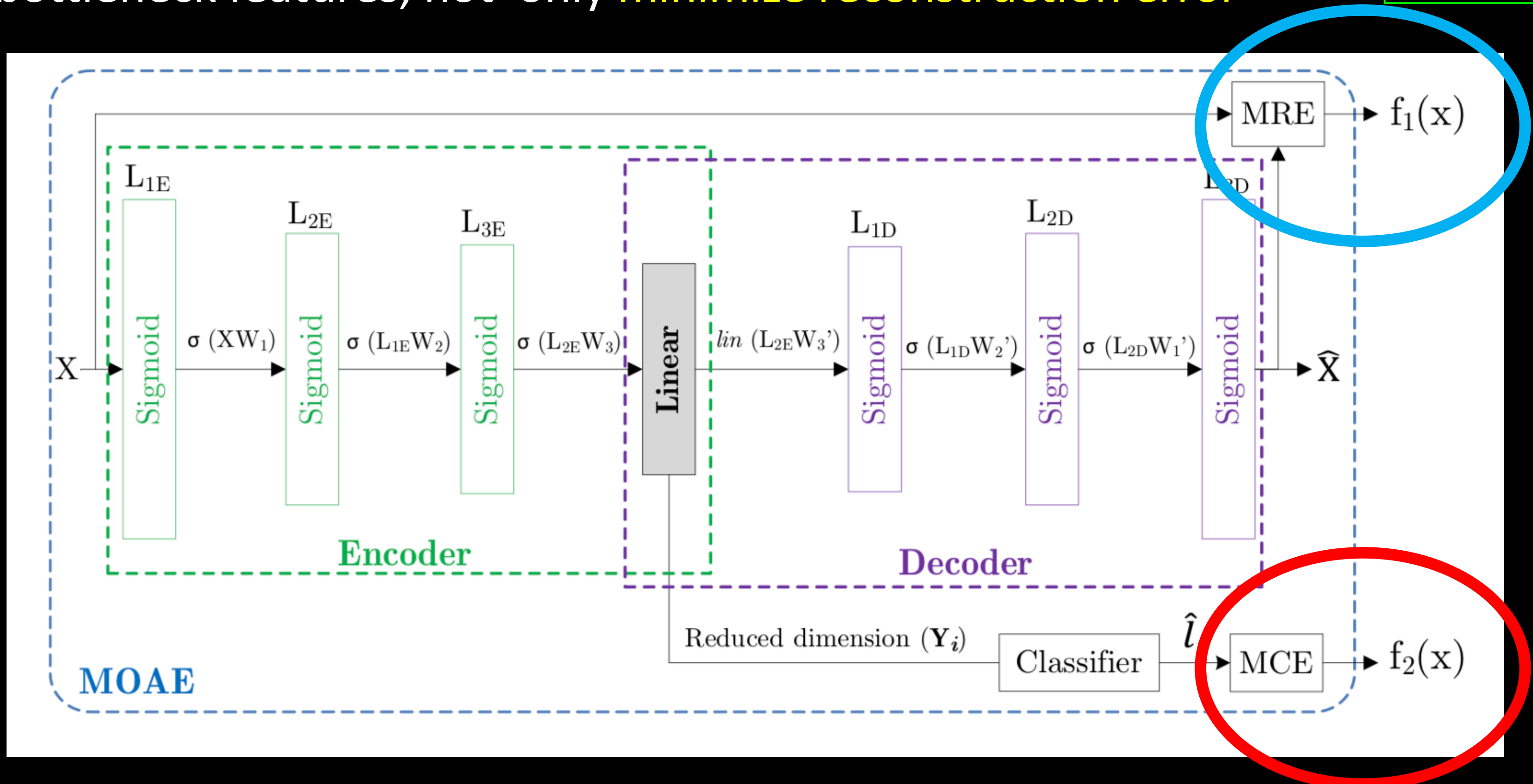




Joint Reconstruction-Classification Loss

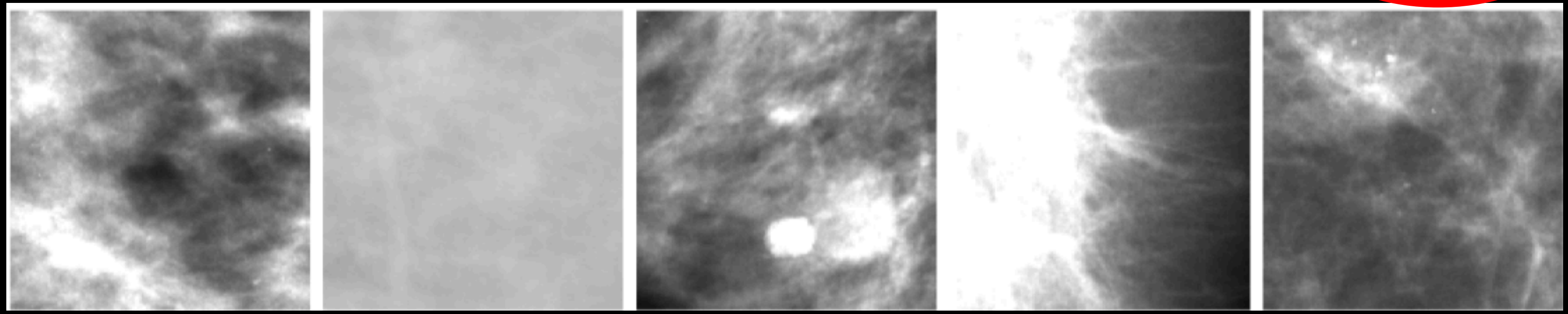
Enhance auto-encoders to minimize classification error using bottleneck features, not only minimize reconstruction error

Asgari, Kawahara, Miles, Hamarneh. CMIG 2017
https://www.cs.sfu.ca/~hamarneh/ecopy/cmpb2017.pdf



$$\mathrm{MRE} = \frac{1}{N}\sum_{i=1}^{N}\sum_{j=1}^{M}(X_{ij} - \hat{X}_{ij})^2$$

$$\mathrm{MCE} = \frac{1}{N}\sum_{i=1}^{N} e_i, \text{ where } e_i = \begin{cases} 0, & l_i = \hat{l}_i \\ 1, & l_i \neq \hat{l}_i \end{cases}$$



		Assessment categories		
		1	2	3
Tissue density classes	I	C_1 (107)	C_2 (41)	C_3 (42)
	II	C_4 (179)	C_5 (46)	C_6 (59)
	III	C_7 (48)	C_8 (142)	C_9 (29)
	IV	C_{10} (51)	C_{11} (144)	C_{12} (61)

Loss to Tackle Input/Output Imbalance

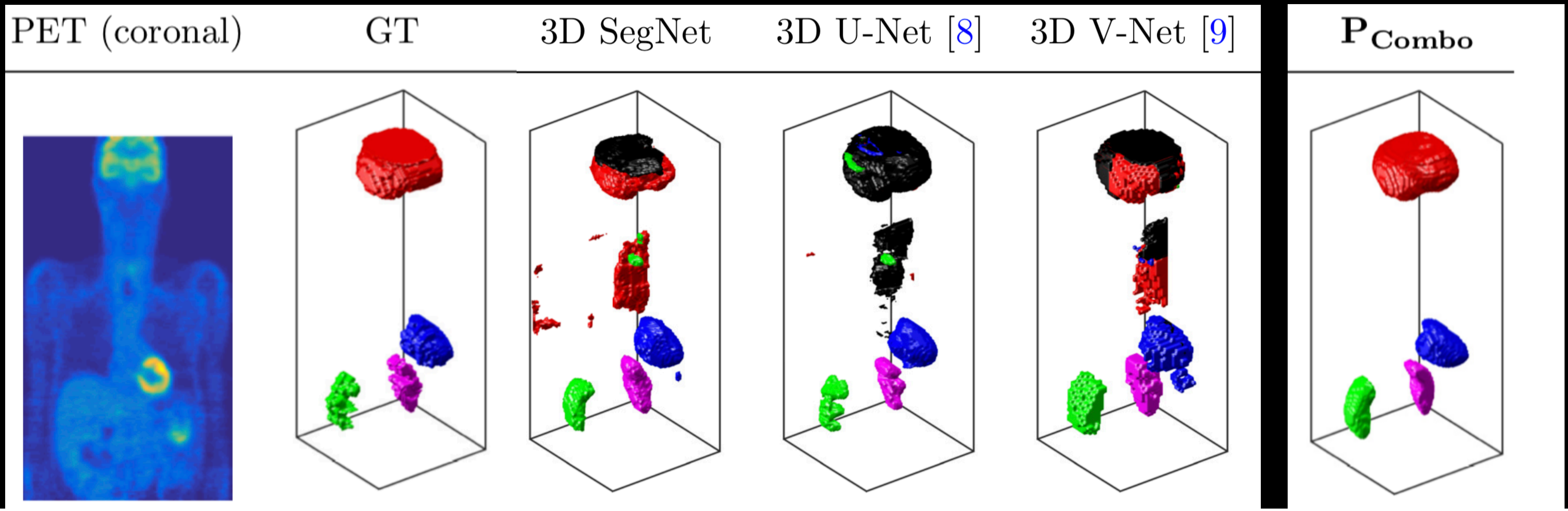
Asgari, Zheng, Zhou, Georgescu, Sharma, Xu, Comaniciu, Hamarneh. CMIG 2019
http://www.cs.sfu.ca/~hamarneh/ecopy/cmig2019.pdf

