

Deep Learning-Based Analysis on Histopathology Images of Lung Cancer

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Outline

- Background and Motivation
- Initial Plan and Methods
- Results
- Future Direction
- Lessons learned

Histopathology

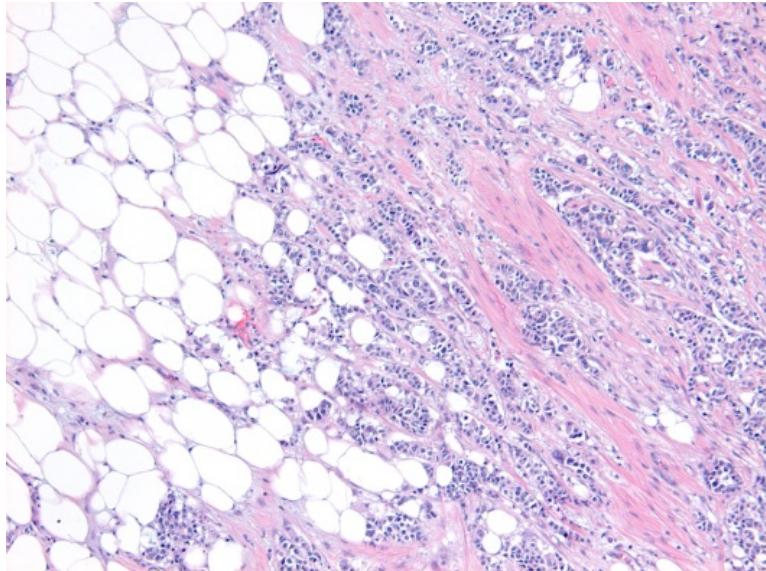


Figure 1: High grade breast cancer

Hematoxylin and Eosin (H&E) section.

Source: Dr. Ala Enno Consultant pathologist at Liverpool Hospital.

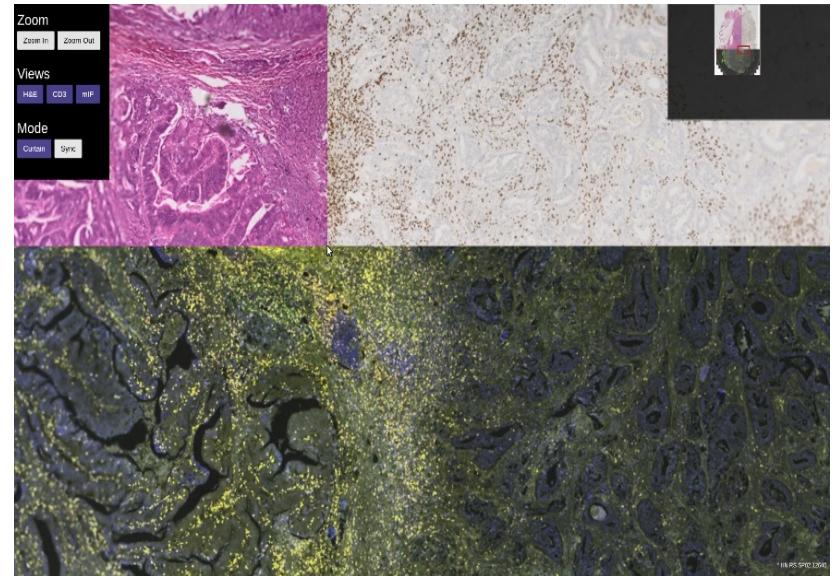


Figure 2: Co-registered H&E (Top Left),

Immunohistochemistry (IHC) (Top Right) and
multispectral Immunofluorescence (Bottom) images
from serialized sections of a patient's tumor sample.

Digital Whole-Slides Image

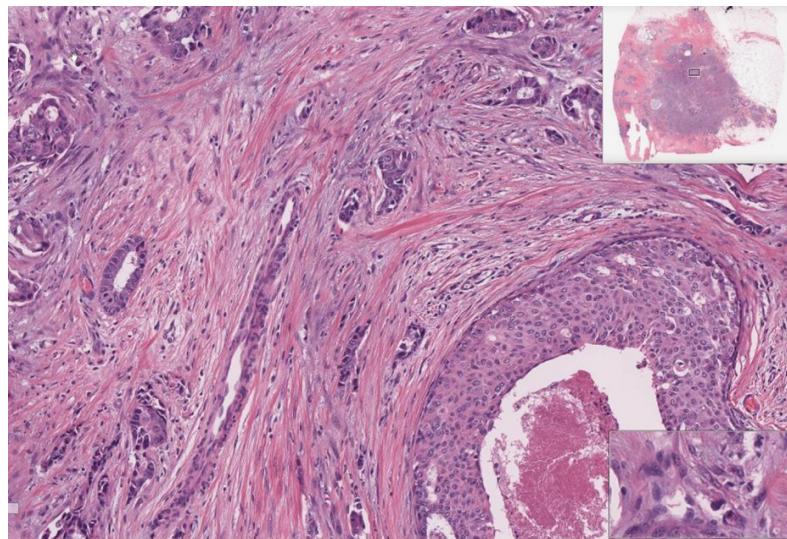


Figure 3: An example
Formalin-Fixed Paraffin-Embedded (**FFPE**) slide
from The Cancer Genome Atlas (TCGA)
digital pathology image repository.

