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Cancer Type/Site Classification using Deep-Learning (Preliminary presentation slides)

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BIDS, FNLCR

(in preparation)

DEPARTMENT OF HEALTH AND HUMAN SERVICES • National Institutes of Health • National Cancer Institute
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  - Maulik Shukla

- **BIDS**
  - Drs. George Zaki, Andrew Weissman, Mark Jensen and Eric Stahlberg
  - Amar Khalsa, Dr. Deb Hope
  - Colleagues who reviewed the material

Feel free to follow-along

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CBIIT

- https://cbiit.github.io/sdsi/workshops **(landing site; creation in progress)**

Github

- https://github.com/ravichas/ML-TC1 **(in progress)**

Introduction

- **This is part of the NCI-DOE knowledge/capability transfer efforts**
- **Share tools/techniques/solutions for cancer related problems. We often take a test-case and show how it works**
- **You would be able to take the test-case (code/scripts) and tune it to your needs**
- **We want to hear from you**

Motivation: Cancer Prediction vs Cancer Detection

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- **Cancer Prediction has been the major focus**
  - Prognosis, Recurrence, Susceptibility

- **Cancer Detection (classification of tumors/cancers) is lagging behind Prediction and we would like to share an application that might be useful**
  - Detect/Identify cancer type at an early stage

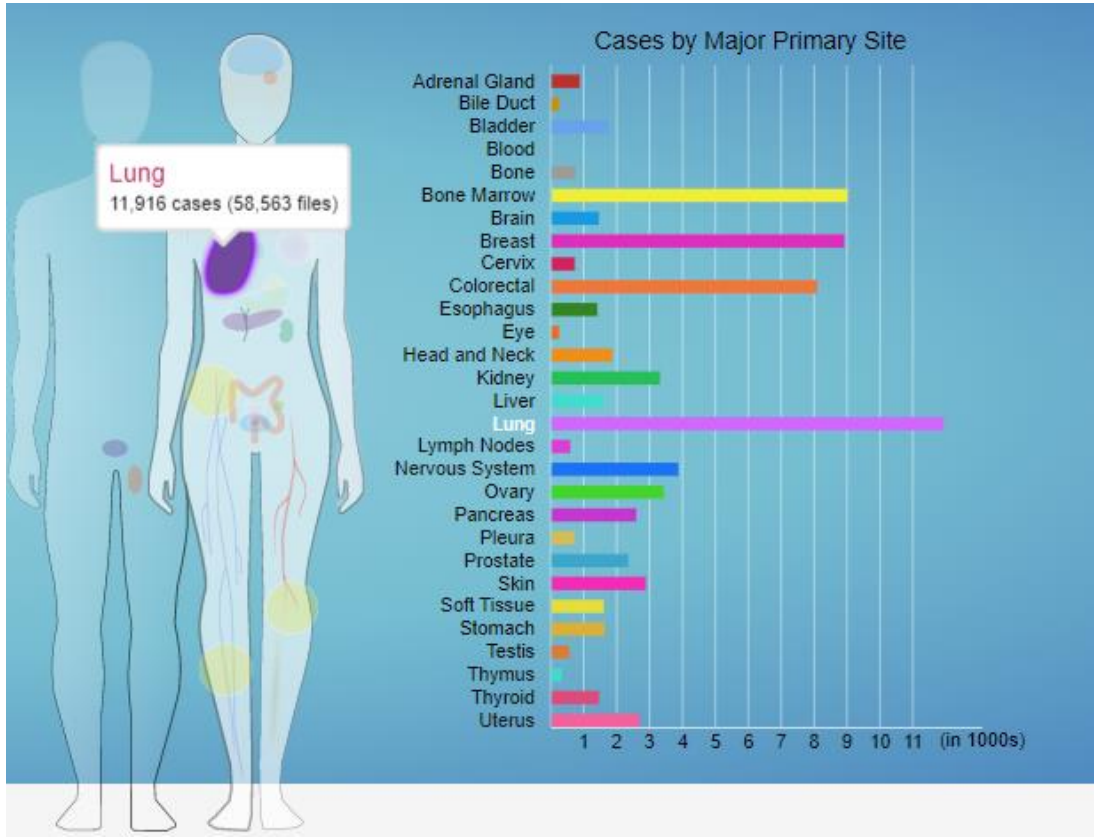
Goal(s)/Questions

- **Take genomic expression data from tumor/cancer samples and apply Deep-Learning to create cancer types/site(s) classifier models**
- **Are the expression profiles unique?**
- **Can we use the model as early cancer type detection**
  - Improving chance of early detection cure/survival?

Cancer Burden

- **Cancer is a group of diseases with world-wide risk**
- **Acquired or somatic changes causes 90-95% of caner (all types)**
  - *Source TCGA*
- **~ 200 forms of cancer**
  - *DOI: 10.5114/wo.2014.47136*
- **For 2020**
  - ~1.8M new cancer cases are expected
  - ~600K deaths will occur

Figure from Genomic Data Commons



Expected New Cases/Deaths in 2020

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New Cancer Cases

Between 2010 and 2020, we expect the number of new cancer cases in the United States to go up about 24% in men to more than 1 million cases per year, and by about 21% in women to more than 900,000 cases per year.

US population gender	Cancers that are expected to increase
Men	Prostrate, Kidney, Liver and Bladder
Women	Lung, Breast, Uterine and Thyroid

Dynamic genomic changes result in Cancer

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Somatic alterations in oncogenes are the source of Transcript alterations

Article

Genomic basis for RNA alterations in cancer

https://doi.org/10.1038/s41586-020-1970-0
Received: 29 March 2018
Accepted: 11 December 2019
Published online: 5 February 2020

Transcript alterations often result from somatic changes in cancer genomes. Various forms of RNA alterations have been described in cancer, including overexpression, altered splicing and gene fusions; however, it is difficult to attribute these to underlying genomic changes owing to heterogeneity among patients and tumor types, and the relatively small cohorts of patients for whom samples have been analyzed by both transcriptome and whole-genome sequencing.

Somatic alterations in the human cancer genome

Barbara Weir, Xiaojun Zhao, and Matthew Meyerson*

CANCER CELL : NOVEMBER 2004 · VOL. 6 · COPYRIGHT © 2004 CELL PRESS

Expression changes in oncogenes; What type of changes?

Hallmarks of cancer: Acquired capabilities (mutations) that drive cancer

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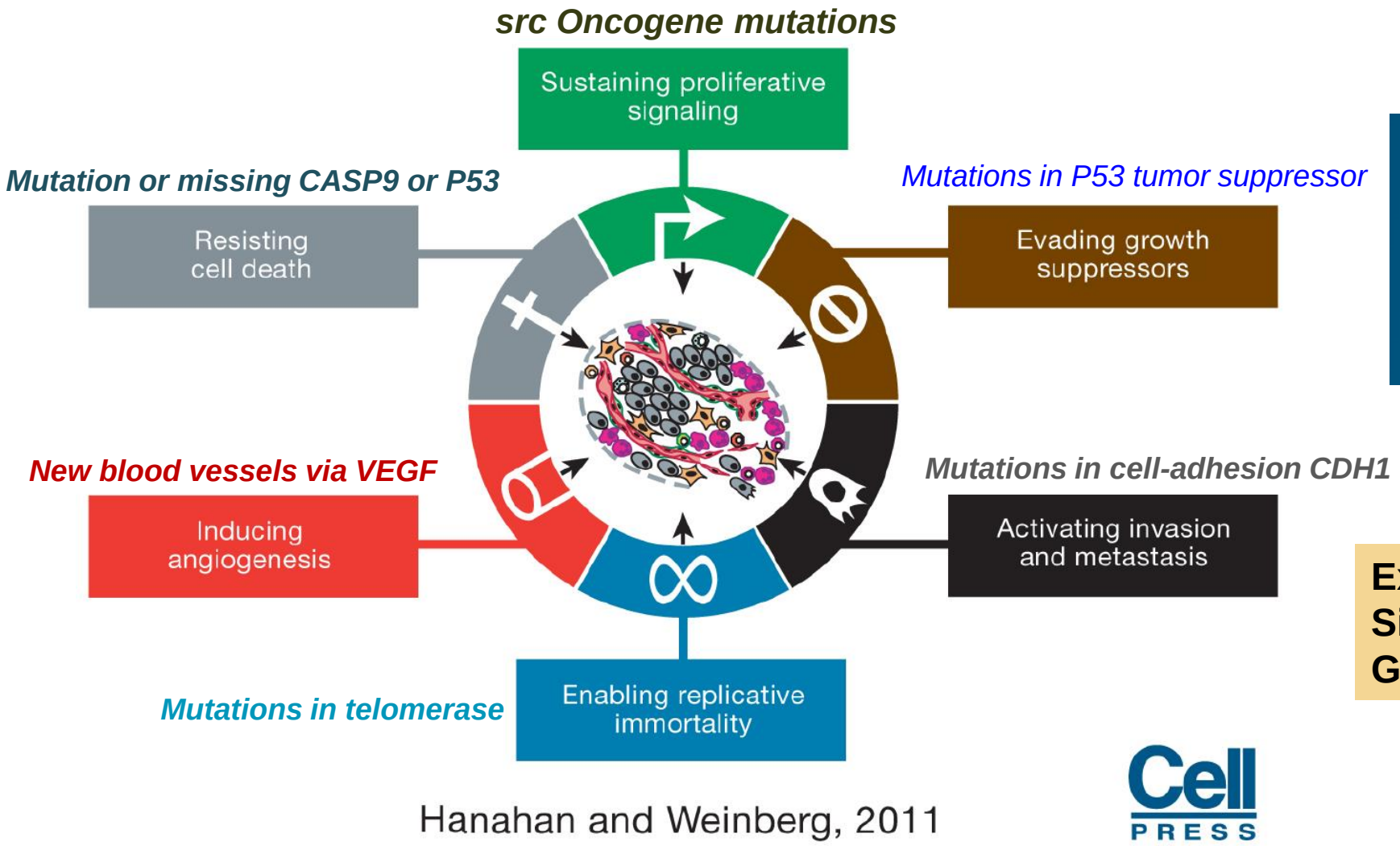
Hallmarks of Cancer: The Next Generation