ComboLoss

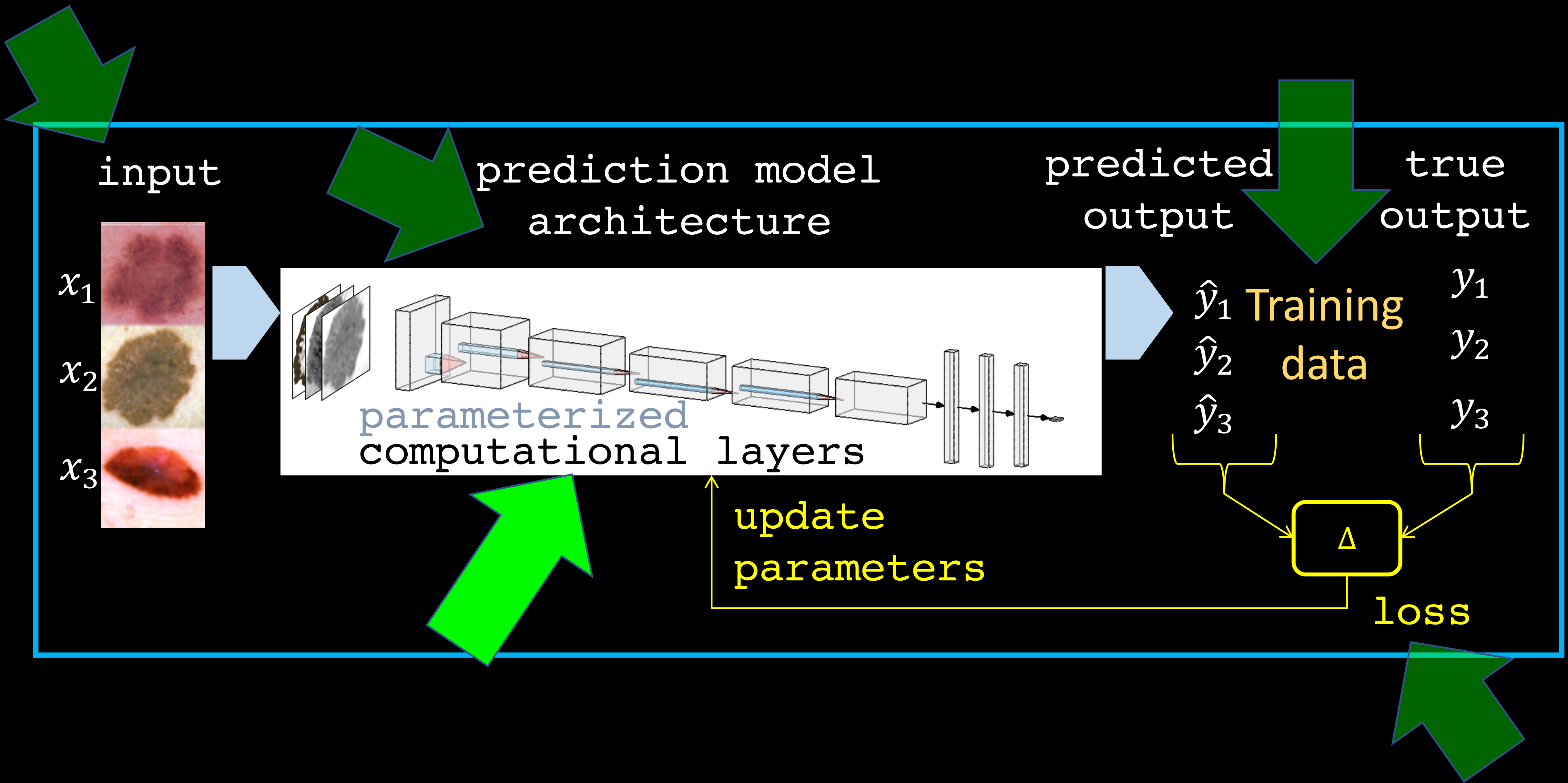
$$L = \alpha \left(-\frac{1}{N} \sum_{i=1}^{N} \beta \left(t_i - \ln p_i \right) + (1-\beta) \left[(1-t_i) \ln (1-p_i) \right] \right) - (1-\alpha) \sum_{i=1}^{K} \left(\frac{2 \sum_{i=1}^{N} p_i t_i + S}{\sum_{i=1}^{N} p_i + \sum_{i=1}^{N} t_i + S} \right)$$

Cross entropy loss
Tackle output-imbalance:
FP & FN in segmentation output

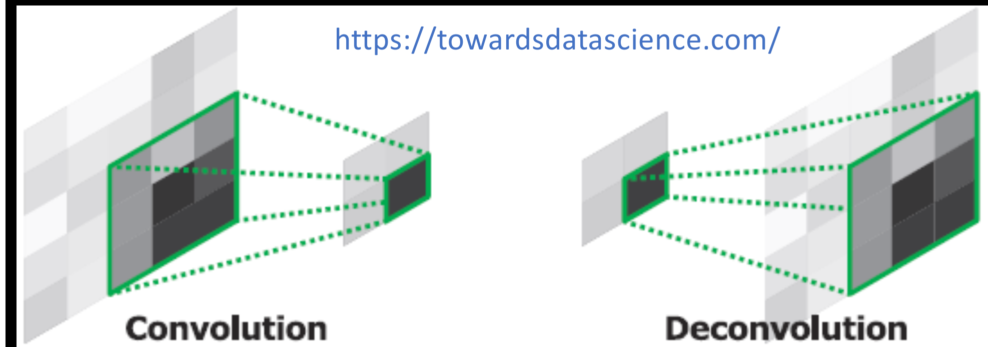
Dice loss
Tackle input-imbalance:
Varying sized objects segments of training data



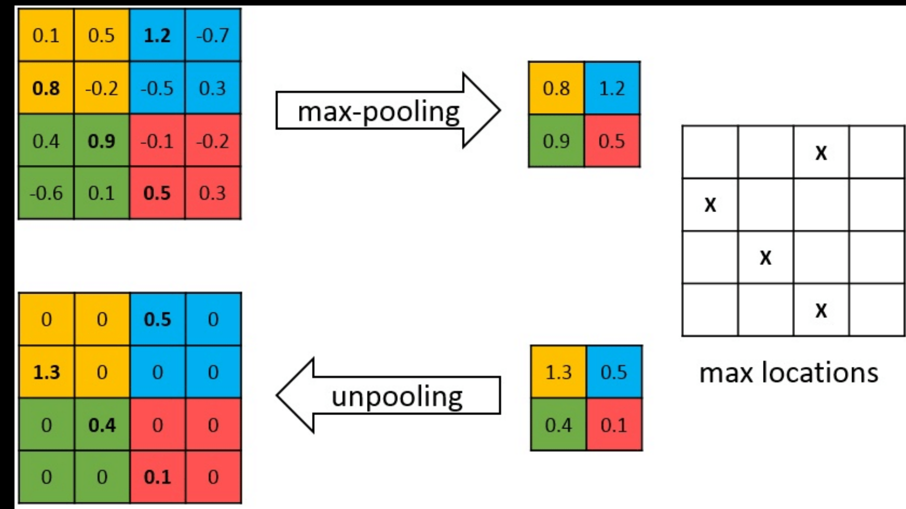
Computational layers



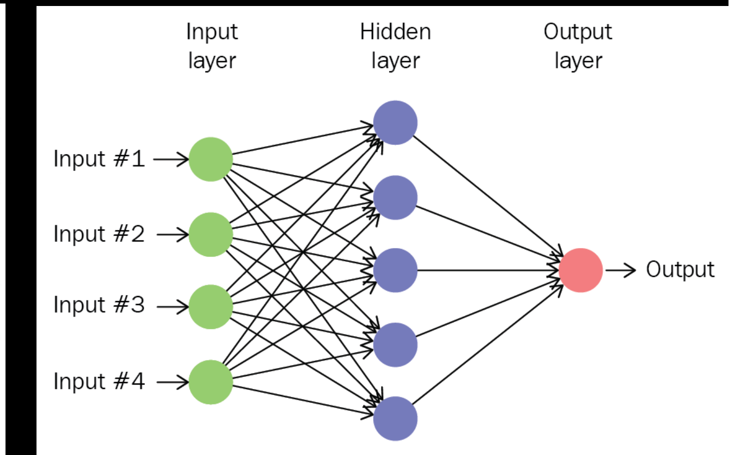
Computational layers



[de]convolution

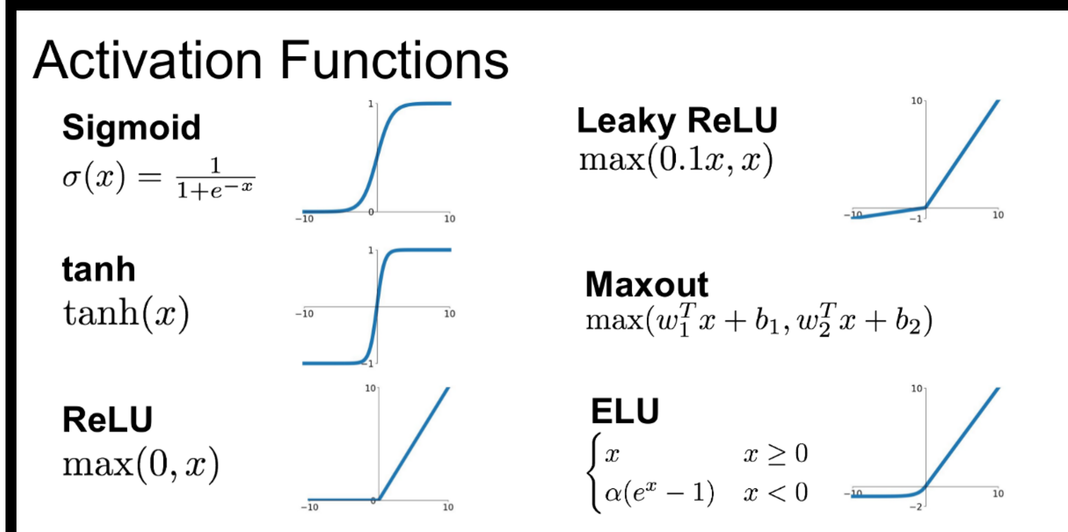


[un]pooing

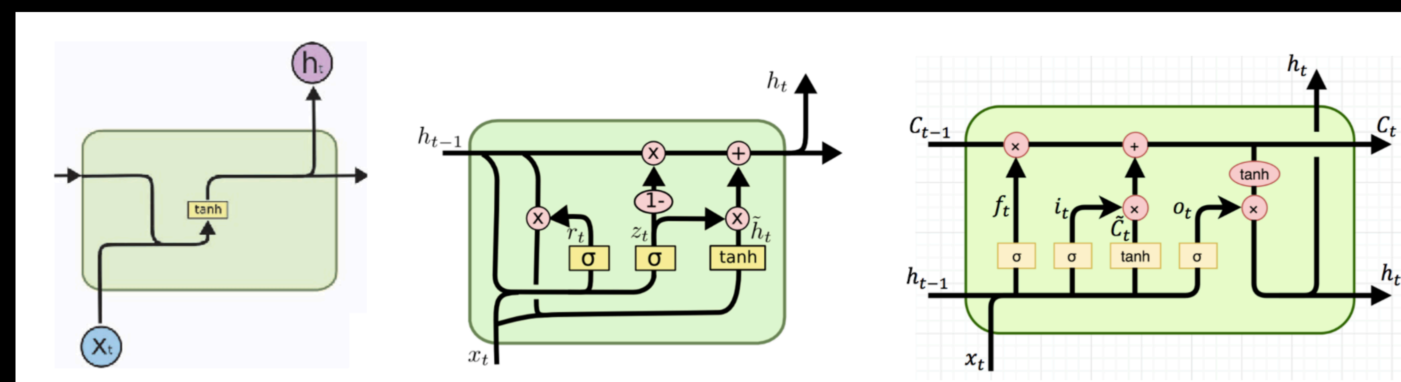


Fully-connected

DOI: 10.1007/978-3-319-44781-0_3



Activation functions

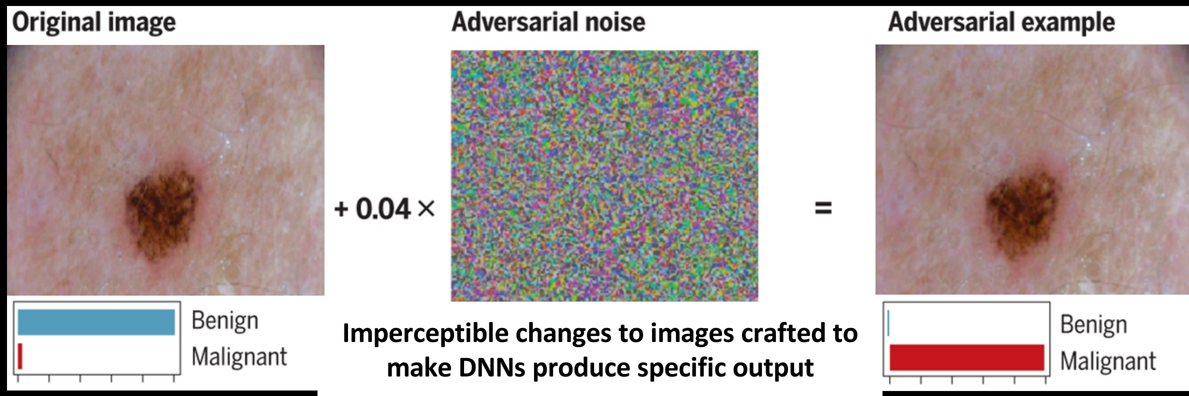


Sequence processing (RNN, LSTM, GRU)