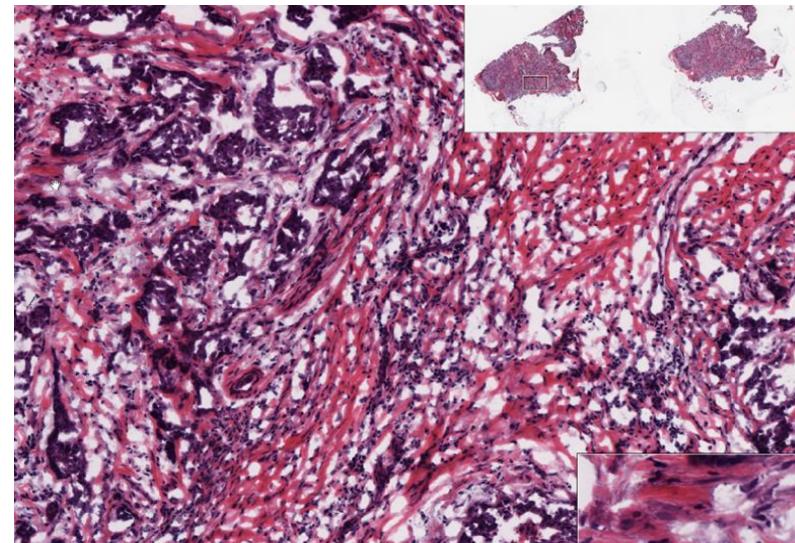
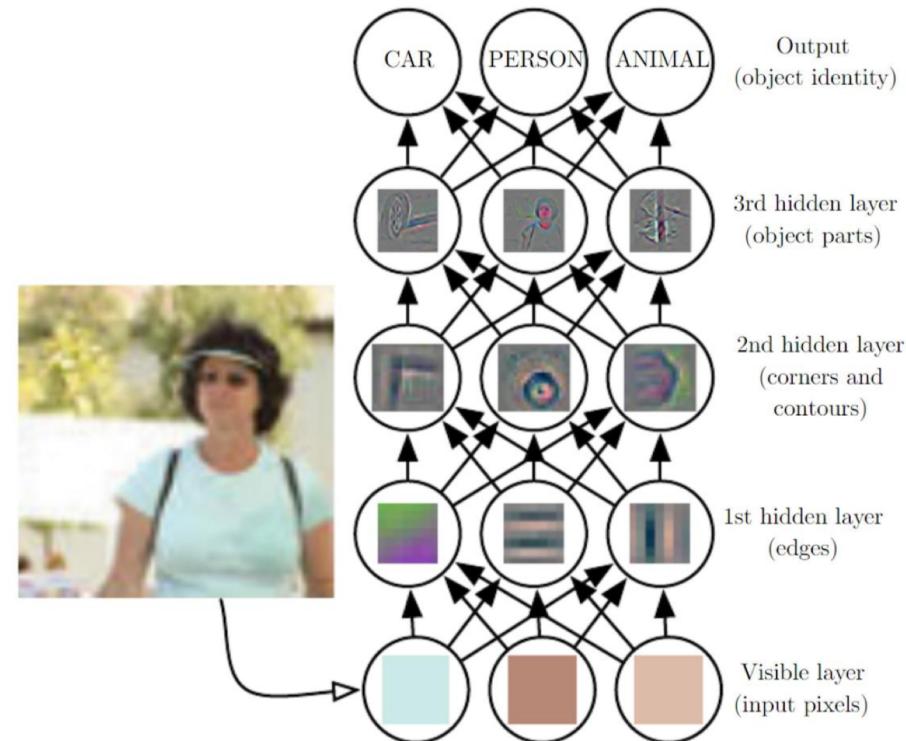


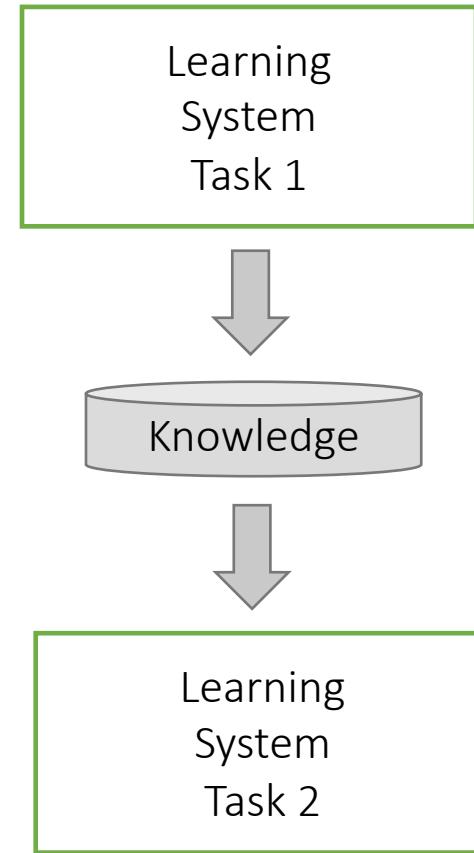
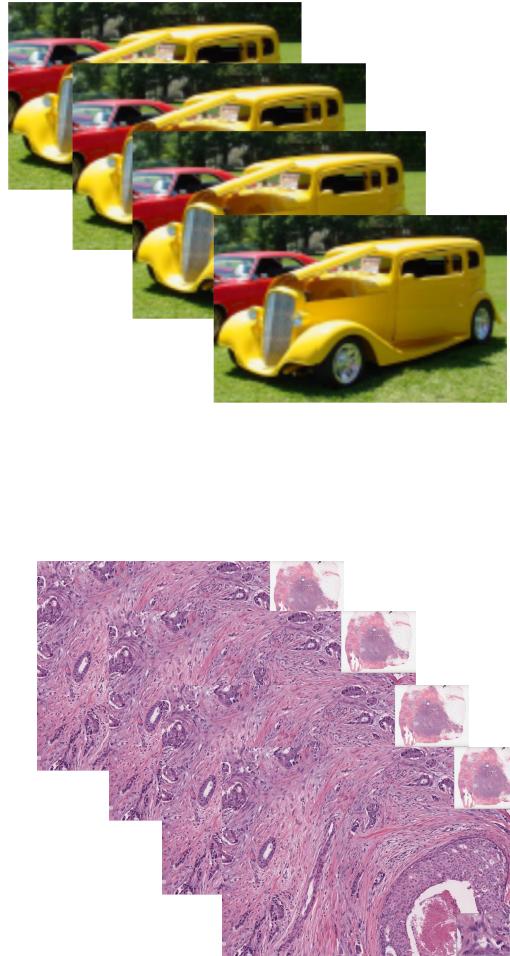
Figure 4: An example **Flash-Frozen** slide
from TCGA digital pathology image repository.