REVIEW | VOLUME 100, ISSUE 1, P57-70, JANUARY 07, 2000

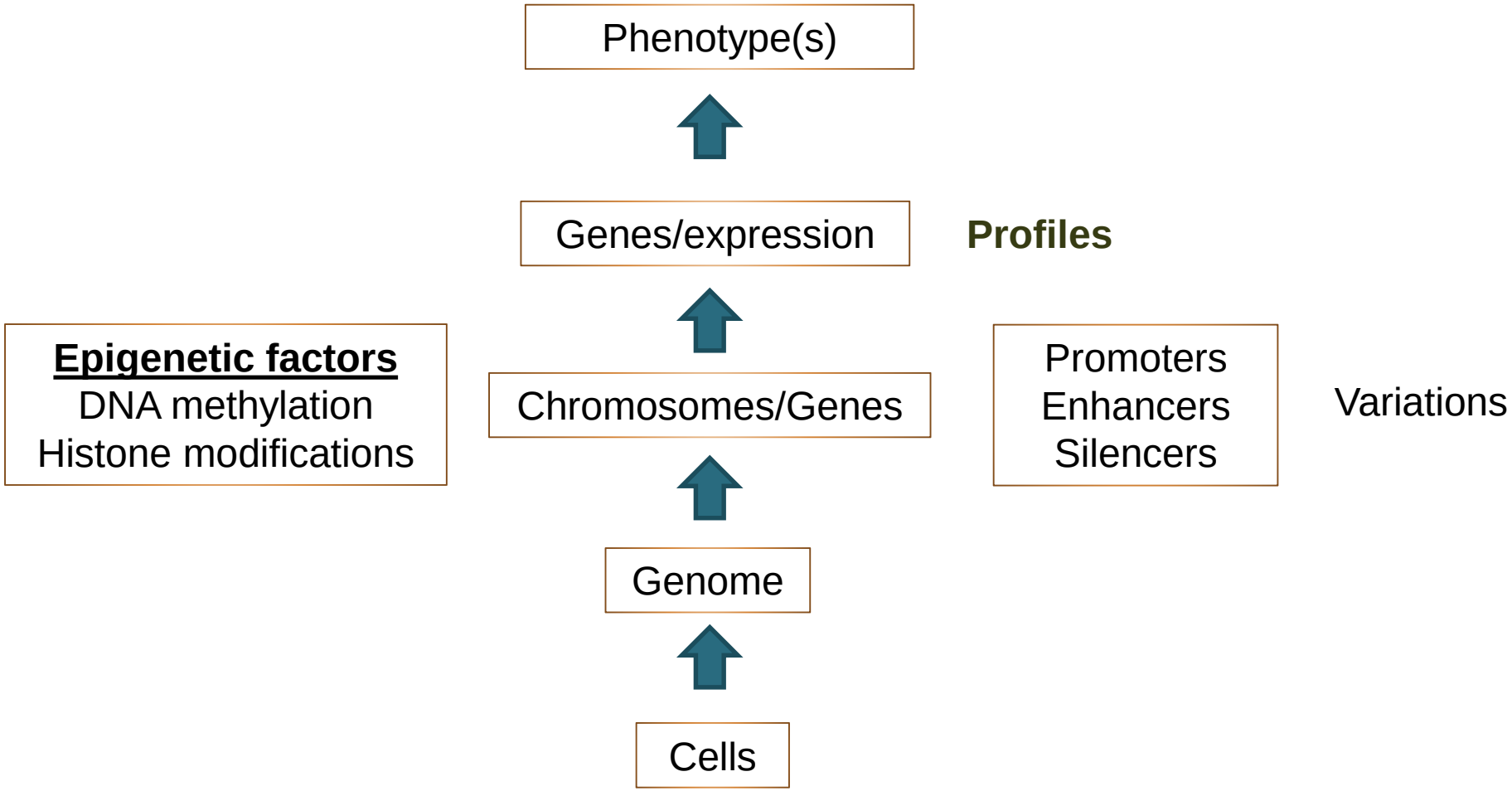
The Hallmarks of Cancer

Douglas Hanahan • Robert A Weinberg

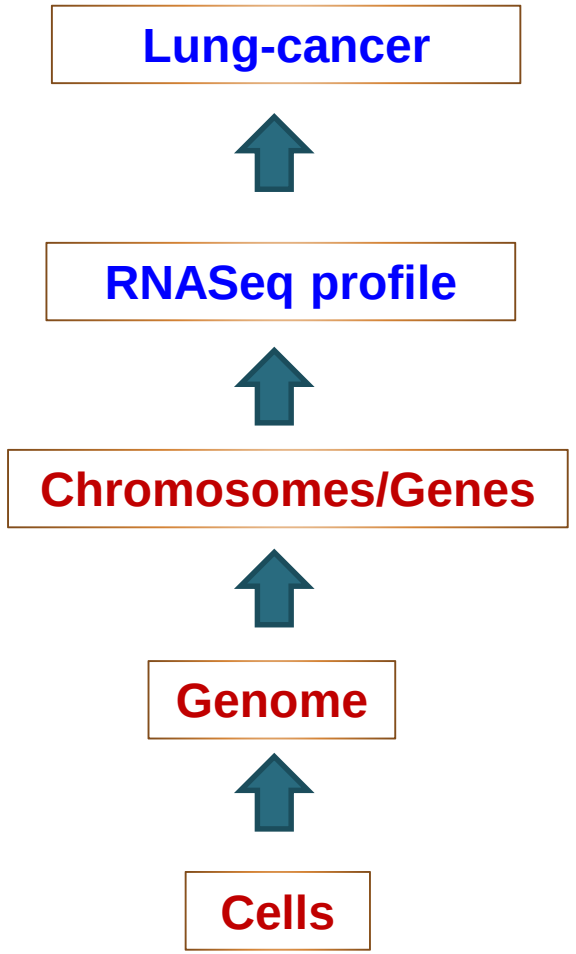
Open Archive • DOI: https://doi.org/10.1016/S0092-8674(00)81683-9

Expression changes in oncogenes; Six capabilities; Overview of Genotype/phenotypes?

Influence of genomic features on phenotypes: An overview



Influence of genomic features on phenotypes: An overview

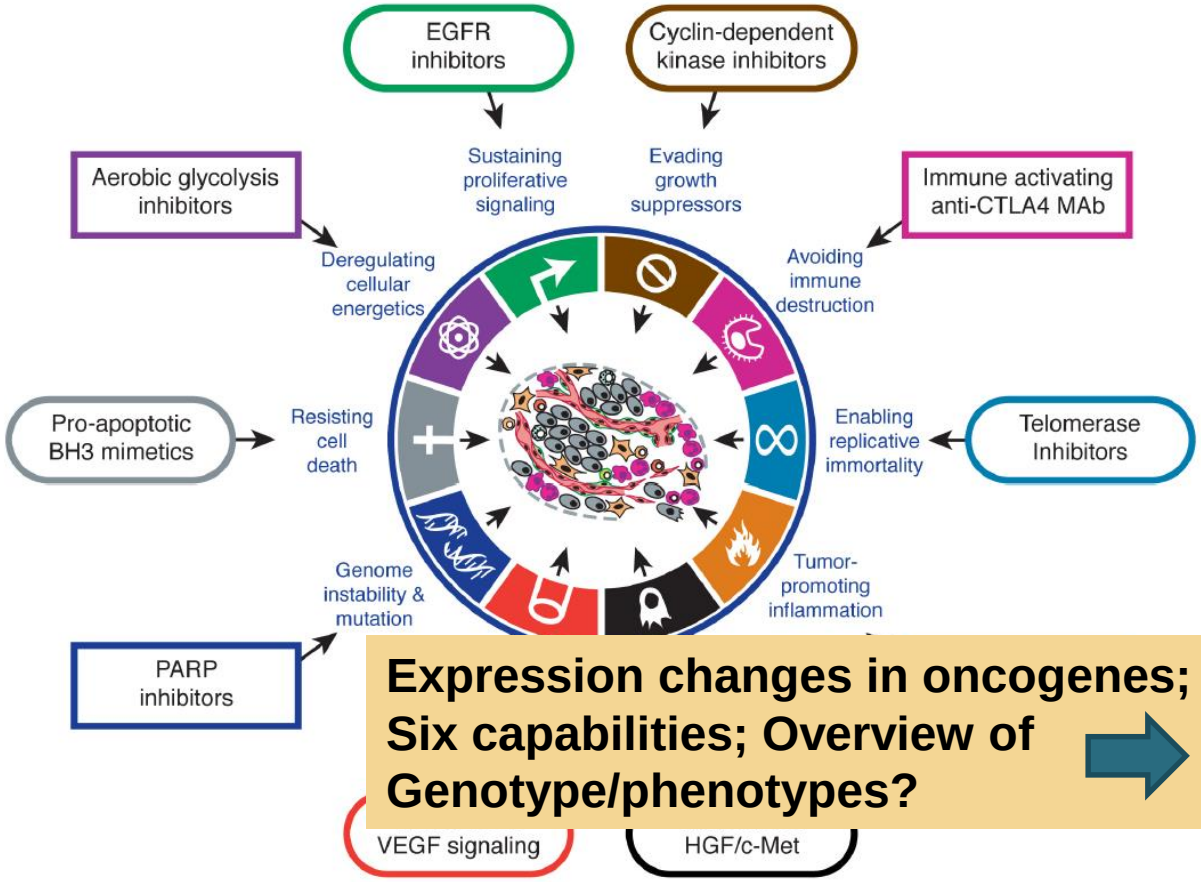


Diagnosis/treatment vs Prediction

Treatment vs Type-Prediction

- **Treatment**
  - Gene-centric (or a slice of pathway)
  - Imatinib targeting BCR/KIT

- **Detecting Type**
  - *"The architecture of occurring genetic aberrations such as somatic mutations, CNVs, changed gene expression profiles, and different epigenetic alterations, is unique for each type of cancer.", DOI: 10.5114/wo.2014.47136*
  - Complex
  - Multi-gene centric



Expression changes in oncogenes; Six capabilities; Overview of Genotype/phenotypes?

Type-Prediction

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The architecture of occurring genetic aberrations such as somatic mutations, CNV, changed gene expression profiles, and different epigenetic alterations, is unique for each type of cancer