23

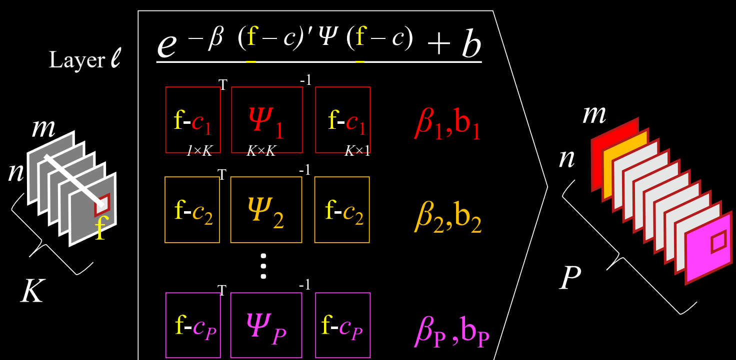
RBF layers to counteract adversarial attacks

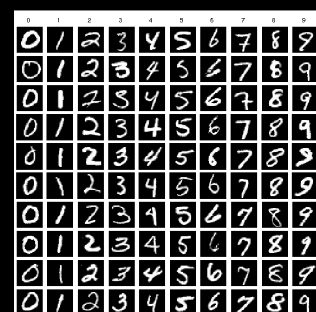
Asgari, Abhishek, Azizi, Hamarneh. CVPR 2019
https://www.cs.sfu.ca/~hamarneh/ecopy/cvpr2019.pdf

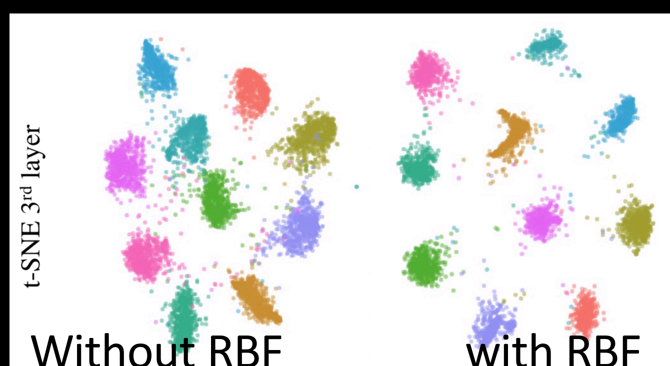


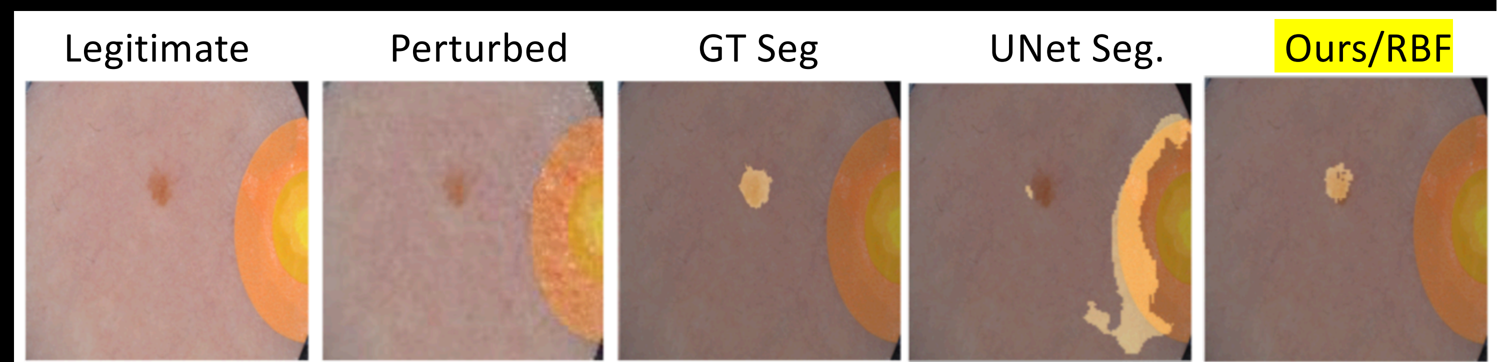
Finlayson, Bowers, Ito, Zittrain, Beam, Kohane. Science 2019

Xiao et al. ECCV 2018

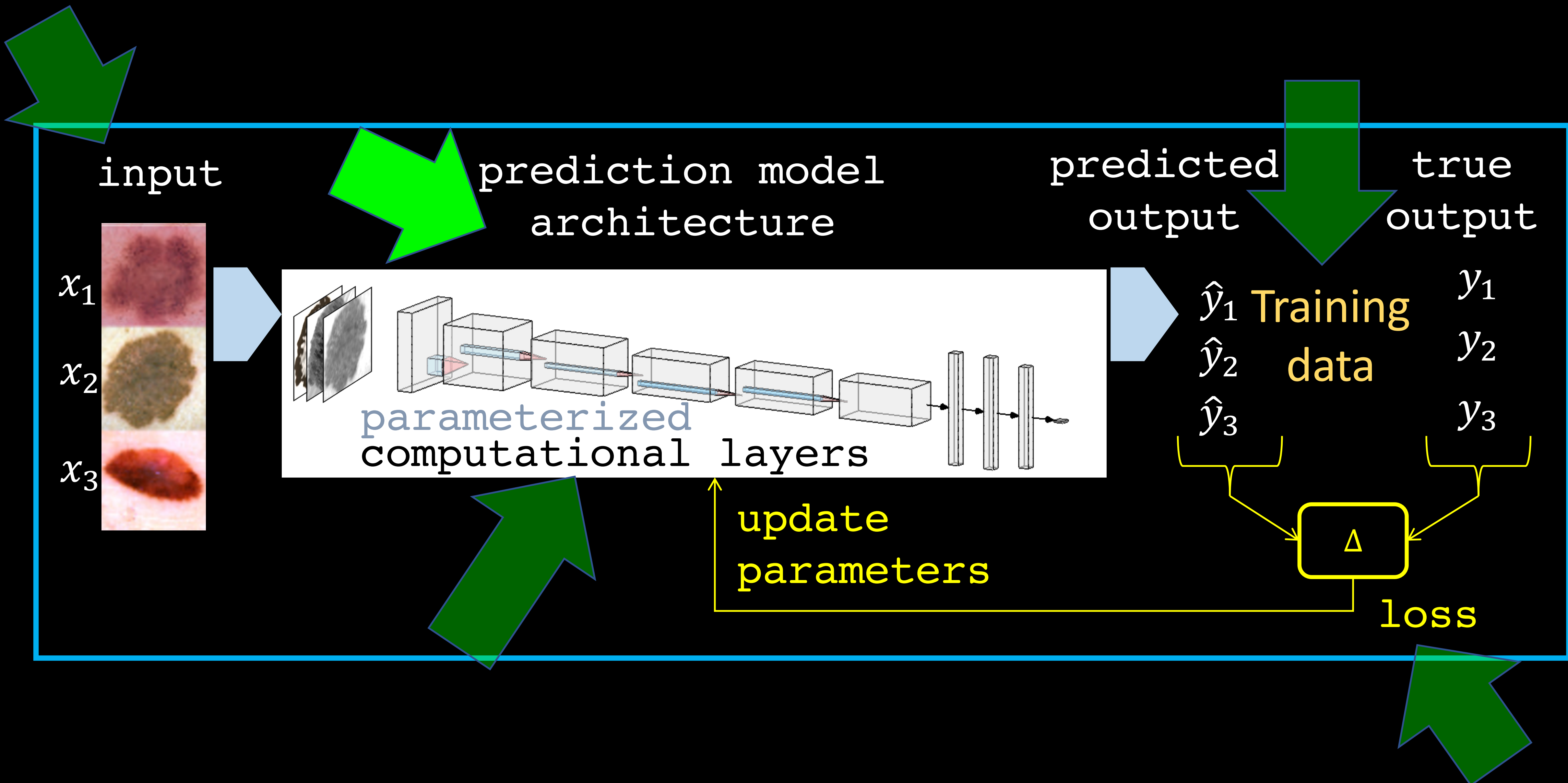






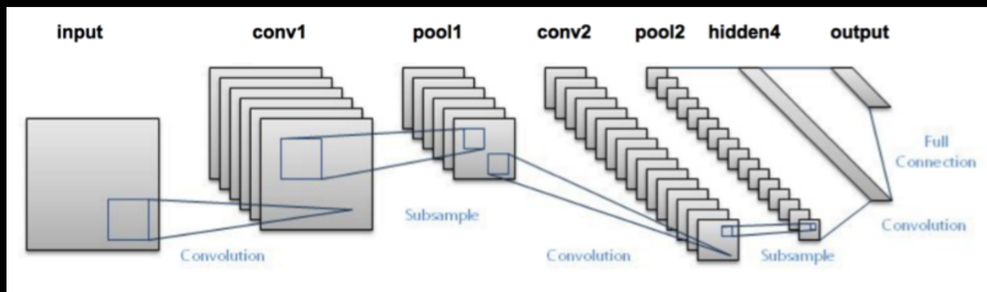


Network architectures



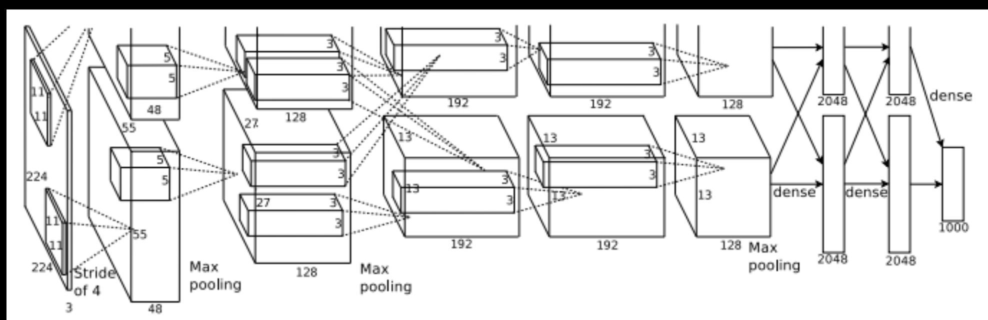
Network architectures

LeNet-5 (1998)