Deep Learning Based Analysis

- A subset of machine learning.
- Deep Learning = Neural Networks.
- Applications:
 - Object Recognition
 - Speech Recognition
 - Natural Language Processing
 - Biomedical Image Analysis
 - ...



Transfer Learning



Motivation

nature
medicine

ARTICLES

<https://doi.org/10.1038/s41591-018-0177-5>

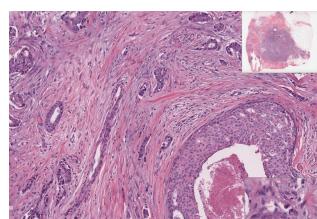
Classification and mutation prediction from non-small cell lung cancer histopathology images using deep learning

Nicolas Coudray  ^{1,2,9}, Paolo Santiago Ocampo ^{3,9}, Theodore Sakellaropoulos ⁴, Navneet Narula ³, Matija Snuderl ³, David Fenyö ^{5,6}, Andre L. Moreira ^{3,7}, Narges Razavian  ^{8*} and Aristotelis Tsirigos  ^{1,3*}

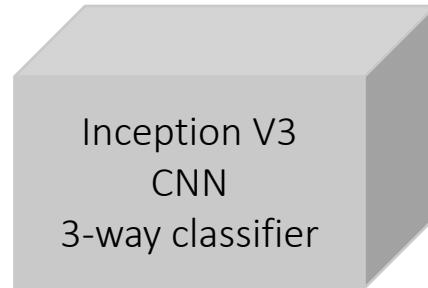
Visual inspection of histopathology slides is one of the main methods used by pathologists to assess the stage, type and subtype of lung tumors. Adenocarcinoma (LUAD) and squamous cell carcinoma (LUSC) are the most prevalent subtypes of lung cancer, and their distinction requires visual inspection by an experienced pathologist. In this study, we trained a deep convolutional neural network (inception v3) on whole-slide images obtained from The Cancer Genome Atlas to accurately and automatically classify them into LUAD, LUSC or normal lung tissue. The performance of our method is comparable to that of pathologists, with an average area under the curve (AUC) of 0.97. Our model was validated on independent datasets of frozen tissues, formalin-fixed paraffin-embedded tissues and biopsies. Furthermore, we trained the network to predict the ten most commonly mutated genes in LUAD. We found that six of them—STK11, EGFR, FAT1, SETBP1, KRAS and TP53—can be predicted from pathology images, with AUCs from 0.733 to 0.856 as measured on a held-out population. These findings suggest that deep-learning models can assist pathologists in the detection of cancer subtype or gene mutations. Our approach can be applied to any cancer type, and the code is available at <https://github.com/ncoudray/DeepPATH>.