DOI: 10.5114/wo.2014.47136

PERSPECTIVE

Understanding Genotype-Phenotype Effects in Cancer via Network Approaches

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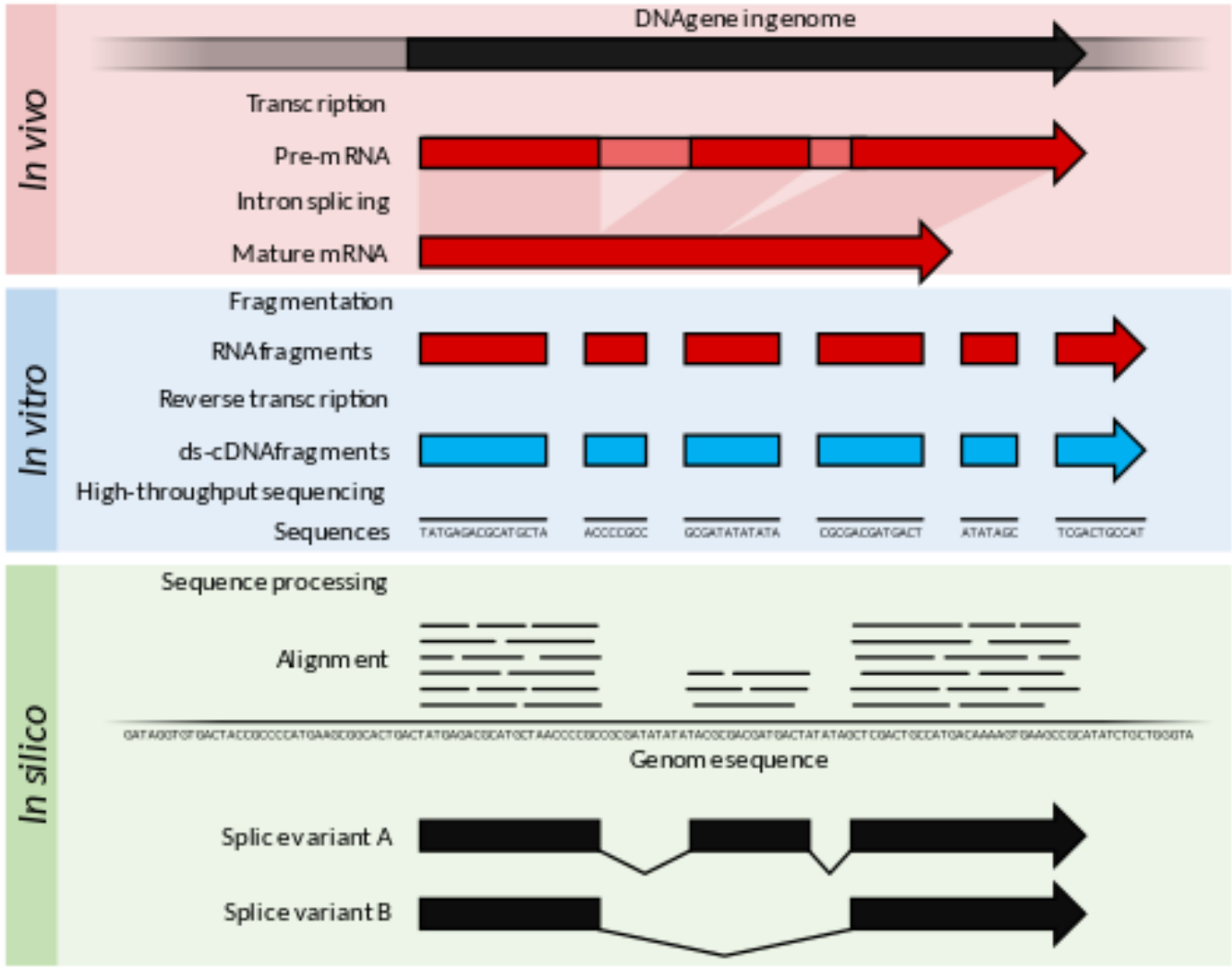
Author Summary

Cancer is now increasingly studied from the perspective of dysregulated pathways, rather than as a disease resulting from mutations of individual genes. A pathway-centric view acknowledges the heterogeneity between genomic profiles from different cancer patients while assuming that the mutated genes are likely to belong to the same pathway and cause similar disease phenotypes. Indeed, network-centric approaches have proven to be helpful for finding genotypic causes of diseases, classifying disease subtypes, and identifying drug targets. In this review, we discuss how networks can be used to help understand patient-to-patient variations and how one can leverage this variability to elucidate interactions between cancer drivers.

What kind of data do we need?

NGS

NGS



READS

Data source: The Cancer Genome Atlas (TCGA)

- NIH launched TCGA Pilot Project – a public funded project
- Goal of creating a comprehensive “atlas” of cancer genomic profiles.
- Large cohorts of over 30 human tumors through large-scale genome sequencing and integrated multi-dimensional analyses.
- Contains Microarray and NGS data
  - RNASeq
  - miRNA seq
  - SNP based platforms
  - …..
- TCGA data is available via GDC

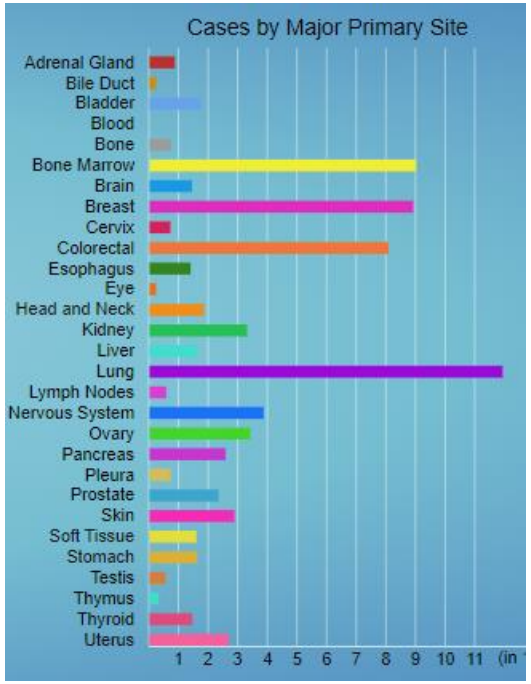
https://www.cancer.gov/about-nci/organization/ccg/research/structural-genomics/tcga

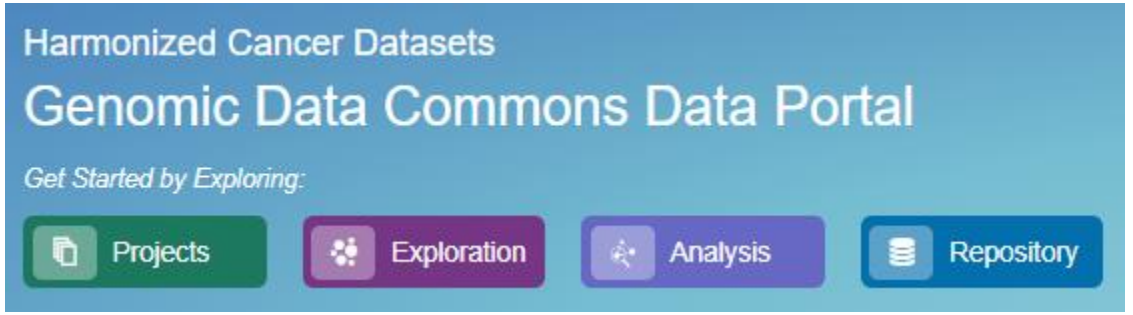
Data Harmonization: GDC (https://gdc.cancer.gov/)

- **Data and metadata is submitted to the GDC in standard data types and file formats. Other data sources (Ex. TCGA) are also included**

- **Data are harmonized against a common reference genome (GRCh38)**

- **For this workshop, we will focus on TCGA Genomic expression data from GDC**

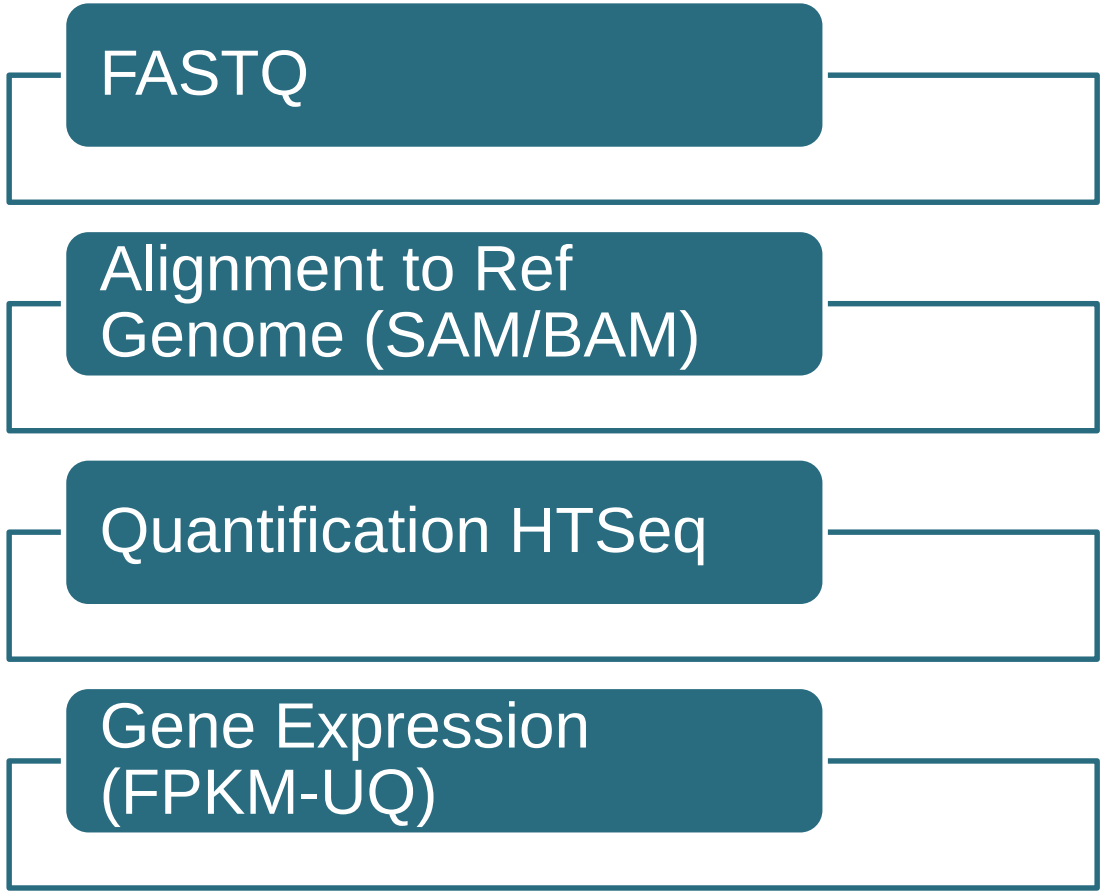




Expression Data Quantification

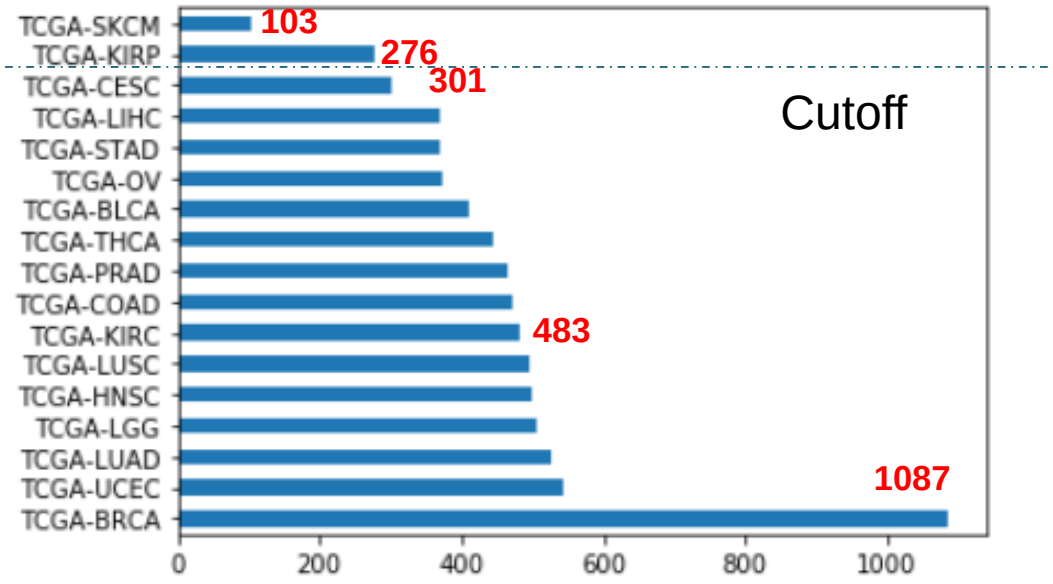
- RC_g: Number of reads mapped to the gene
- RC_{g75}: The 75th percentile read count value for genes in the sample
- L: Length of the gene in base pairs; Calculated as the sum of all exons in a gene

$$\text{FPKM-UQ} = \frac{\text{RC}_g \times 10^9}{\text{RC}_{g75} \times \text{L}}$$



Fragments Per Kilobase of transcript per Million mapped reads

How much data for modeling?