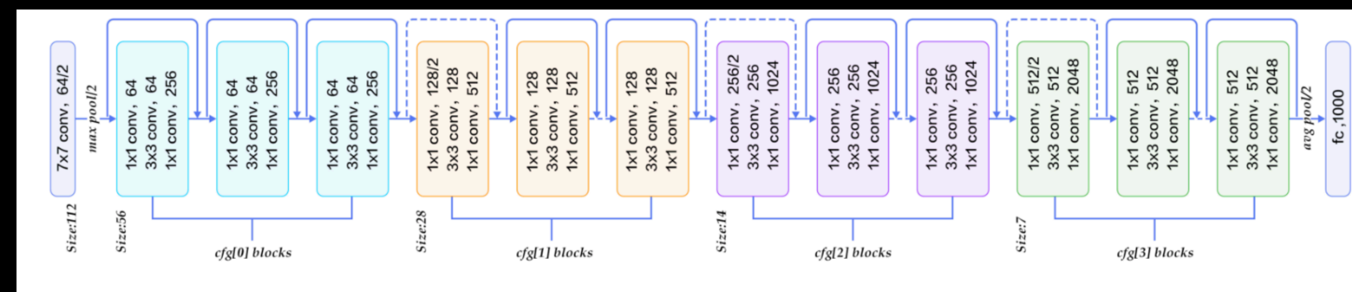


VGGNet (2014)

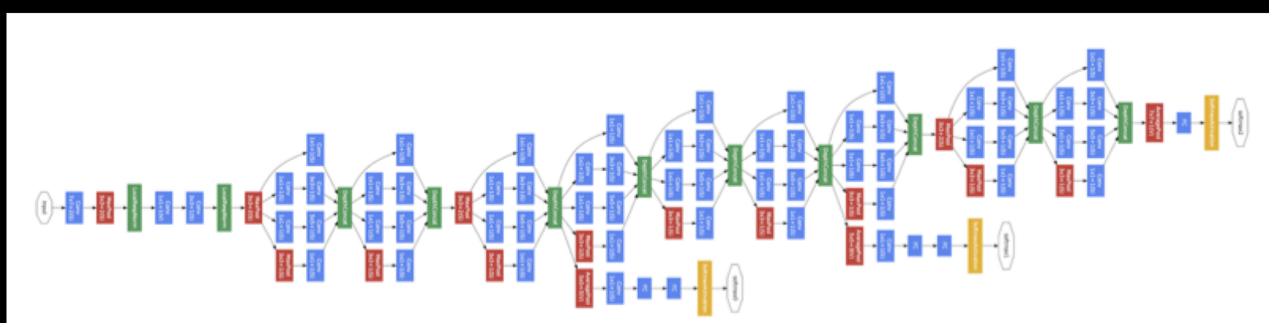
AlexNet (2012)



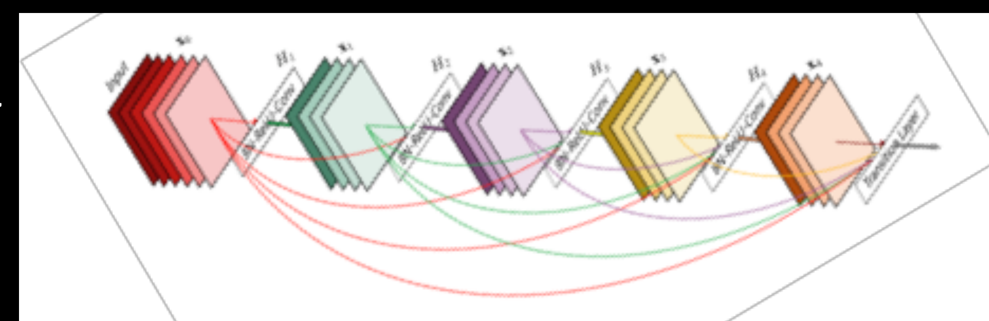
ResNet(2015)



GoogleNet Inception(2014)

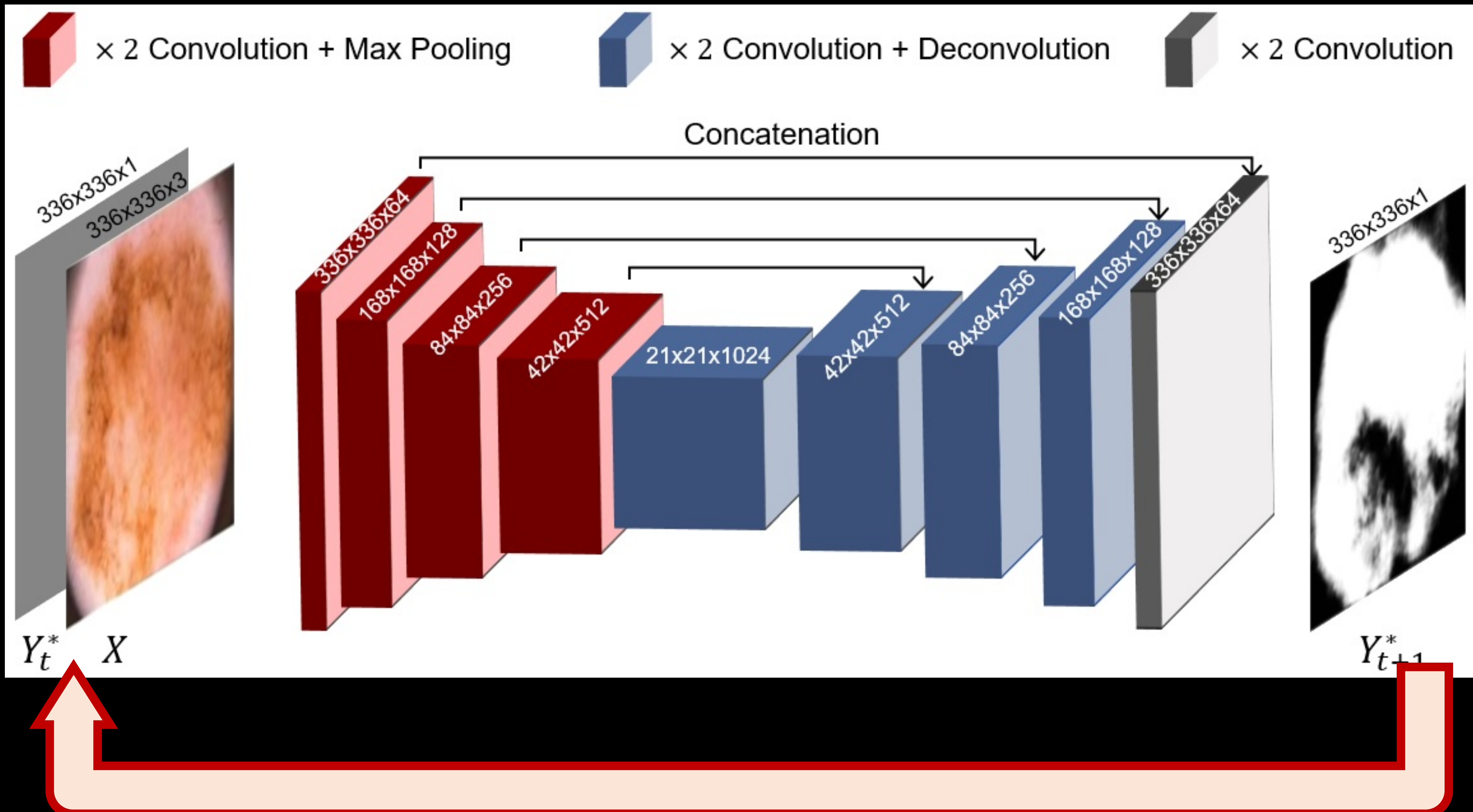


DenseNet (2018)



Auto-Context Network

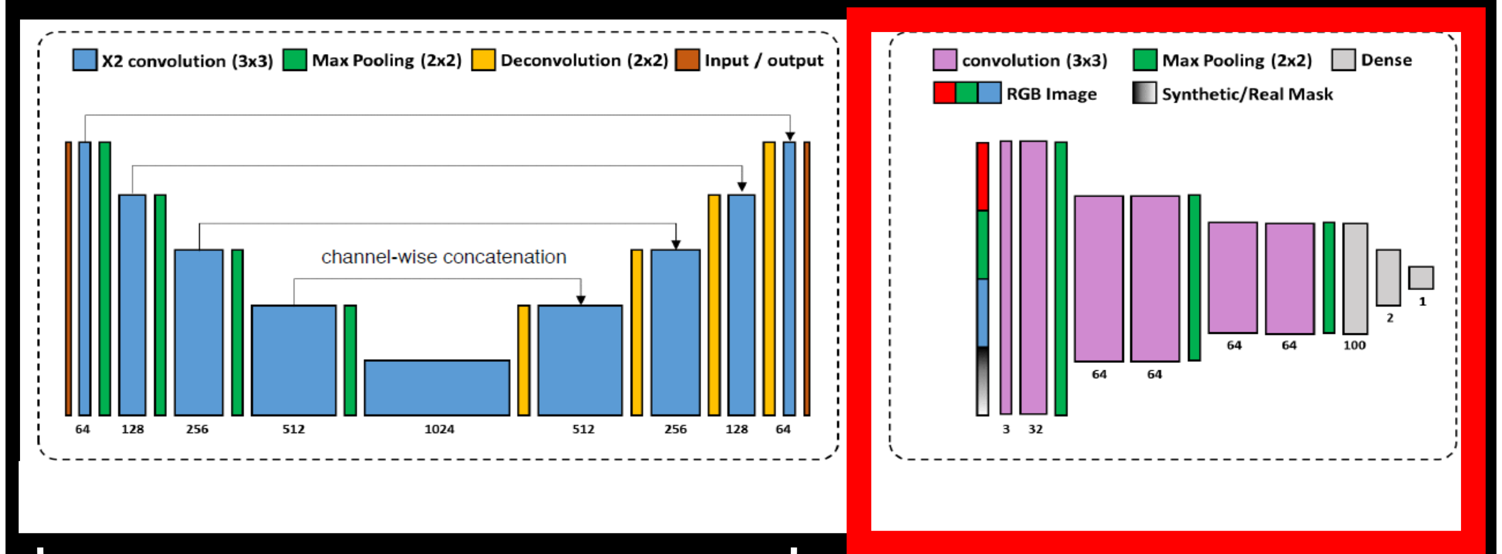
Mirikharaji, Izadi, Kawahara, Hamarneh. ISBI2018
https://www.cs.sfu.ca/~hamarneh/ecopy/isbi2018a.pdf