Motivation

Model 1: lung cancer type classification



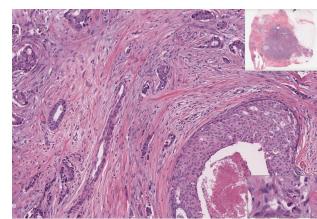
TCGA



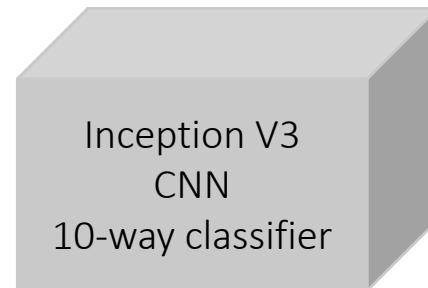
AUC = 0.97

- 1 - Normal
- 2 - LUAD
- 3 - LUSC

Model 2: gene mutation status prediction



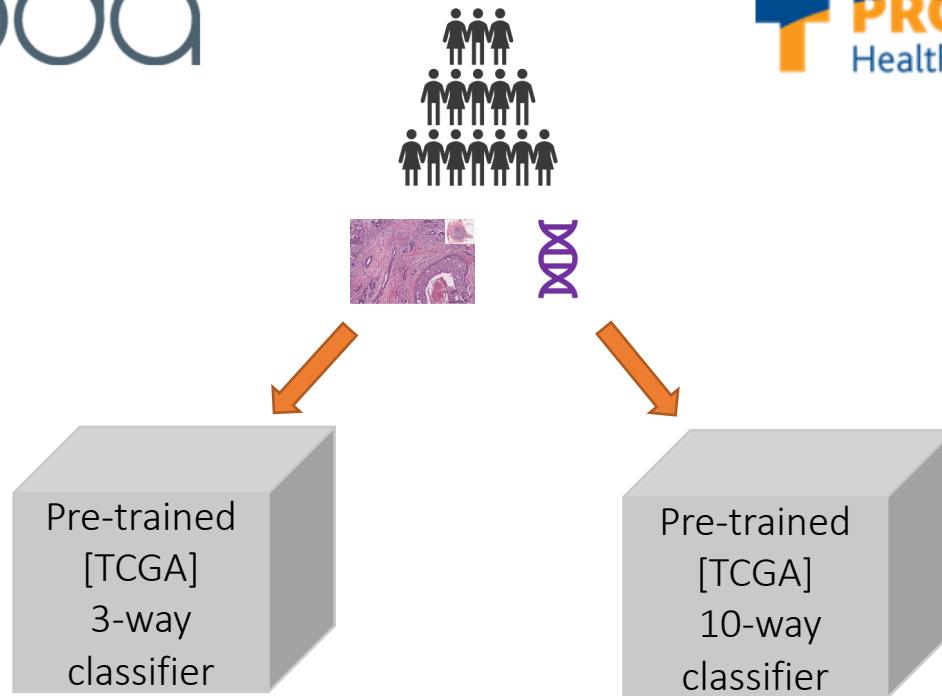
TCGA



AUC > 0.74

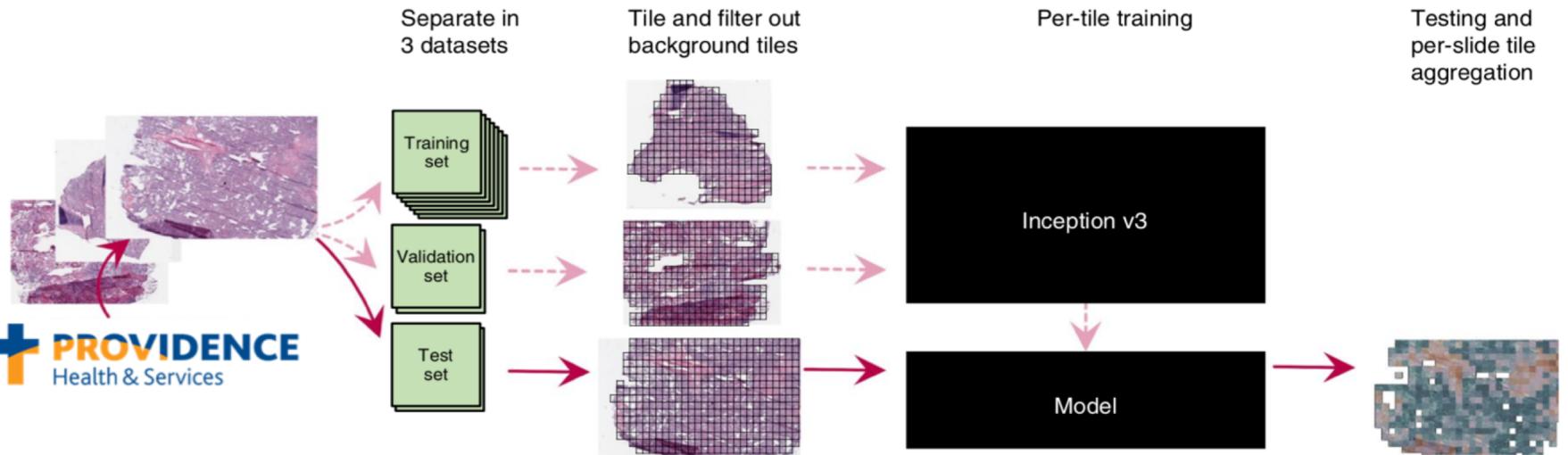
- 1 - STK11
- 2 - EGFR
- 3 - SETBP1
- 4 - TP53
- 5 - FAT1
- 6 - KRAS
- 7 - KEAP1
- 8 - LRP1B
- 9 - FAT4
- 10 - NF1

Initial Plan



1. Run prediction using Providence dataset.
2. Transfer learning using Providence dataset.

Methods



GitHub / DeepPATH

Code Issues 10 Pull requests 3 Actions Projects 0 Wiki Security 0 Insights

Classification of Lung cancer slide images using deep-learning

228 commits 7 branches 0 packages 0 releases 3 contributors

Branch: master New pull request Create new file Upload files Find file Clone or download

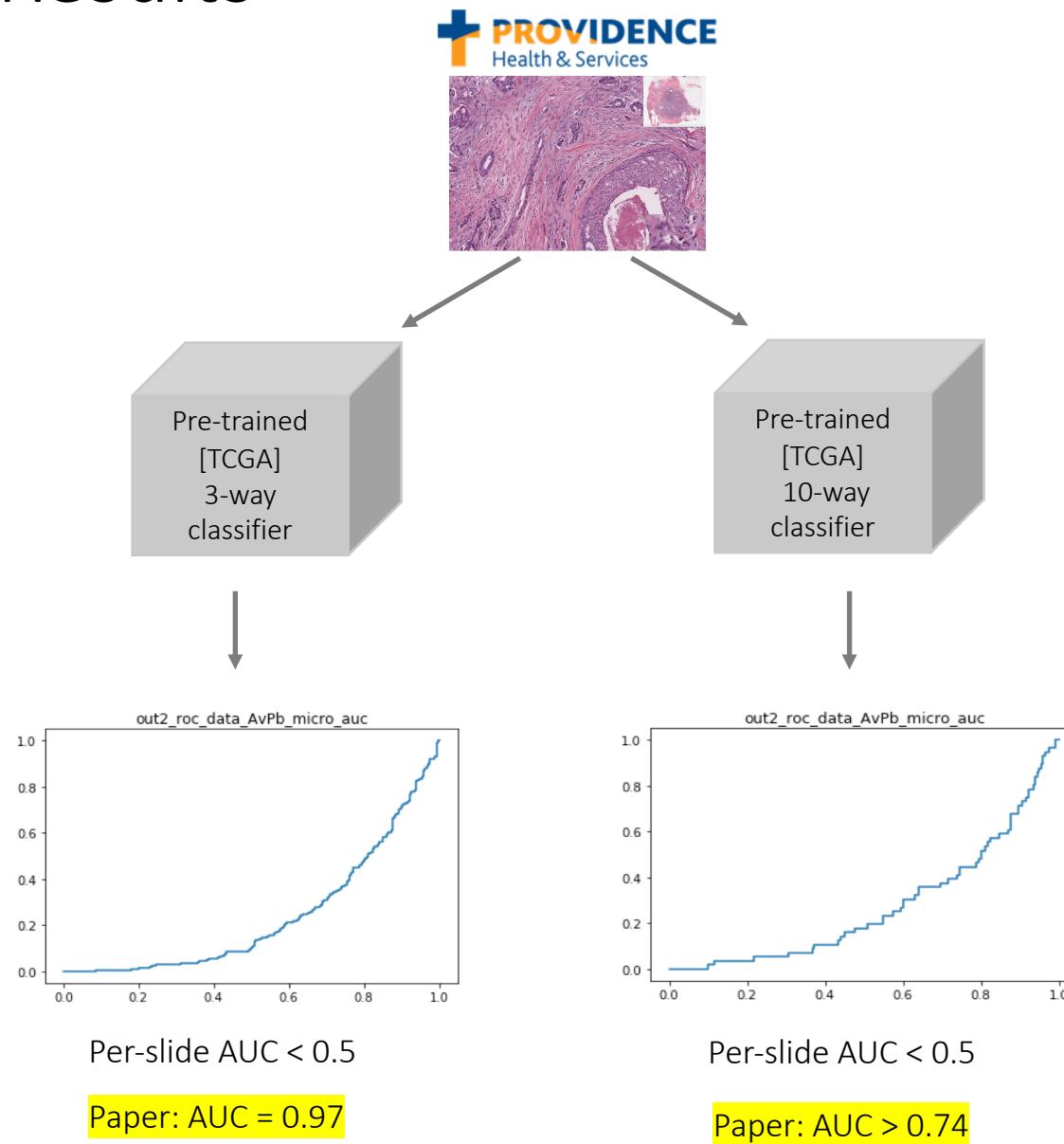
Coudray Yahadane s normalization Latest commit a1106a1 on Apr 22

DeepPATH_code	Vahadane s normalization	last month
.gitignore	remove folder	3 years ago
README.md	references	2 years ago

README.md

The DeepPATH framework gathers the codes that have been used to study the use of a deep learning architecture (inception v3 from Google) to classify Lung cancer images.