CODE	Cancer Site/Type
BRCA	Breast invasive carcinoma
UCEC	Uterine Corpus Endometrial Carcinoma
LUAD	Lung adenocarcinoma
LGG	Brain Lower Grade Glioma
HNSC	Head and Neck squamous cell carcinoma
LUHSC	Lung squamous cell carcinoma
KIRC	Kidney renal clear cell carcinoma
PRAD	Prostate adenocarcinoma
COAD	Colon adenocarcinoma
THCA	Thyroid carcinoma
BLCA	Bladder Urothelial Carcinoma
OV	Ovarian serous cystadenocarcinoma
STAD	Stomach adenocarcinoma
LIHC	Liver hepatocellular carcinoma
CEC	Cervical squamous cell carcinoma and endocervical adenocarcinoma

300 samples each

Expression data from a sample

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Gene: AC090241.2 ENSG00000270112

Description	novel transcript, antisense to ST8SIA5
Location	Chromosome 18: 46,756,487-46,802,449 forward strand. GRCh38:CM000680.2
About this gene	This gene has 8 transcripts (splice variants)
Transcripts	Hide transcript table

Gene: DNAH3 ENSG00000158486

Description	dynein axonemal heavy chain 3 [Source:HGNC Symbol;Acc:HGNC:2949]
Gene Synonyms	DKFZp434N074, DLP3, Dnahc3b, Hsadhc3
Location	Chromosome 16: 20,933,111-21,159,441 reverse strand. GRCh38:CM000678.2
About this gene	This gene has 6 transcripts (splice variants), 371 orthologues, 14 paralogues and is a member of 1 Ensembl protein family.
Transcripts	Hide transcript table

TCGA-BRCA

Genes	Expression
ENSG00000242268.2	1658.464179
ENSG00000270112.3	460.2343433
ENSG00000167578.15	52440.10096
ENSG00000273842.1	0
ENSG00000078237.5	68165.45626
ENSG00000146083.10	255959.2351
ENSG00000225275.4	0
ENSG00000158486.12	104.9473768
ENSG00000198242.12	4968556.658
ENSG00000259883.1	6108.999052
ENSG00000231981.3	0
ENSG00000269475.2	0
ENSG00000201788.1	0
ENSG00000134108.11	957330.2056
ENSG00000263089.1	3484.027373
ENSG00000172137.17	41485.9507
ENSG00000167700.7	226717.4208
ENSG00000234943.2	2082.245035
ENSG00000240423.1	310.5246749
ENSG00000060642.9	155863.9216
ENSG00000271616.1	0
ENSG00000234881.1	0
ENSG00000236040.1	394.4755669
ENSG00000231105.1	1583.312582
ENSG00000243044.1	0
ENSG00000182141.8	45538.60648
ENSG00000269416.4	119.0847054
ENSG00000264981.1	0

60,483 transcripts

Data Preparation

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Breast Cancer

60,484 transcripts

	Sample1	Sample2	Sample3	Sample4		Sample297	Sample298	Sample299	Sample300
Genes	Expression	Genes	Expression	Genes	Expression	Genes	Expression	Genes	Expression	Genes	Expression	Genes	Expression	Genes	Expression
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ENSG00000167578.15	52440.10096	ENSG00000167578.15	52440.10096	ENSG00000167578.15	52440.10096	ENSG00000167578.15	52440.10096	ENSG00000167578.15	52440.10096	ENSG00000167578.15	52440.10096	ENSG00000167578.15	52440.10096	ENSG00000167578.15	52440.10096
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ENSG00000078237.5	68165.45626	ENSG00000078237.5	68165.45626	ENSG00000078237.5	68165.45626	ENSG00000078237.5	68165.45626	ENSG00000078237.5	68165.45626	ENSG00000078237.5	68165.45626	ENSG00000078237.5	68165.45626	ENSG00000078237.5	68165.45626
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Data Preparation

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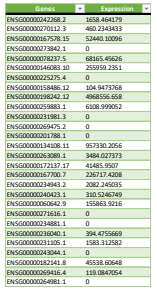
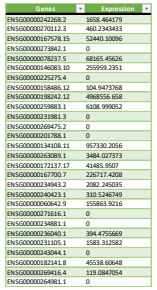
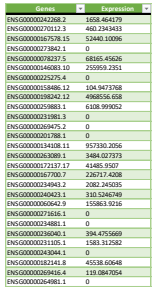
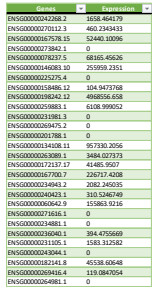
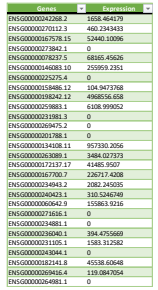
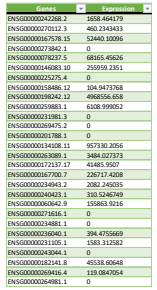
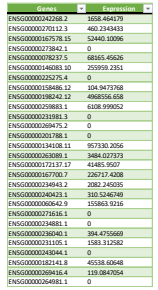
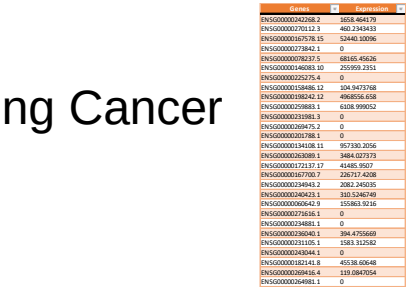
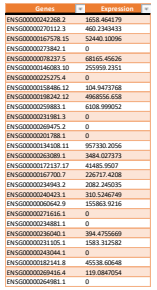
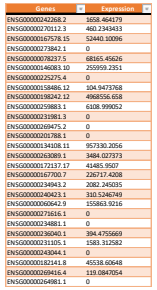
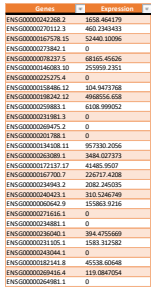
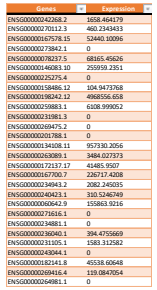
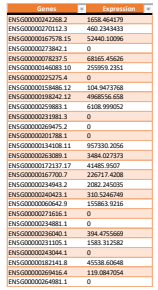
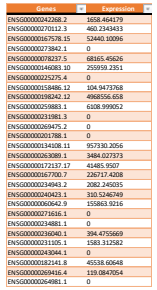
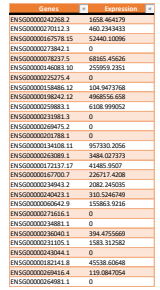
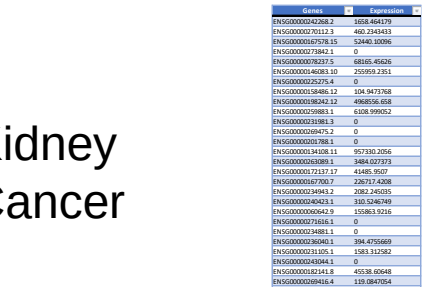
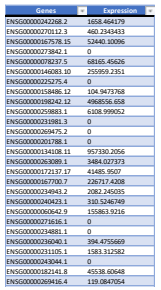
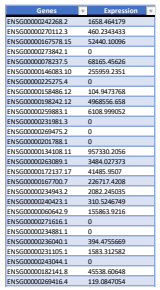
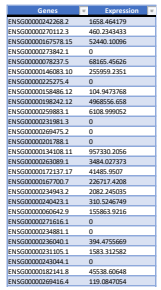
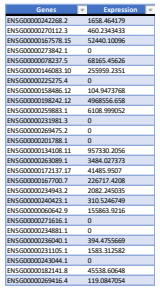
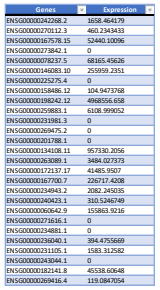
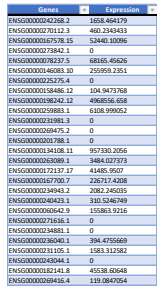
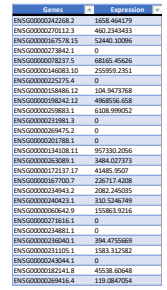
sponsored by the National Cancer Institute

	Sample1	Sample2	Sample3	Sample4	Sample297	Sample298	Sample299	Sample300
Breast Cancer								
Lung Cancer								
Kidney Cancer								

Merged Sample Expression Data

Genes

SAMPLES

	0	1	2	3	4	5	6	7	8	9	...	60474	60475	60476	60477	60478	60479	60480	60481	60482	submitter_id
0	574548	2263.14	983212	69718	54834.9	19718.1	175853	735123	38662.4	233190	...	0	0	0	0	0	0	0	0	0	TCGA-04-1331-01A-01R-1569-13
1	352295	4592.37	663107	39745.4	36553.5	41147.1	241313	396423	37567	128693	...	0	0	0	0	0	0	0	0	0	TCGA-04-1332-01A-01R-1564-13
2	295162	649.026	1.21115e+06	57385.5	33097.4	58051.8	228615	346066	105567	408267	...	0	0	0	0	0	0	0	0	0	TCGA-04-1338-01A-01R-1564-13
3	329580	1835.59	1.08437e+06	33812.3	24516.1	22330.6	42134.4	895558	56178	83847.3	...	0	0	0	0	0	0	0	0	0	TCGA-04-1341-01A-01R-1564-13
4	289269	40061.7	2.44837e+06	26399.5	18248	49610	74761.1	571992	71951.9	98726.4	...	0	0	0	0	0	0	0	0	0	TCGA-04-1343-01A-01R-1564-13
...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
4495	1.18093e+06	0	1.01139e+06	67877.2	15005.7	50527.3	6.21536e+06	1.47373e+06	459656	167488	...	0	0	0	0	0	0	0	0	0	TCGA-ZS-A9CD-01A-11R-A37K-07
4496	929228	0	869800	95607.5	17188.6	9352.12	7.61121e+06	196838	354465	138074	...	0	0	0	0	0	0	0	0	0	TCGA-ZS-A9CE-01A-11R-A37K-07
4497	469276	476.683	516938	110051	34469.4	37334.7	5.95811e+06	427832	323833	154861	...	0	0	0	0	0	0	0	0	0	TCGA-ZS-A9CF-01A-11R-A38B-07
4498	2.44119e+06	18282.7	853547	79288.7	106926	42593.9	4.80111e+06	955338	331924	177020	...	0	0	0	0	0	0	0	0	0	TCGA-ZS-A9CG-01A-11R-A37K-07
4499	259853	505.488	591328	74253.7	42553.5	118772	148978	508465	153862	170412	...	0	0	0	0	0	0	0	0	0	TCGA-ZX-AA5X-01A-11R-A42T-07