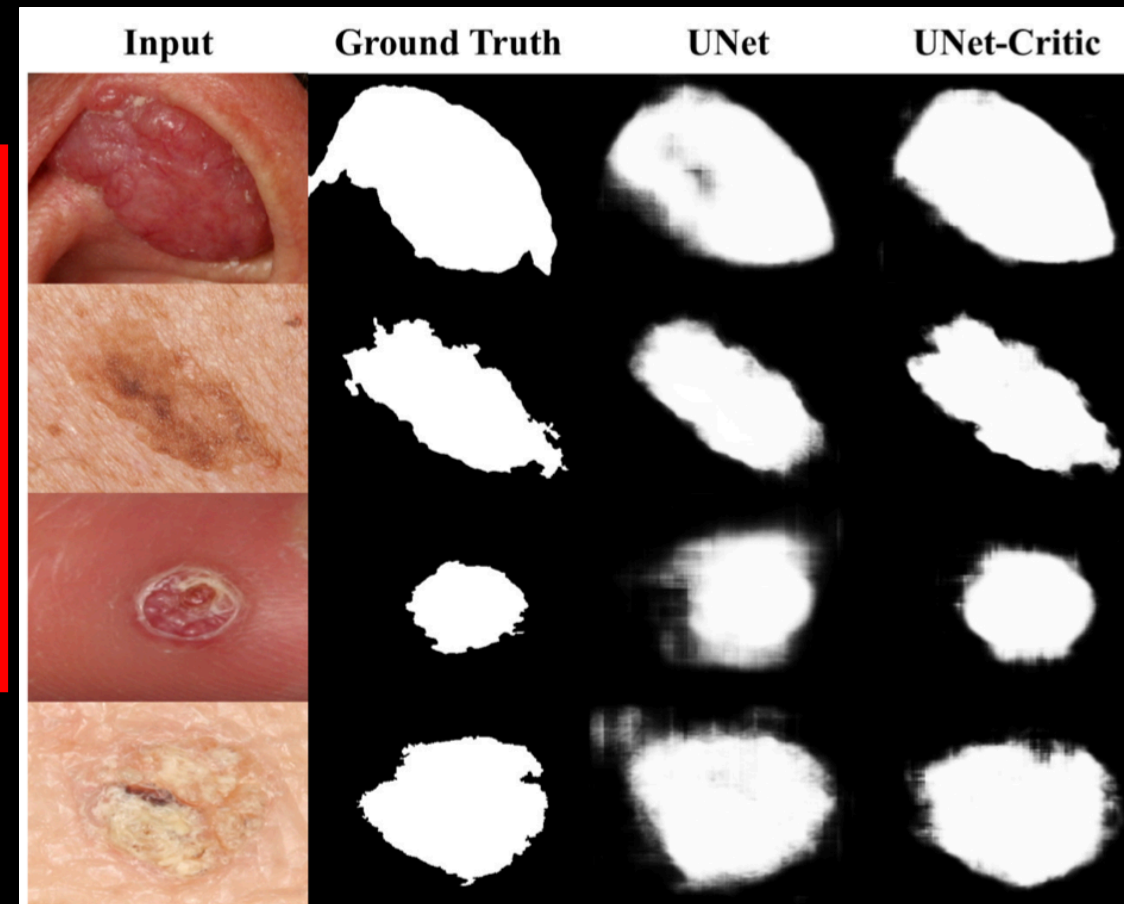
Critic Adversarial Networks

Izadi, Mirikharaji, Kawahara, Hamarneh. ISBI 2018

https://www.cs.sfu.ca/~hamarneh/ecopy/isbi2018b.pdf

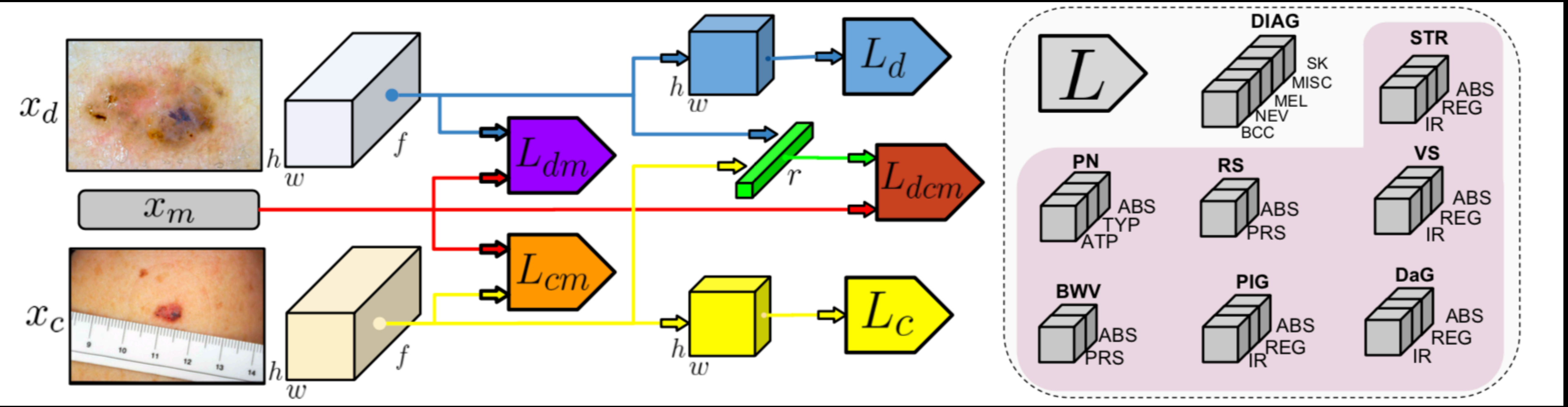


Segmenter **Critic**



Multi-modal input multi-label output network

Kawahara, Daneshvar, Argenziano, Hamarneh
IEEE JBHI 2019
http://www.cs.sfu.ca/~hamarneh/ecopy/jbhi2019a.pdf



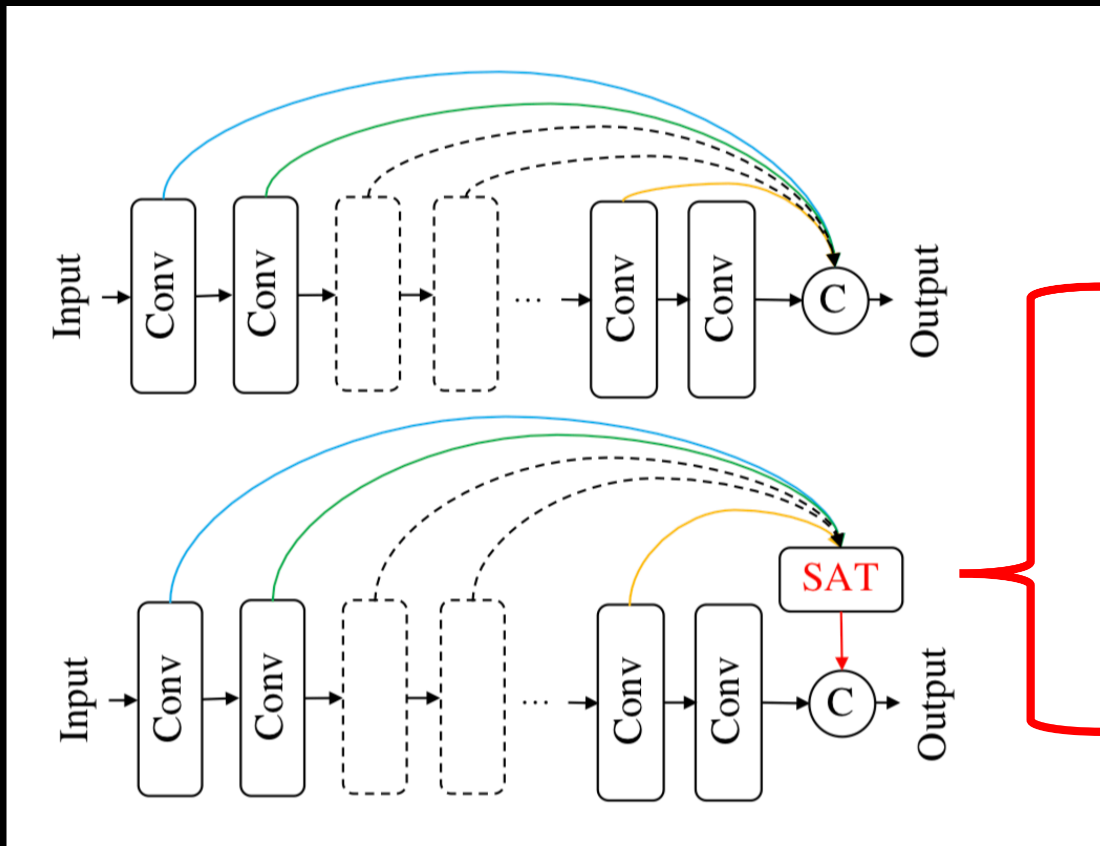
Dermoscopic image
Metadata
Clinical image

Handling missing data

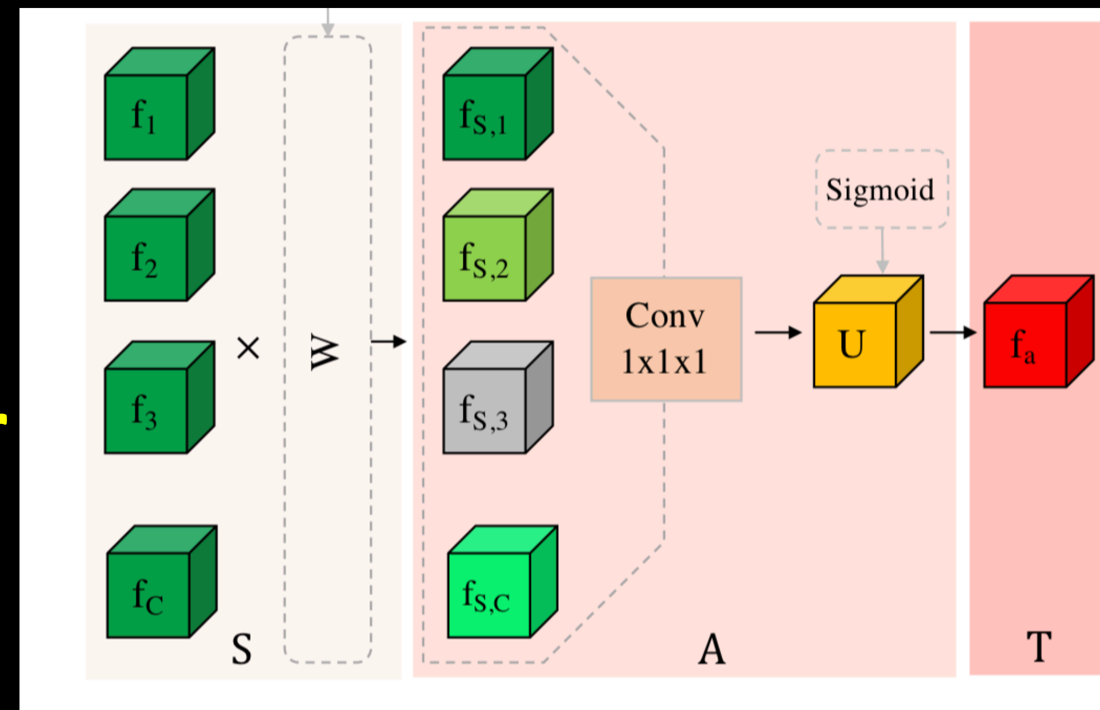
Binary diagnosis &
7 dermoscopic criteria