Prediction Results



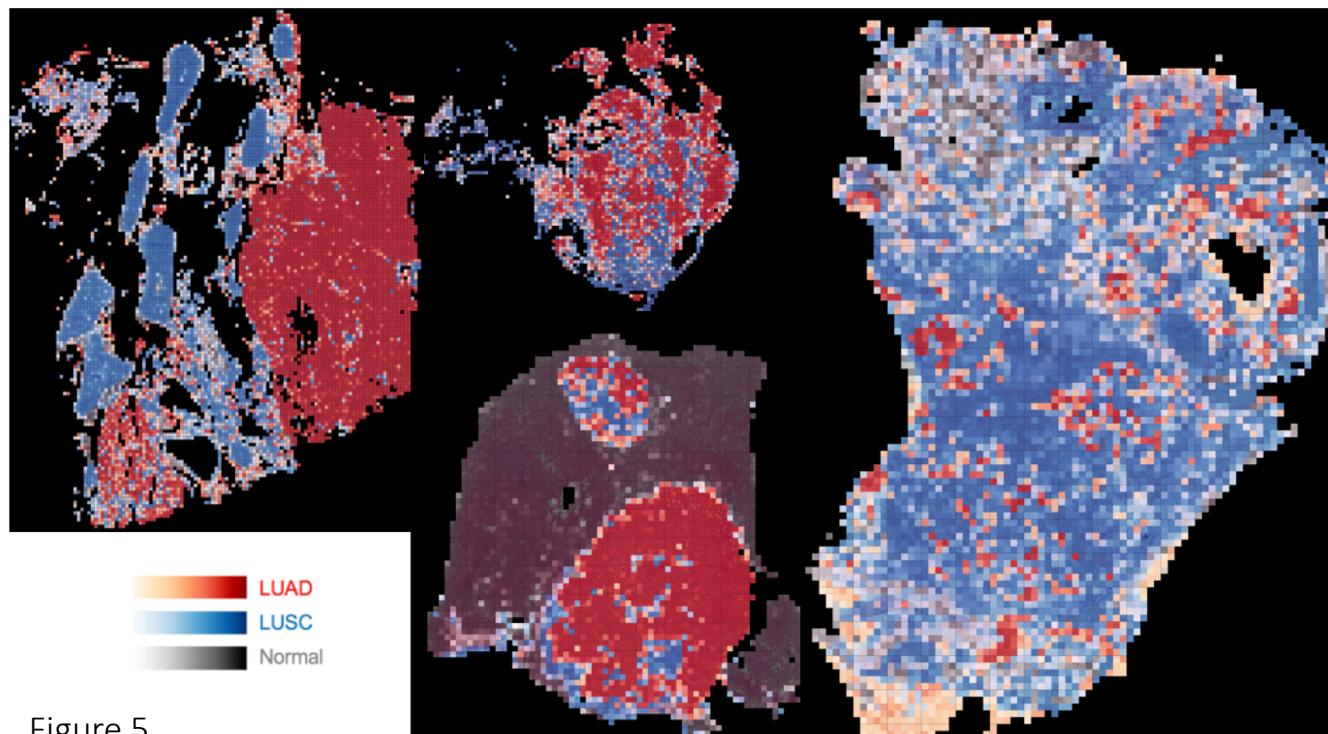
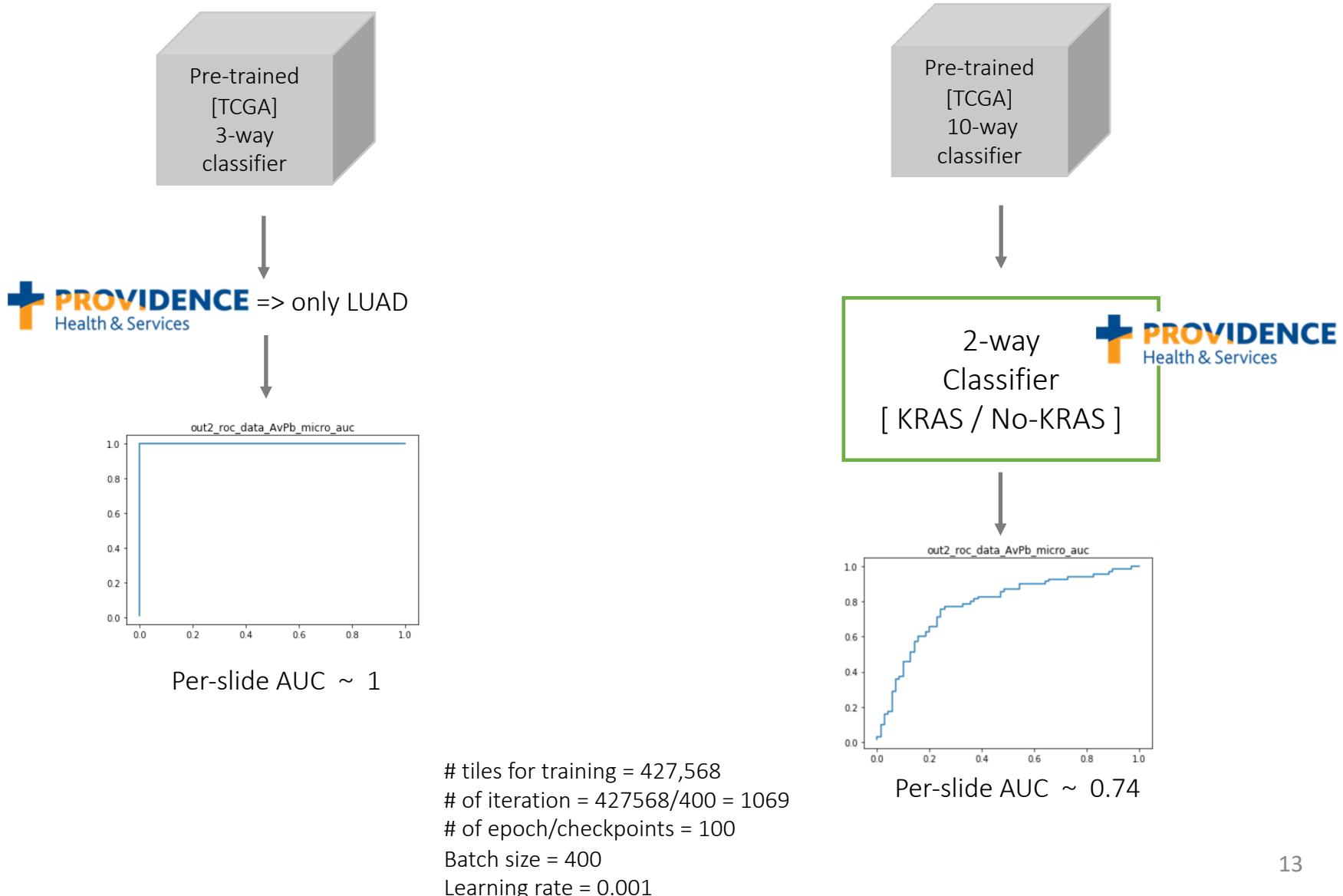