4500 rows × 60484 columns

Transpose and add as a row

Quantifying mRNA abundance and Scaling

- **GDC harmonization data is provided in FPKM-UQ**

- **In our code, FPKM-UQ is rescaled to TPM using the following formula.**

$$\mathrm{TPM}_i = \left(\frac{\mathrm{FPKM}_i}{\Sigma_j \mathrm{FPKM}_j}\right) \cdot 10^6$$

- **TPM has nice mathematical properties and a stable entity**

https://docs.gdc.cancer.gov/Encyclopedia/pages/HTSeq-FPKM-UQ/

Mapping and quantifying mammalian transcriptomes by RNA-Seq

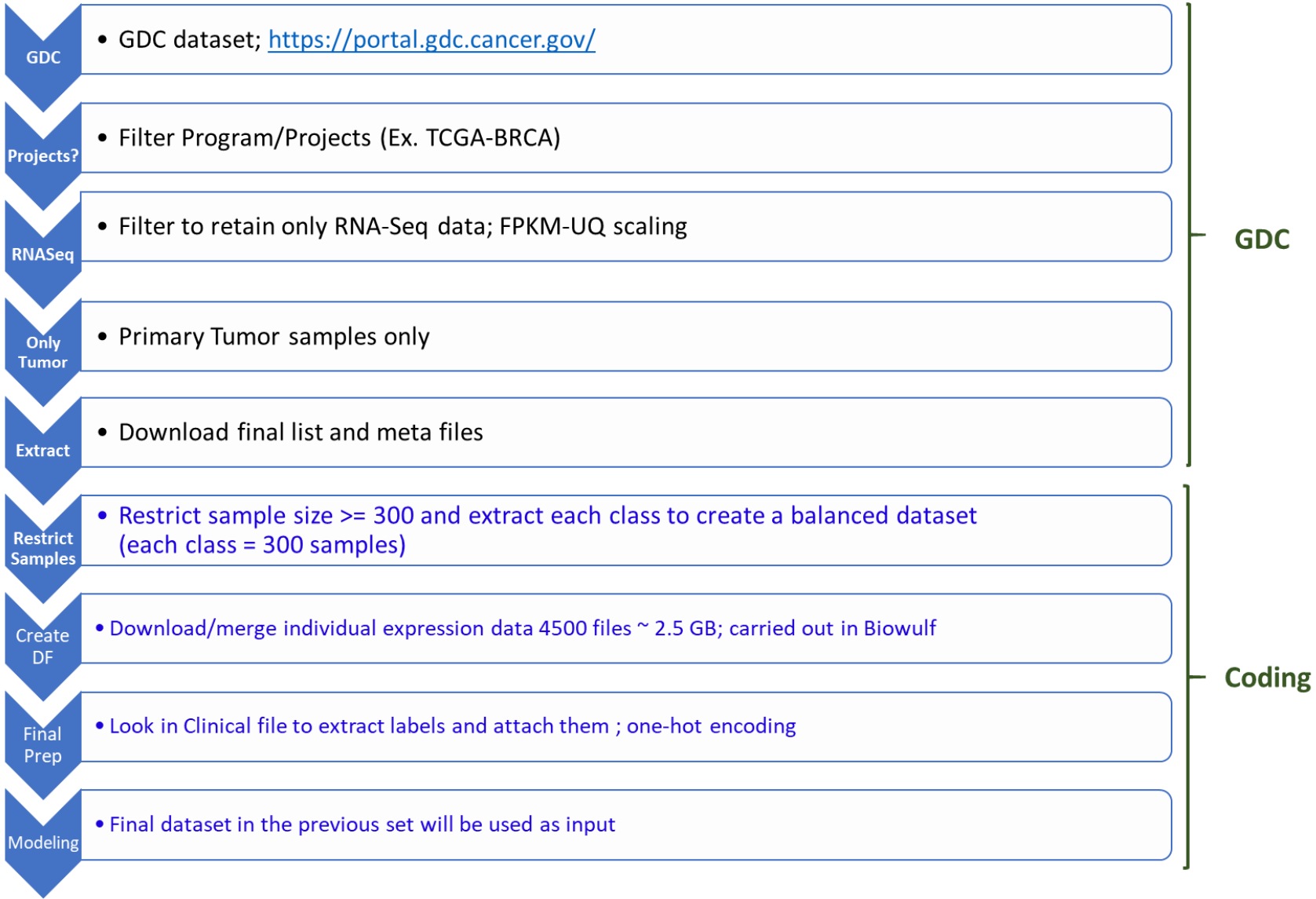
Ali Mortazavi[1,2], Brian A Williams[1,2], Kenneth McCue[1], Lorian Schaeffer[1] & Barbara Wold[1]

One-hot encoding to convert Cancer types to numbers

- **Convenient to transform categorical variables into a numerical quantity for computations**
  - BRCA to 0 ; LUAD to 1 etc.
  - 0, 1, 2, 3, …, 13, 14, 15

```
>>> encoded
array([[1., 0., 0., 0., 0., 0., 0., 0., 0., 0., 0., 0., 0., 0., 0., 0.],
       [0., 1., 0., 0., 0., 0., 0., 0., 0., 0., 0., 0., 0., 0., 0., 0.],
       [0., 0., 1., 0., 0., 0., 0., 0., 0., 0., 0., 0., 0., 0., 0., 0.],
       [0., 0., 0., 1., 0., 0., 0., 0., 0., 0., 0., 0., 0., 0., 0., 0.],
       [0., 0., 0., 0., 1., 0., 0., 0., 0., 0., 0., 0., 0., 0., 0., 0.],
       [0., 0., 0., 0., 0., 1., 0., 0., 0., 0., 0., 0., 0., 0., 0., 0.],
       [0., 0., 0., 0., 0., 0., 1., 0., 0., 0., 0., 0., 0., 0., 0., 0.],
       [0., 0., 0., 0., 0., 0., 0., 1., 0., 0., 0., 0., 0., 0., 0., 0.],
       [0., 0., 0., 0., 0., 0., 0., 0., 1., 0., 0., 0., 0., 0., 0., 0.],
       [0., 0., 0., 0., 0., 0., 0., 0., 0., 1., 0., 0., 0., 0., 0., 0.],
       [0., 0., 0., 0., 0., 0., 0., 0., 0., 0., 1., 0., 0., 0., 0., 0.],
       [0., 0., 0., 0., 0., 0., 0., 0., 0., 0., 0., 1., 0., 0., 0., 0.],
       [0., 0., 0., 0., 0., 0., 0., 0., 0., 0., 0., 0., 1., 0., 0., 0.],
       [0., 0., 0., 0., 0., 0., 0., 0., 0., 0., 0., 0., 0., 1., 0., 0.],
       [0., 0., 0., 0., 0., 0., 0., 0., 0., 0., 0., 0., 0., 0., 1., 0.],
       [0., 0., 0., 0., 0., 0., 0., 0., 0., 0., 0., 0., 0., 0., 0., 1.]],
      dtype=float32)
```

Data preparation steps summary



Before we break for hands-on

- **Python as the programming language for this workshop, but similar libraries are available in R or other languages**

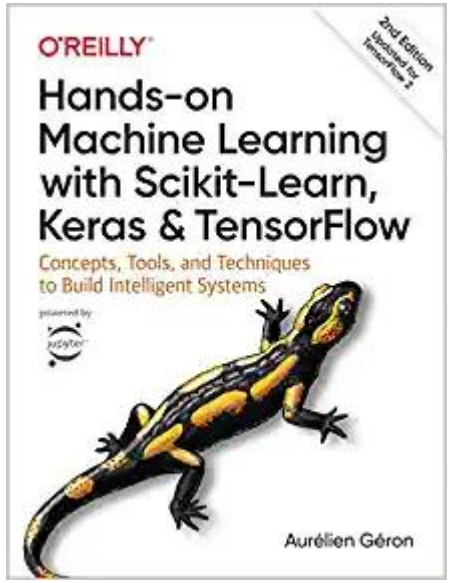
- **Will use Jupyter Notebook for sharing the code**
  - With little effort one can convert the Python code into R and still use Jupyter Notebook

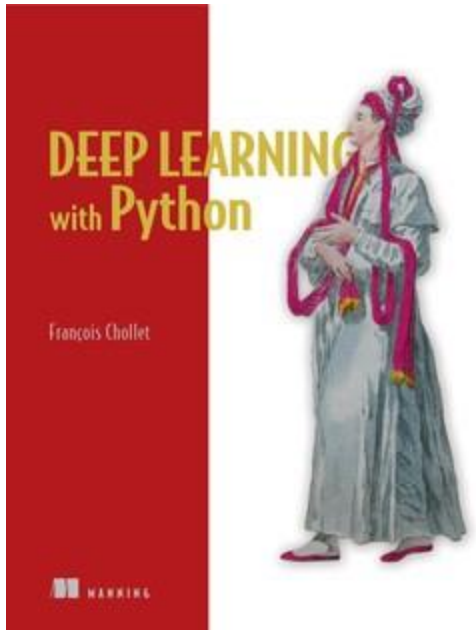
To be continued after hands-on

https://github.com/ravichas/ML-TC1

Before we begin the modeling section …

- **Due to lack of time, I wont be covering the basics of Neural Network**





These are good books for beginners and up

Keras is a high-level NN package that is built on top of popular high-level libraries (TF, Theano). Works well with CPU/GPU