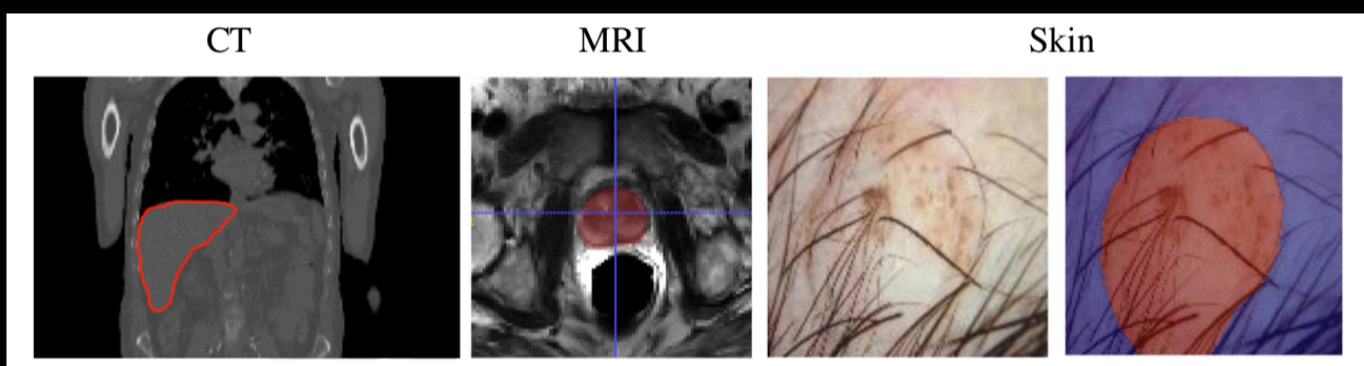
Networks with light, learnable skip connection

Asgari, BenTaieb, Sharma, Zhou, Zheng, Georgescu, Sharma, Xu, Comaniciu, Hamarneh. MICCAI MLMI 2019
http://www.cs.sfu.ca/~hamarneh/ecopy/miccai_mlmi2019b.pdf



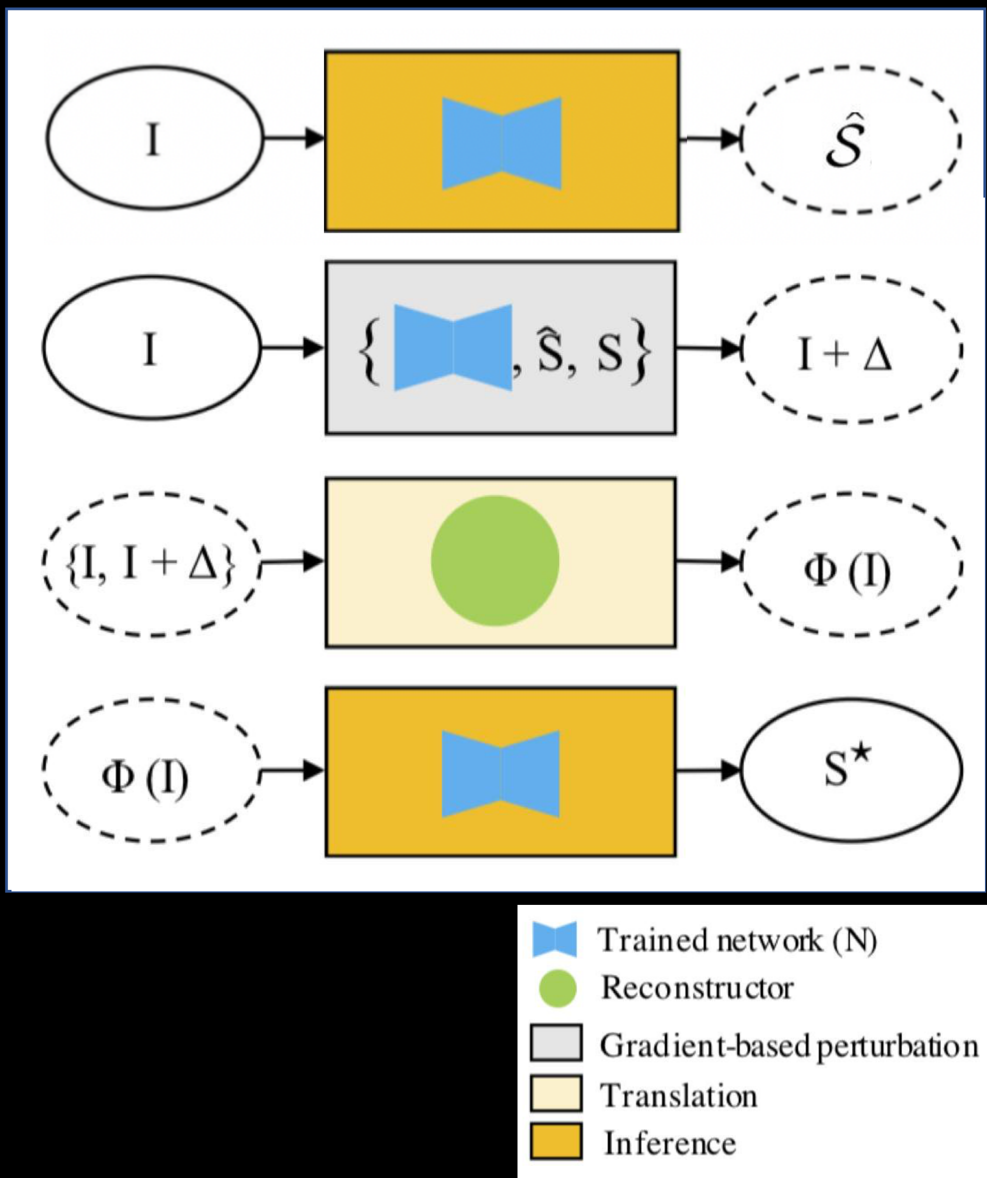
SAT:
Select
Attend
Transfer





Learn to modify input to cause improved output

Asgari, Abhishek, Hamarneh. MICCAI2019
http://www.cs.sfu.ca/~hamarneh/ecopy/miccai2019b.pdf