Figure 5



Figure 6

Transfer Learning Results



Future Direction



About Keras

Getting started

Developer guides

Keras API reference

Models API

Layers API

Callbacks API

Data preprocessing

Search Keras documentation...

» Keras API reference / Keras Applications

Available models

Keras Applications

Keras Applications are deep learning models that are built on top of Keras. These models can be used for prediction, feature extraction and more.

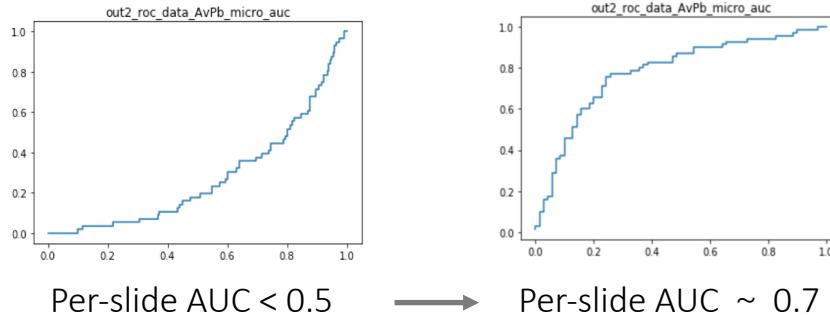
Weights are downloaded automatically when instantiating the model. Upon instantiation, the models will be built according to the TensorFlow data format convention, unless a configuration file at `~/.keras/keras.json` specifies `image_data_format=channels_last`, then any model will be built according to the TensorFlow data format convention.

Model	Size	Top-1 Accuracy	Top-5 Accuracy	Parameters	Depth
Xception	88 MB	0.790	0.945	22,910,480	126
VGG16	528 MB	0.713	0.901	138,357,544	23
VGG19	549 MB	0.713	0.900	143,667,240	26
ResNet50	98 MB	0.749	0.921	25,636,712	-
ResNet101	171 MB	0.764	0.928	44,707,176	-
ResNet152	232 MB	0.766	0.931	60,419,944	-
ResNet50V2	98 MB	0.760	0.930	25,613,800	-
ResNet101V2	171 MB	0.772	0.938	44,675,560	-
ResNet152V2	232 MB	0.780	0.942	60,380,648	-
InceptionV3	92 MB	0.779	0.937	23,851,784	159
InceptionResNetV2	215 MB	0.803	0.953	55,873,736	572
MobileNet	16 MB	0.704	0.895	4,253,864	88
MobileNetV2	14 MB	0.713	0.901	3,538,984	88
DenseNet121	33 MB	0.750	0.923	8,062,504	121
DenseNet169	57 MB	0.762	0.932	14,307,880	169
DenseNet201	80 MB	0.773	0.936	20,242,984	201
NASNetMobile	23 MB	0.744	0.919	5,326,716	-
NASNetLarge	343 MB	0.825	0.960	88,949,818	-
EfficientNetB0	29 MB	-	-	5,330,571	-
EfficientNetB1	31 MB	-	-	7,856,239	-
EfficientNetB2	36 MB	-	-	9,177,569	-
EfficientNetB3	48 MB	-	-	12,320,535	-
EfficientNetB4	75 MB	-	-	19,466,823	-
EfficientNetB5	118 MB	-	-	30,562,527	-
EfficientNetB6	166 MB	-	-	43,265,143	-
EfficientNetB7	256 MB	-	-	66,658,687	-

The top-1 and top-5 accuracy refers to the model's performance on the ImageNet validation dataset.

Depth refers to the topological depth of the network. This includes activation layers, batch normalization layers etc.

Lessons Learned



- By transfer learning, performance improved on Providence dataset.