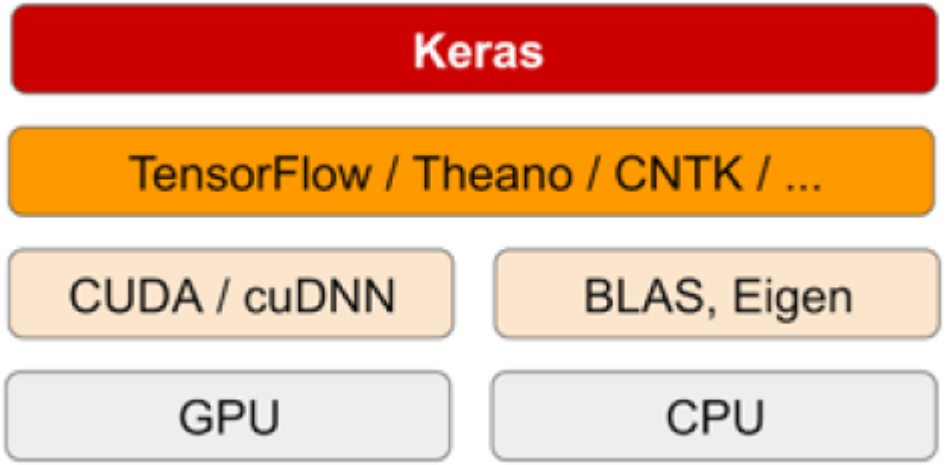


Figure from Deep Learning with Python

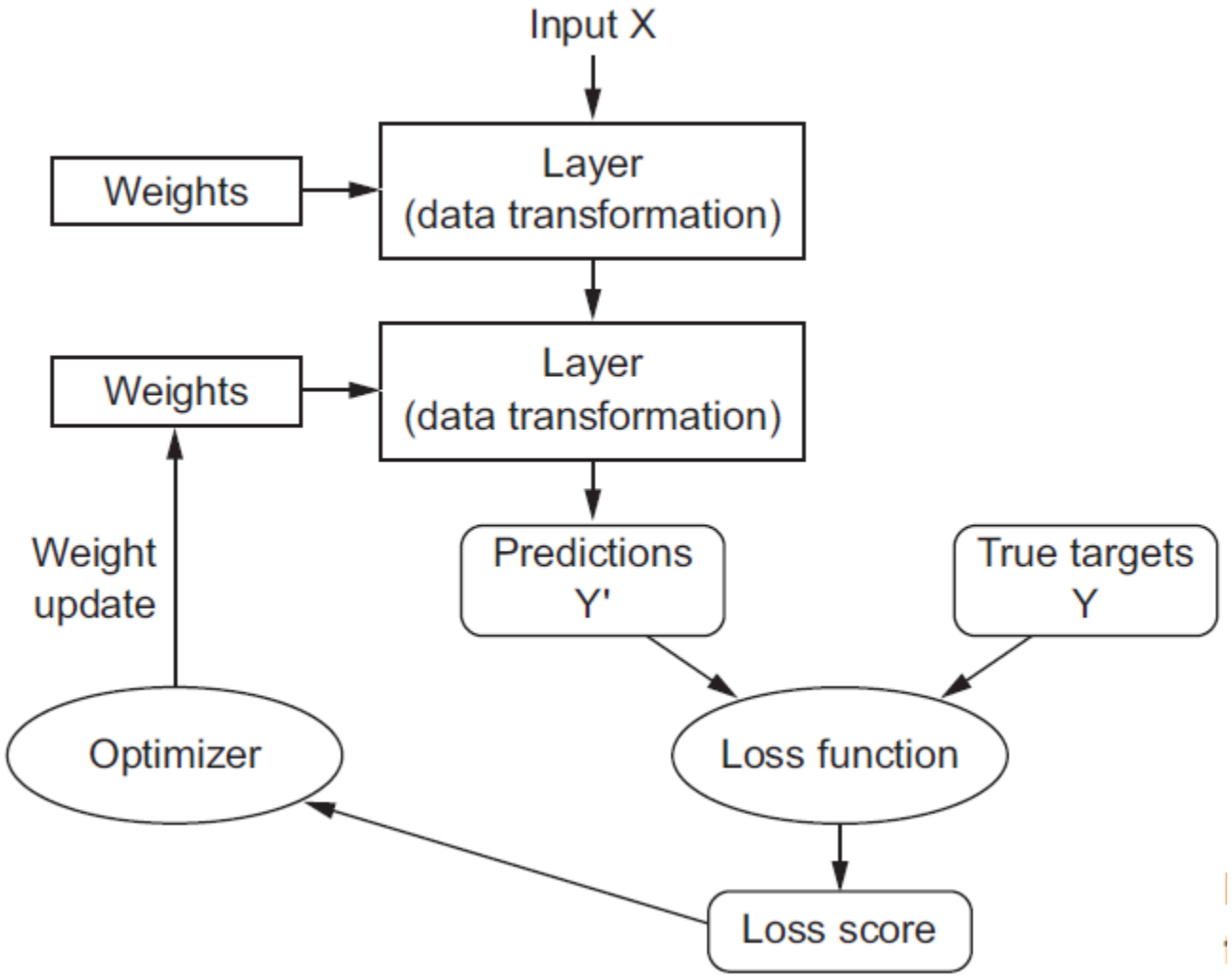
Supervised Learning

- Goal
  - Construct a model that takes in input features/target pair to return a prediction for target/outcome

- Train a machine learning
  - Model refers to learning its parameters, which typically involves minimizing a loss function on training data with the aim of making accurate predictions on unseen (test) data

Deep Learning Procedure

Taken from Deep Learning with Keras book



Terminology

	0	1	2	3	4	5	6	7	8	9	...	60474	60475	60476	60477	60478	60479	60480	60481	60482	submitter_id
0	574548	2263.14	983212	69718	54834.9	19718.1	175853	735123	38662.4	233190	...	0	0	0	0	0	0	0	0	0	TCGA-04-1331-01A-01R-1569-13
1	352295	4592.37	663107	39745.4	36553.5	41147.1	241313	396423	37567	128693	...	0	0	0	0	0	0	0	0	0	TCGA-04-1332-01A-01R-1564-13
2	295162	649.026	1.21115e+06	57385.5	33097.4	58051.8	228615	346066	105567	408267	...	0	0	0	0	0	0	0	0	0	TCGA-04-1338-01A-01R-1564-13
3	329580	1835.59	1.08437e+06	33812.3	24516.1	22330.6	42134.4	895558	56178	83847.3	...	0	0	0	0	0	0	0	0	0	TCGA-04-1341-01A-01R-1564-13
4	289269	40061.7	2.44837e+06	26399.5	18248	49610	74761.1	571992	71951.9	98726.4	...	0	0	0	0	0	0	0	0	0	TCGA-04-1343-01A-01R-1564-13

- **Columns**
  - input variables or features or attributes
- **Outcome column**
  - Outcome variables or targets
- **Rows**
  - Training example or instance
- **Whole table Training data set**

A Simple Network

Input	Output
0.125	0.39
0.25	0.40
0.5	0.43
1	0.48
2	0.58
3	???

Data based on Mary Attenborough, in Mathematics for Electrical Engineering and Computing, 2003

What is different about Neural Network?

- **If you know the equation (algorithm), then you feed in the input and you get the output. You can code the function yourself**

```
def function(m):
    L = 0.1 * m + 0.38
    return(L)
```

- **You can choose to use linear modeling and use the data to figure the relationship**

```
Model ← lm( L ~ m)
```

- **Neural Network using the data learn the algorithm.**

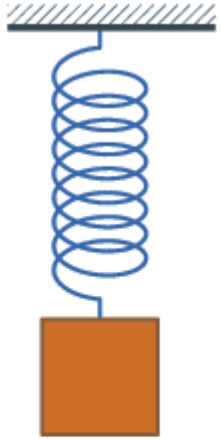
INPUT

ALGORITHM

OUTPUT

A Simple Network

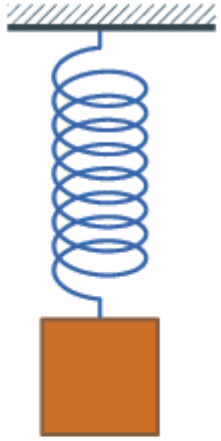
Input: Mass or M (kg)
Output: Length or L (m)



M	L
Input	Output
0.125	0.39
0.25	0.40
0.5	0.43
1	0.48
2	0.58
3	???

Based on Mary Attenborough, in Mathematics for Electrical Engineering and Computing, 2003

A Simple Network



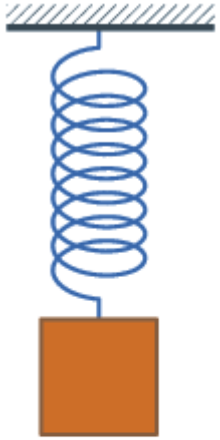
M	L
0.125	0.39
0.25	0.40
0.5	0.43
1	0.48
2	0.58
3	0.68

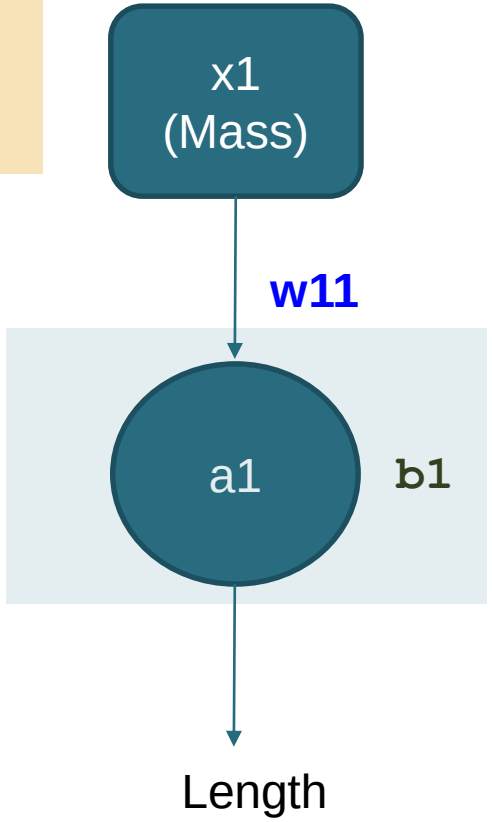
```
L = 0.1 * Mass + 0.38
```


Mary Attenborough, in Mathematics for Electrical Engineering and Computing, 2003

A Simple Network


```
a1 = x1   * w11   +  b1
 L = M    * 0.1   + 0.38
```



Hidden Layer

M	L
0.125	0.39
0.25	0.40
0.5	0.43
1	0.48
2	0.58
3	0.68

```
These are the model variables: [array([[0.10058284]], dtype=float32), array([0.37793916], dtype=float32)]
```

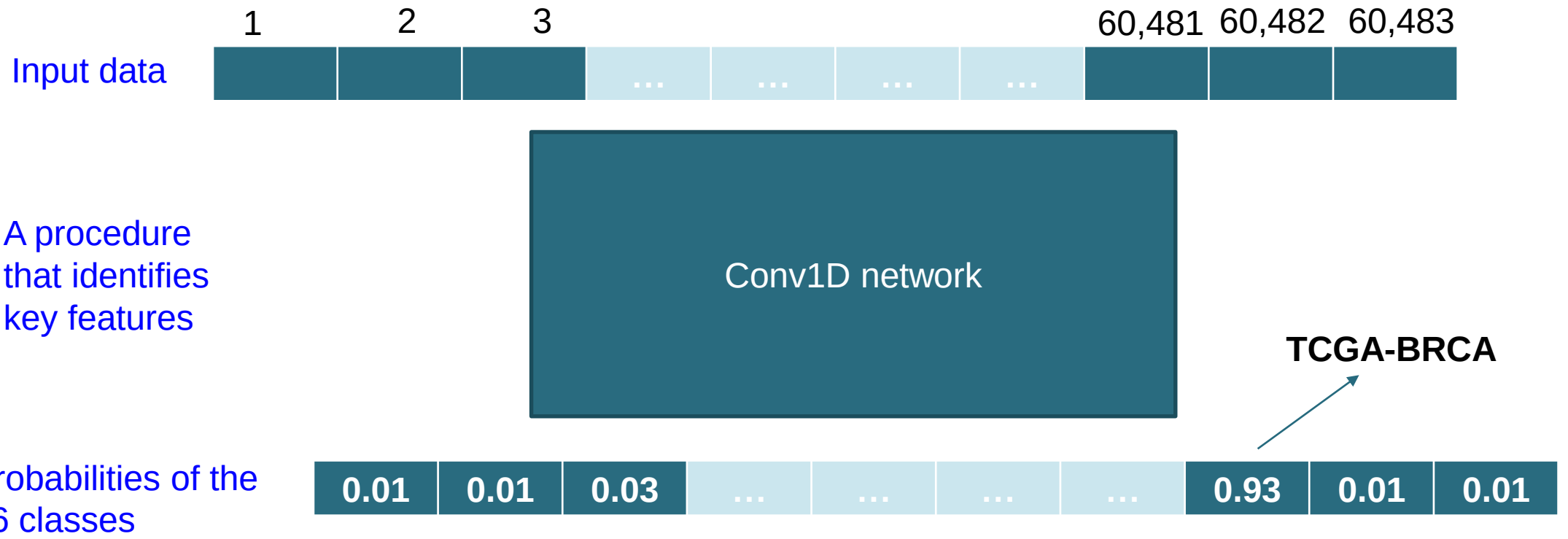
Based on Mary Attenborough, in Mathematics for Electrical Engineering and Computing, 2003