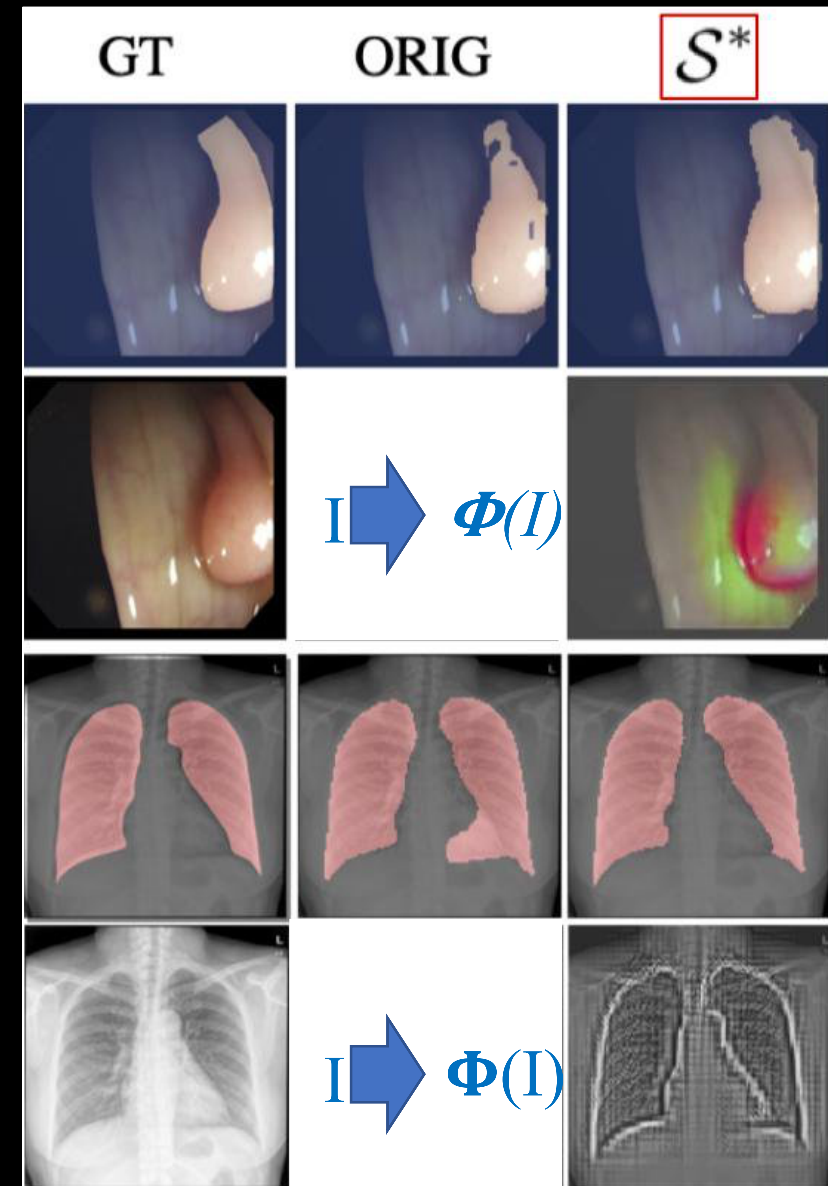


Feeding input through network gives sub-optimal output

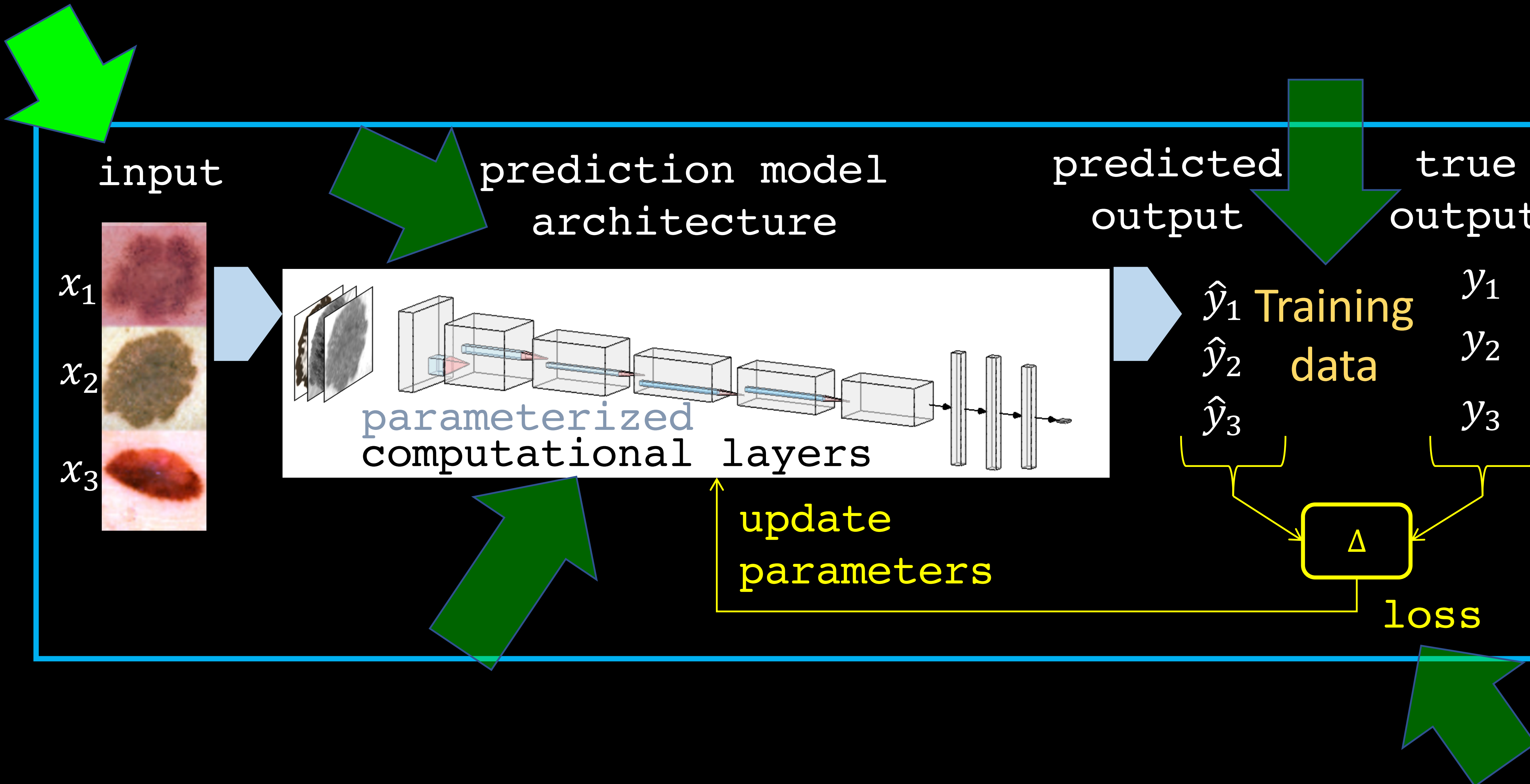
We modify input to produce *known* optimal output

Train network to estimate modification

Feeding estimated modification improves output



Input data (data shift and missing data)

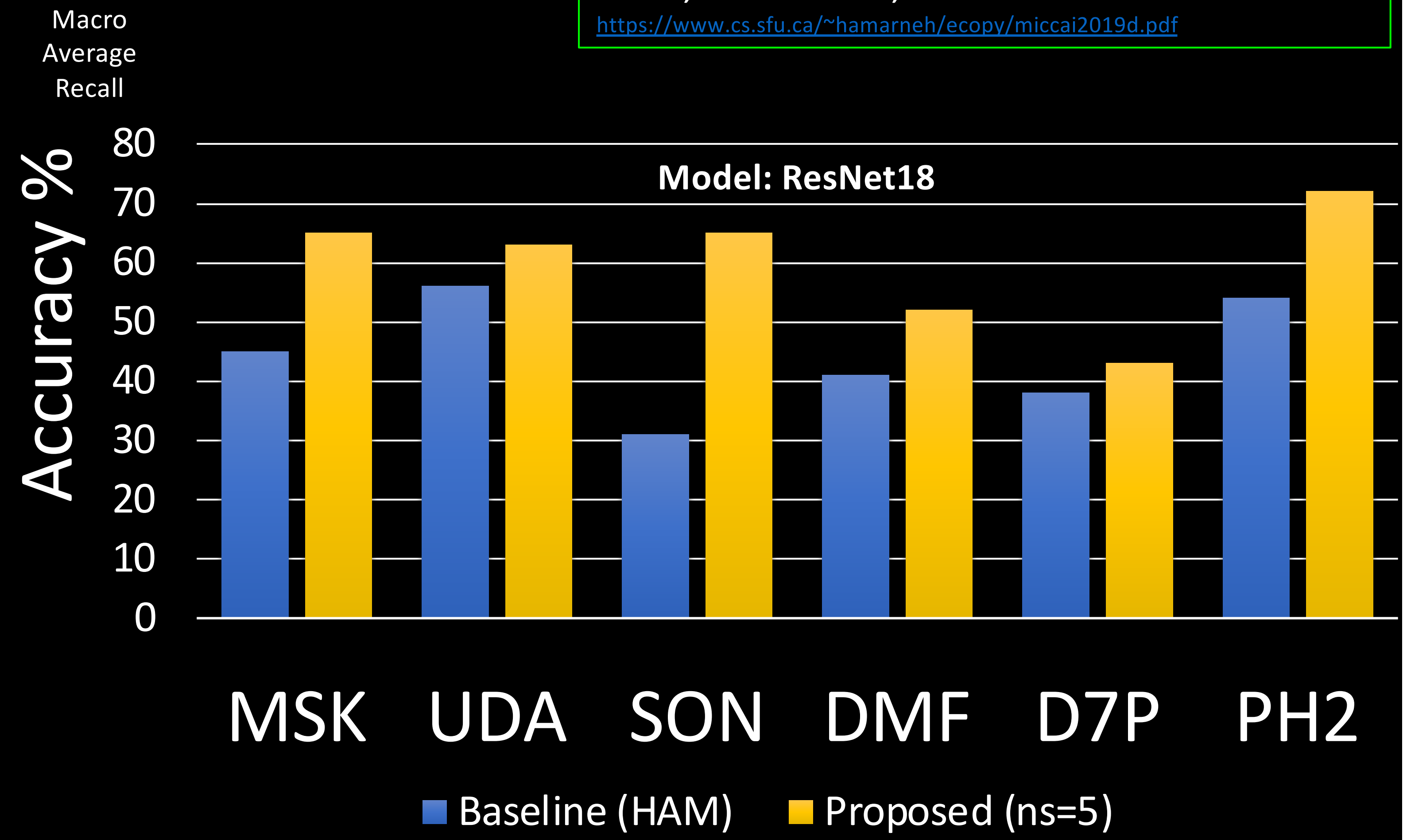


Skin dataset shift

Yoon, Hamarneh, Garbi. MICCAI 2019
https://www.cs.sfu.ca/~hamarneh/ecopy/miccai2019d.pdf

7 Domains:
1 primary: HAM10000
6 secondary: Dermofit+MSK+UDA+ONIC+Derm7pt+PH2
n_s samples/class

CCSA loss: classification & contrastive semantic alignment [Motiian ICCV 2017] CE loss + feature alignment/separation losses

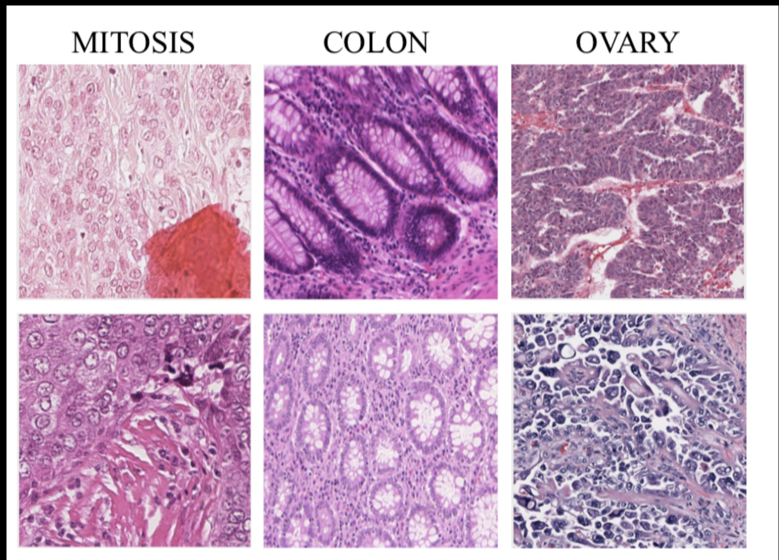


Class imbalance:
Intra-domain P(nevus) >> P(melanoma)
Inter-domain dermatofibroma ∉ Domain2

Dynamic sampling
two image-label pairs across domain: $(x_1, y_1), (x_2, y_2)$
Adaptive weighting
of CCSA loss based on $P(y = c_i)$ and $P(y_1 = c_i, y_2 = c_j)$