- Expectation vs. Reality
- Academic vs. Industry
- Technology vs. Business / Market



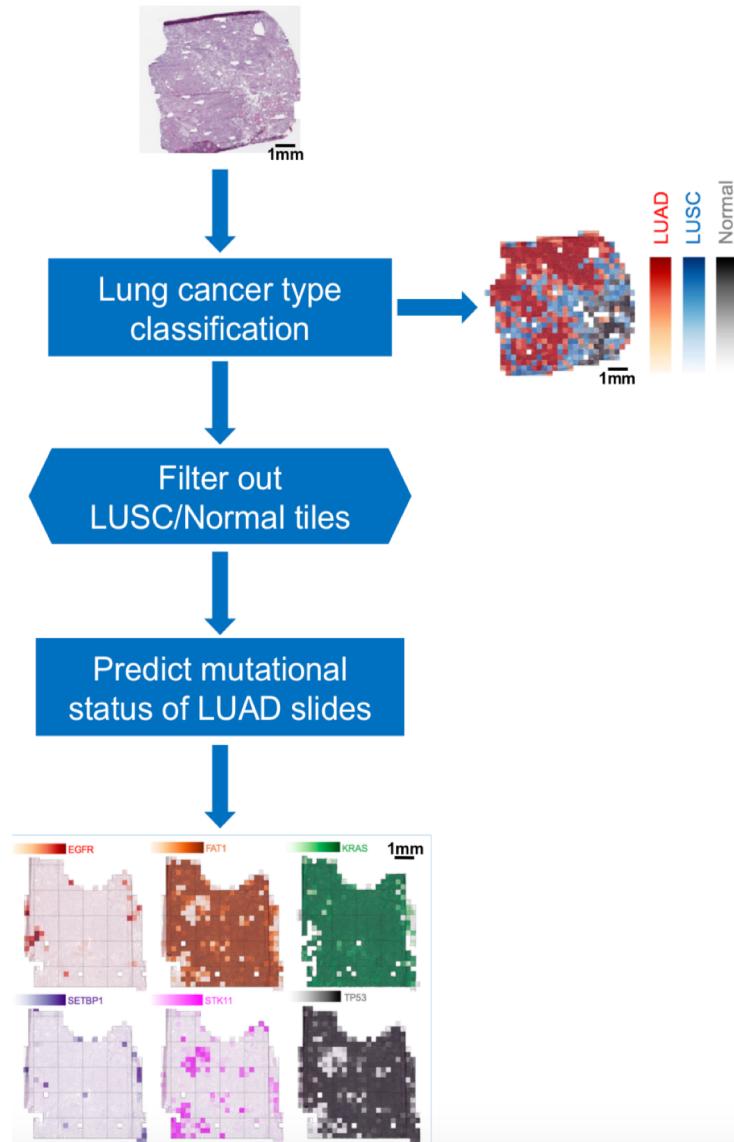
Acknowledgements



Diane Doctor
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Kevin Matlock
Xubo Song

...

Backup Slides



Convolutional Neural Network (CNN)

- CONV layer:
 - Filter size, padding, stride, number of filters, activations, weights, bias.
- POOL layer:
 - Filter size, stride, max or average pooling.
- FC (fully connected) layer:
 - Weight matrix, bias parameter.

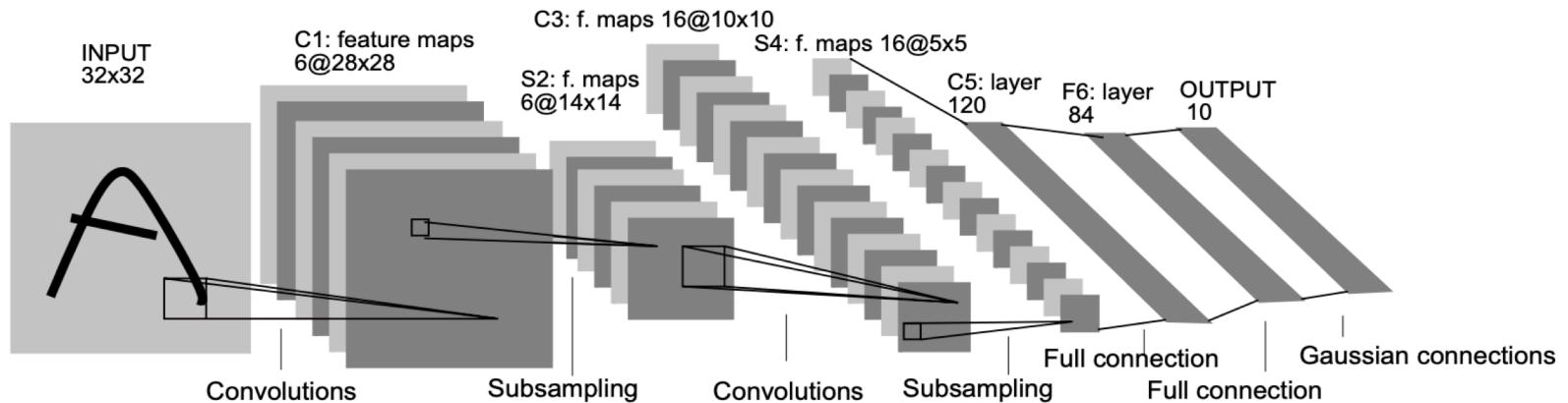
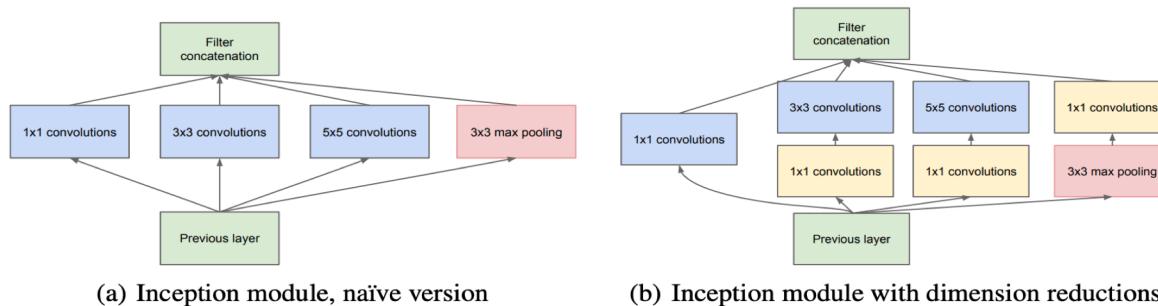
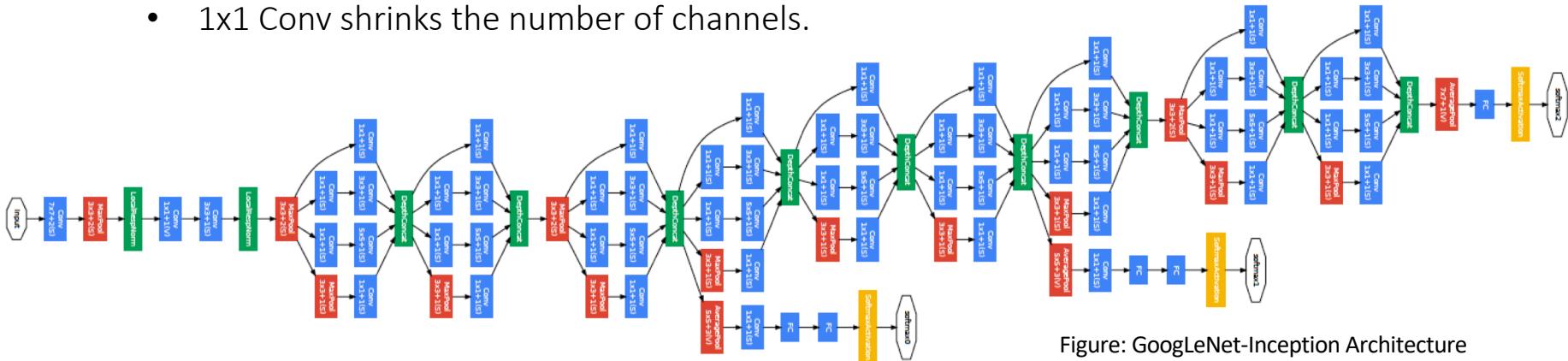