Error minimization

- Goal is to choose Ws such that predictions of the network should be close to y
- Error function or cost function a measure how good our predictions are
- Eventually, we wan to pick a set of w that minimizes the error function

Convolutional Neural Network

- **We are going to take a vector of genomic expression values and feed them into a network with a series of operations to create a model**
- **Model is what we call convolutional-1D network**

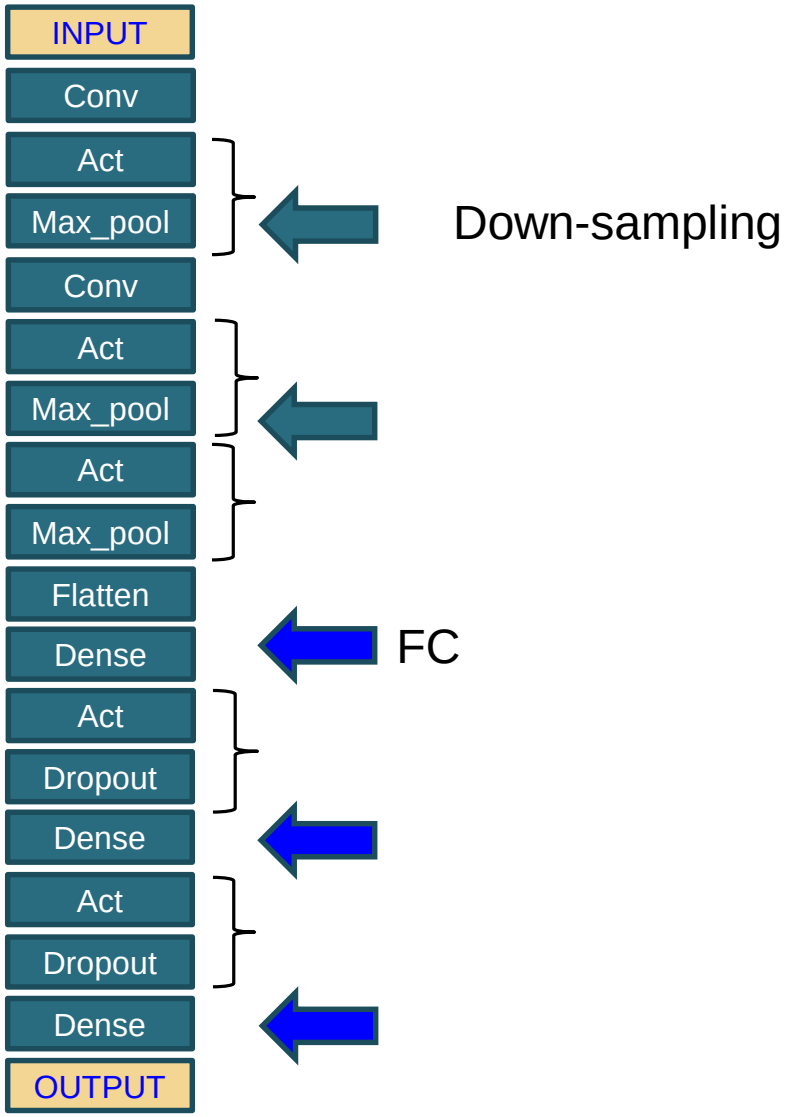


Components of conv1D

1. **Activation (Act)**
2. **Convolution (Conv)**
3. **Maxpooling (Max_pool)**
4. **Flatten**
5. **Dense**
6. **Dropout**

Topology of a network defines a “hypothesis space”

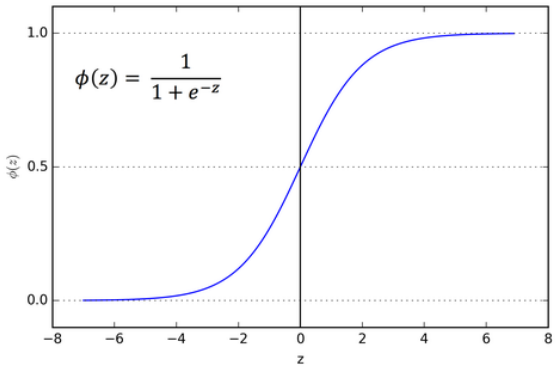
Choosing a specific topology is usually not straight-forward and comes with practice.



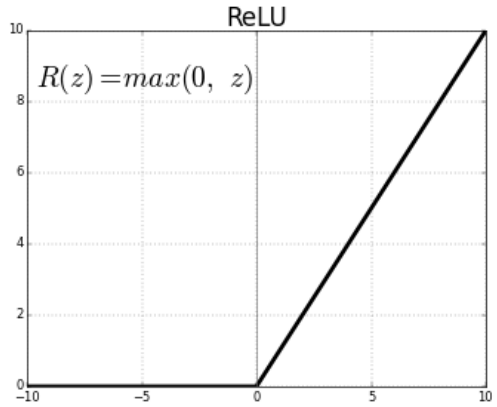
1. Activation Function

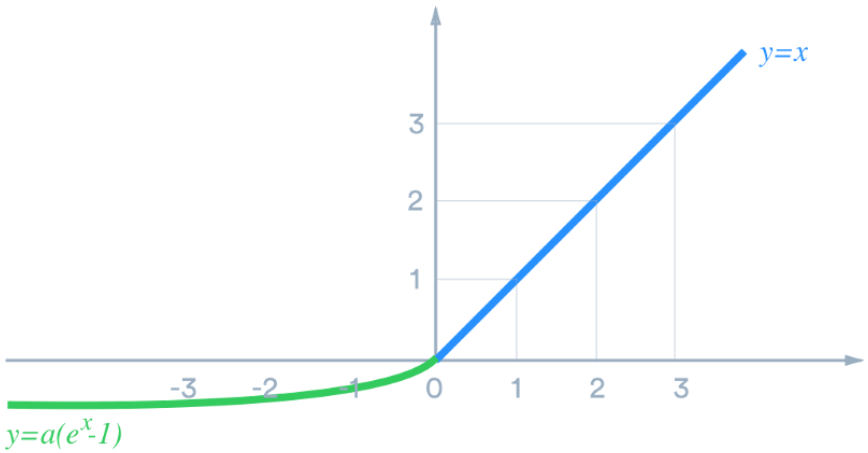
- **Activation functions are included to create non-linearity**

- **Sigmoid**
- **ReLU**
- **Leaky ReLU**
- **ELU**
- **Maxout**
- **Tanh**



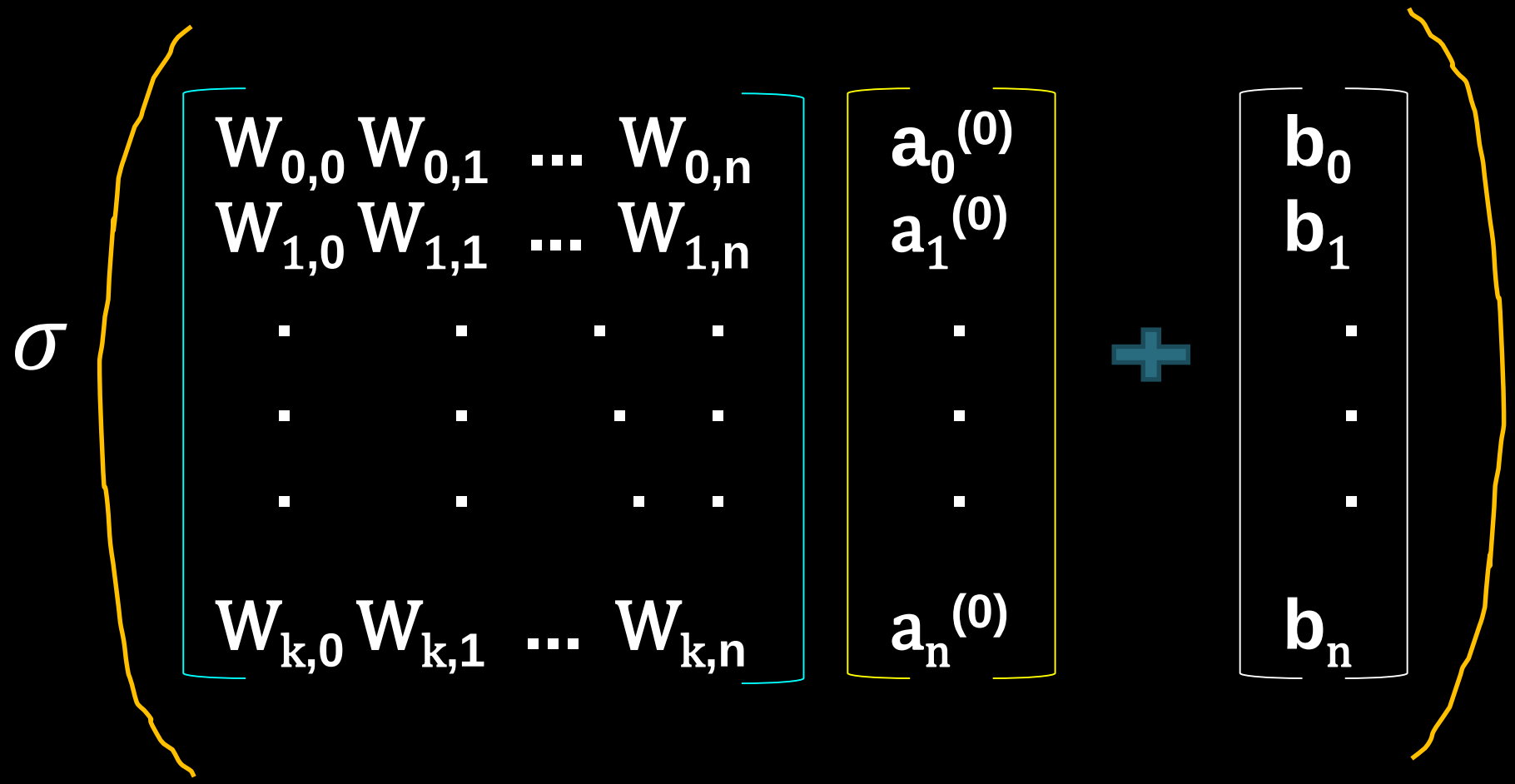
Squashes the #s to [0, 1]