Adversarial Stain Transfer in Histopathology

BenTaieb, Hamarneh. TMI 2018
https://www.cs.sfu.ca/~hamarneh/ecopy/tmi2018.pdf

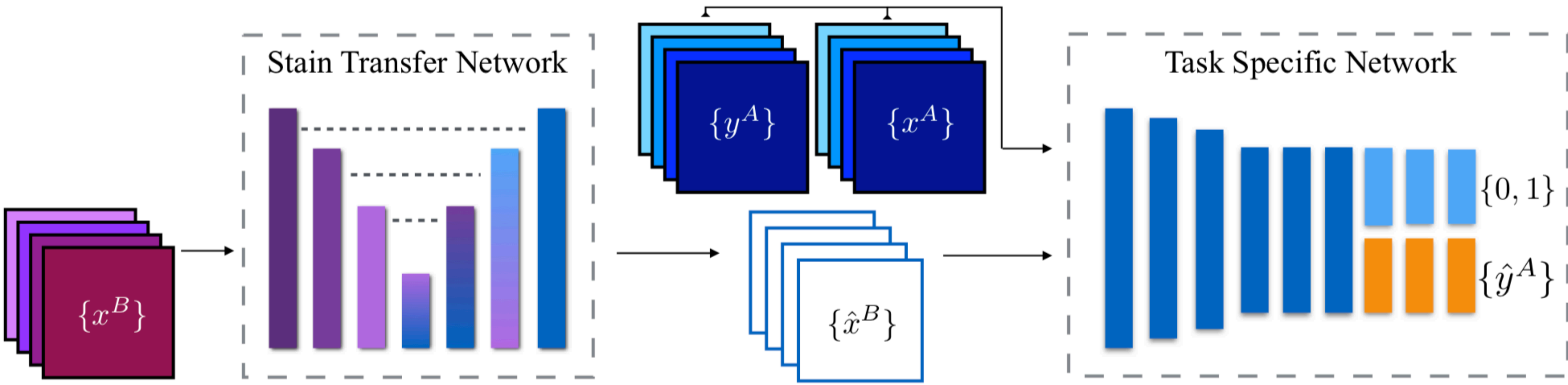


A

B

A and B refer to different staining procedures

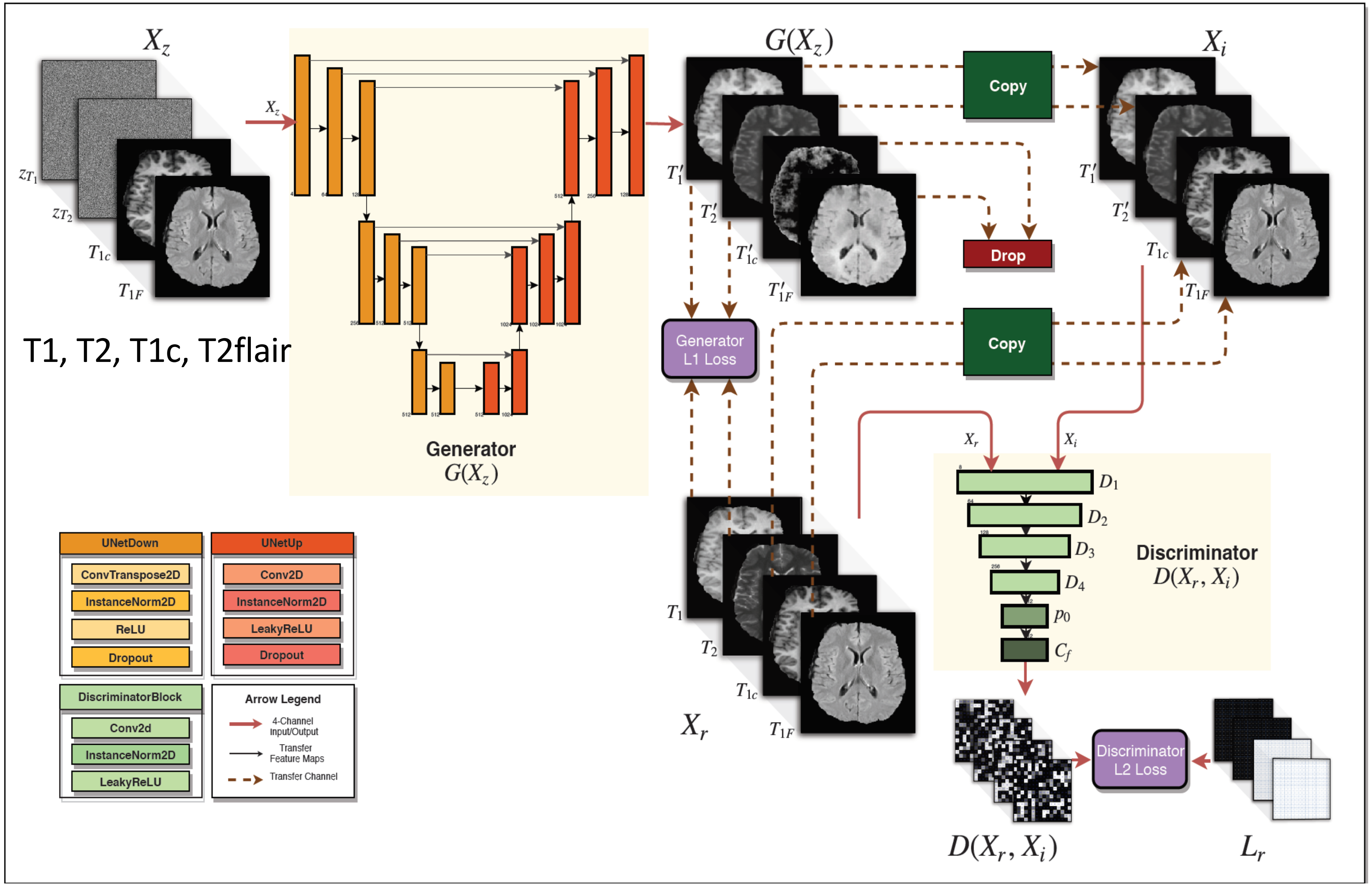
- Learns to discriminate real from fake 'A staining'
- Learns to perform the task, e.g. classification

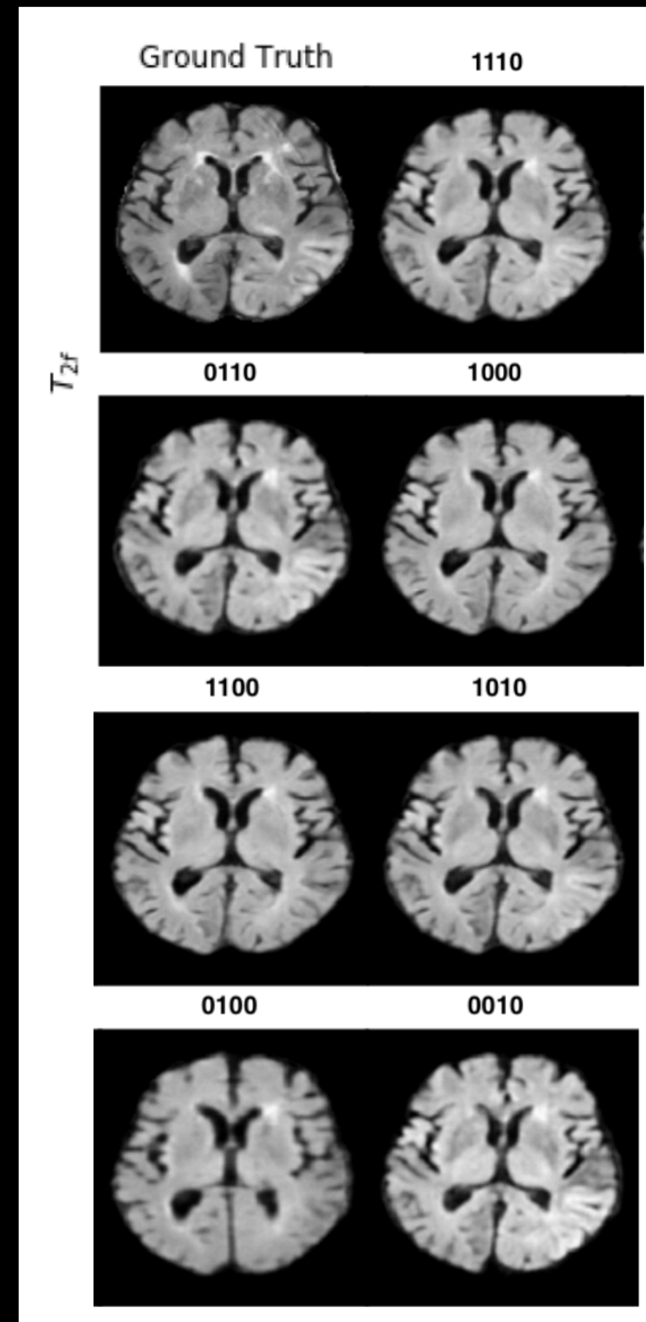


Missing MRI Pulse Sequence Synthesis

Multi-input, multi-output, adversarial training

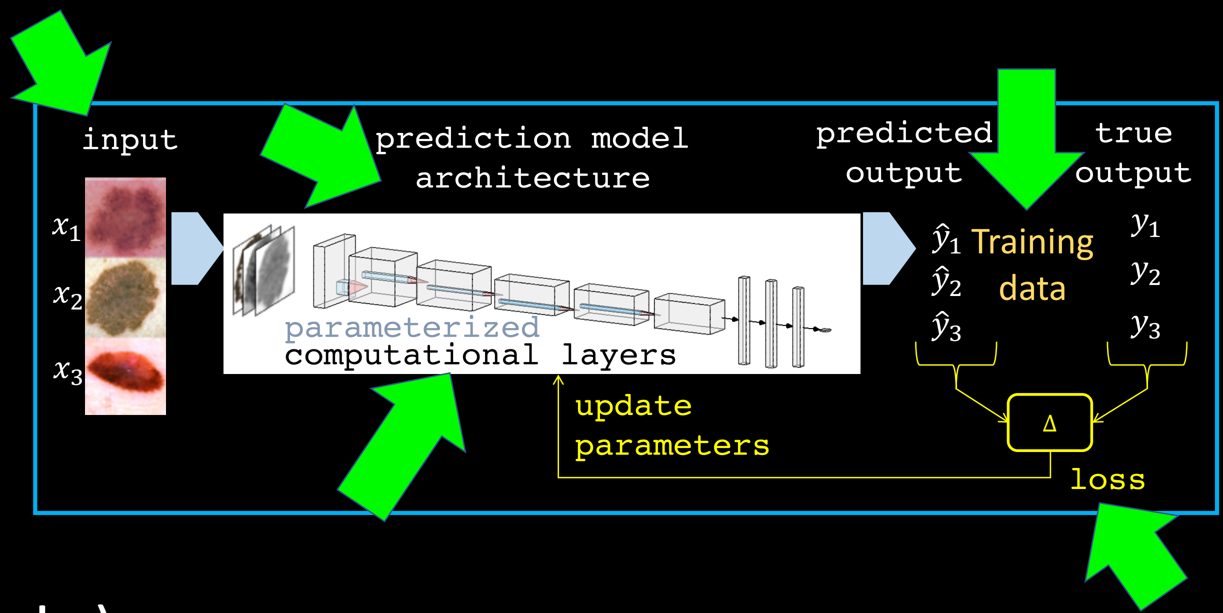
Sharma, Hamarneh. arXiv (rev. TMI)
www.cs.sfu.ca/~hamarneh/ecopy/arxiv_1904_12200.pdf





Some things we talked about...

- Medical image interpretation tasks (segmentation, classification)
- Promising deep learning approach
- ...but with many moving parts
  - Training data (synthesize/augment, active learning, crowdsourcing, weak labels)
  - Loss function
  - Computational layers (adversarial attacks)
  - Neural architecture
  - Input data (shift, missing, multi-modal)



Many things we didn't…

- Interpretability / explainability and trust
- Fairness and bias
- Neural architecture search
- Handling new/unseen disease classes (in training)
- complex hierarchy of large number of disease classes
- Uncertainty and Bayesian neural nets
- Self-learning, curriculum learning
- DL for medical image reconstruction from sensor data
- Predict ultimate task from image data or directly from sensor data
- Hybrid data- and expert knowledge/model-driven methods
- Legal, ethical, societal, economic challenges
- Other: most promising applications, inter-disciplinary collaboration…

Thank you!

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www. Medical Image Analysis .com

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