Figure: LeNet-5 Architecture. Each plane is a feature map, i.e. a set of units whose weights are constrained to be identical.

GoogLeNet-Inception



- Inception module using all of the choices for CNN (5x5 Conv or 3x3 Conv).
- The output of the module is the concatenation of all.
- 1x1 Conv shrinks the number of channels.



- Inception networks composed of multiple inception modules.
- There are 3 SoftMax branches at different positions.
- It helps to ensure the intermediate features are good enough.
- Regularization effect on Inception network and prevent overfitting.

Inception V3

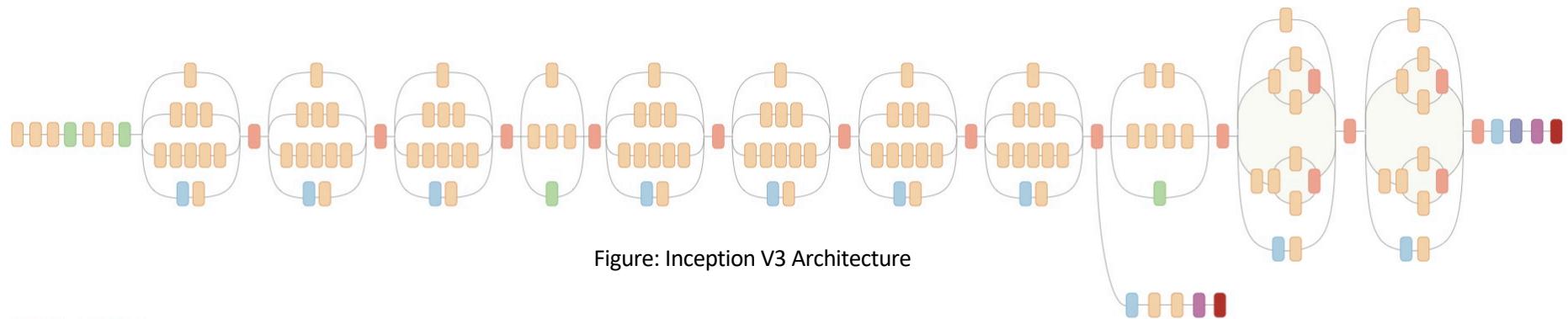
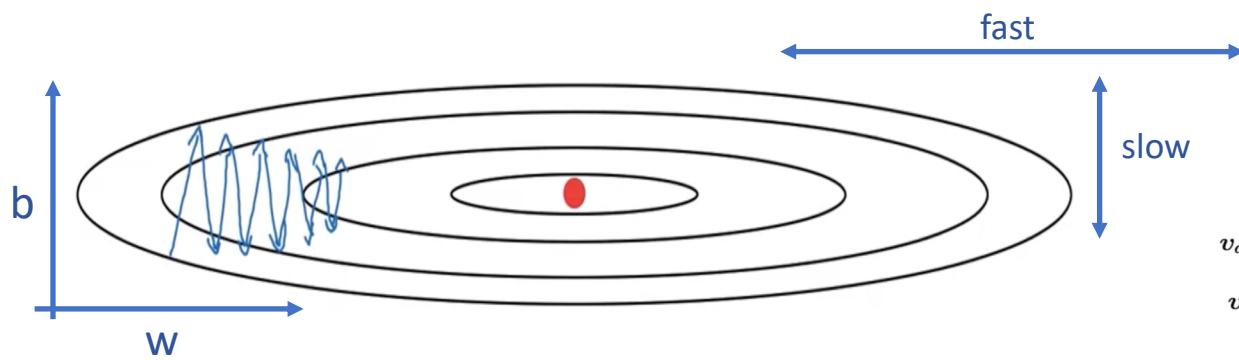


Figure: Inception V3 Architecture

- Convolution
- AvgPool
- MaxPool
- Concat
- Dropout
- Fully connected
- Softmax

RMSProp Optimizer



$$v_{dw} = \beta \cdot v_{dw} + (1 - \beta) \cdot dw^2$$

$$v_{db} = \beta \cdot v_{db} + (1 - \beta) \cdot db^2$$

$$W = W - \alpha \cdot \frac{dw}{\sqrt{v_{dw}} + \epsilon}$$

$$b = b - \alpha \cdot \frac{db}{\sqrt{v_{db}} + \epsilon}$$