1. Activation function

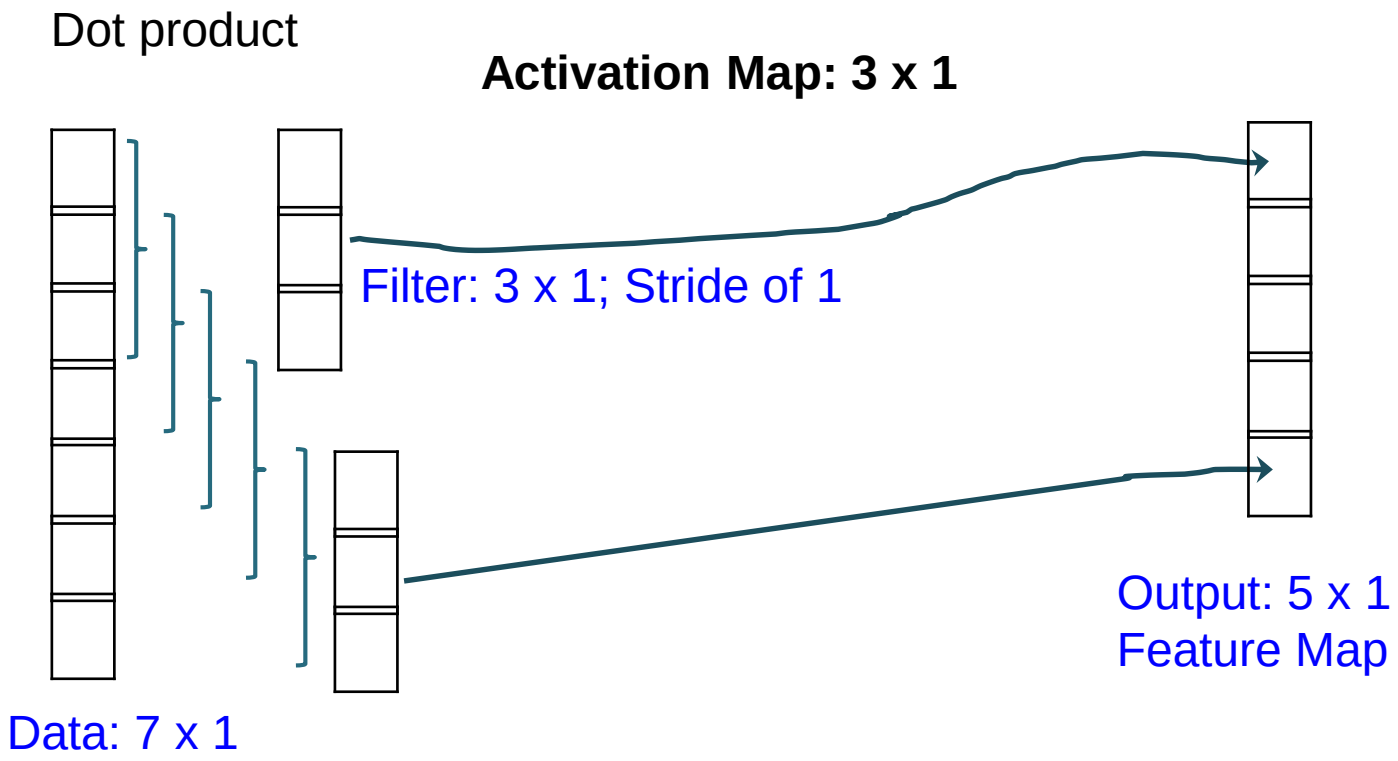
$$a^{(L)} = \sigma(w^{(L)} a^{(L-1)} + b^{(L)})$$



2. Convolution

Process of applying filter (kernel) to the data for the purpose of subsampling. Kernel is a matrix that has a smaller dimension than the input data creates chunks

Reduces the number of parameters and allow creation of deeper networks



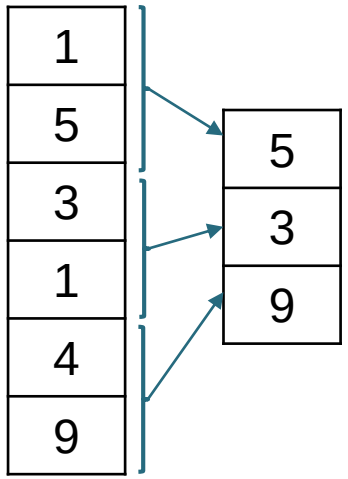
Convolutional Layer

# of HP

- # of filters
- Spatial Extent
- Stride
- Amount of zero padding

3. Pooling

- **Pooling makes the representations smaller/manageable (downsampling) by retaining only important features; creates smaller clusters of manageable size**
- **Each activation map will be pooled separately.**
- **Common approach is Max Pooling**



Max-pooling with filter size of 2x1 and stride of 2

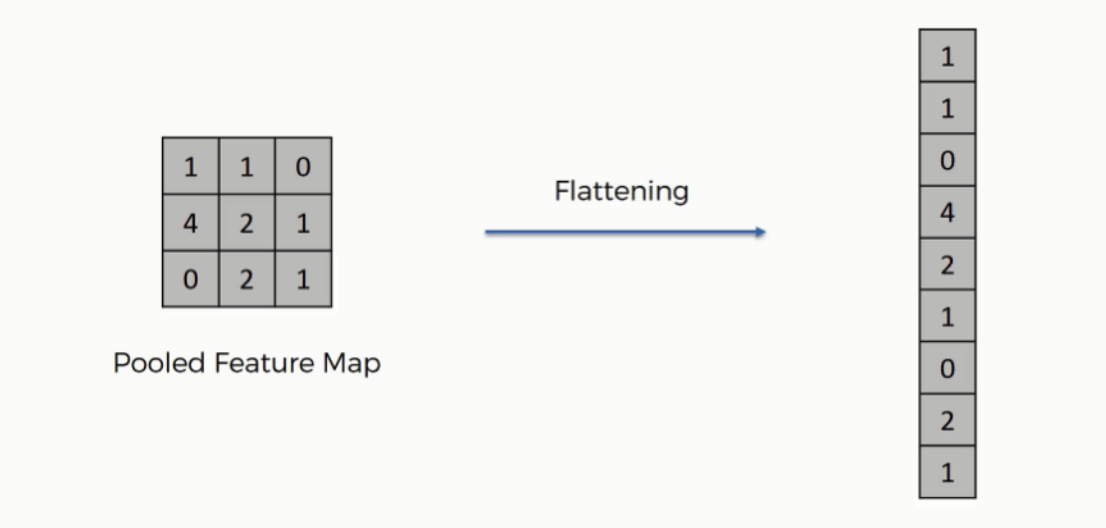
Max Pooling Intuition:
Enhancing the signals by looking at a region and pick the maximum activation value

Each of these are activation and we are looking for

Research shows that zero-padding is not followed. Because we are interested in down-sampling

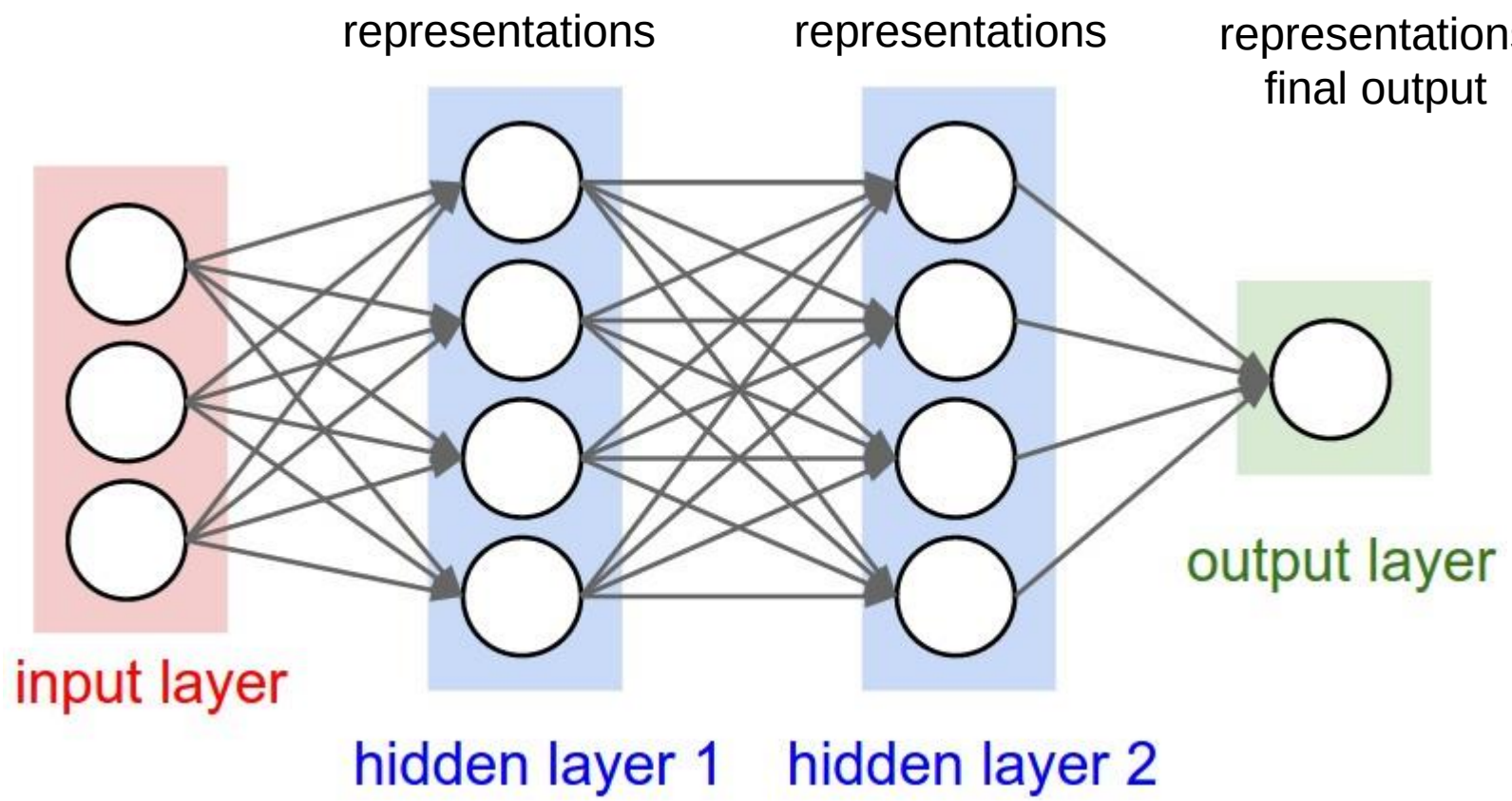
4. Flatten

Procedure to transform a 2D matrix (features) to a 1D vector which in turn can be fed into a fully-connected layer (dense)

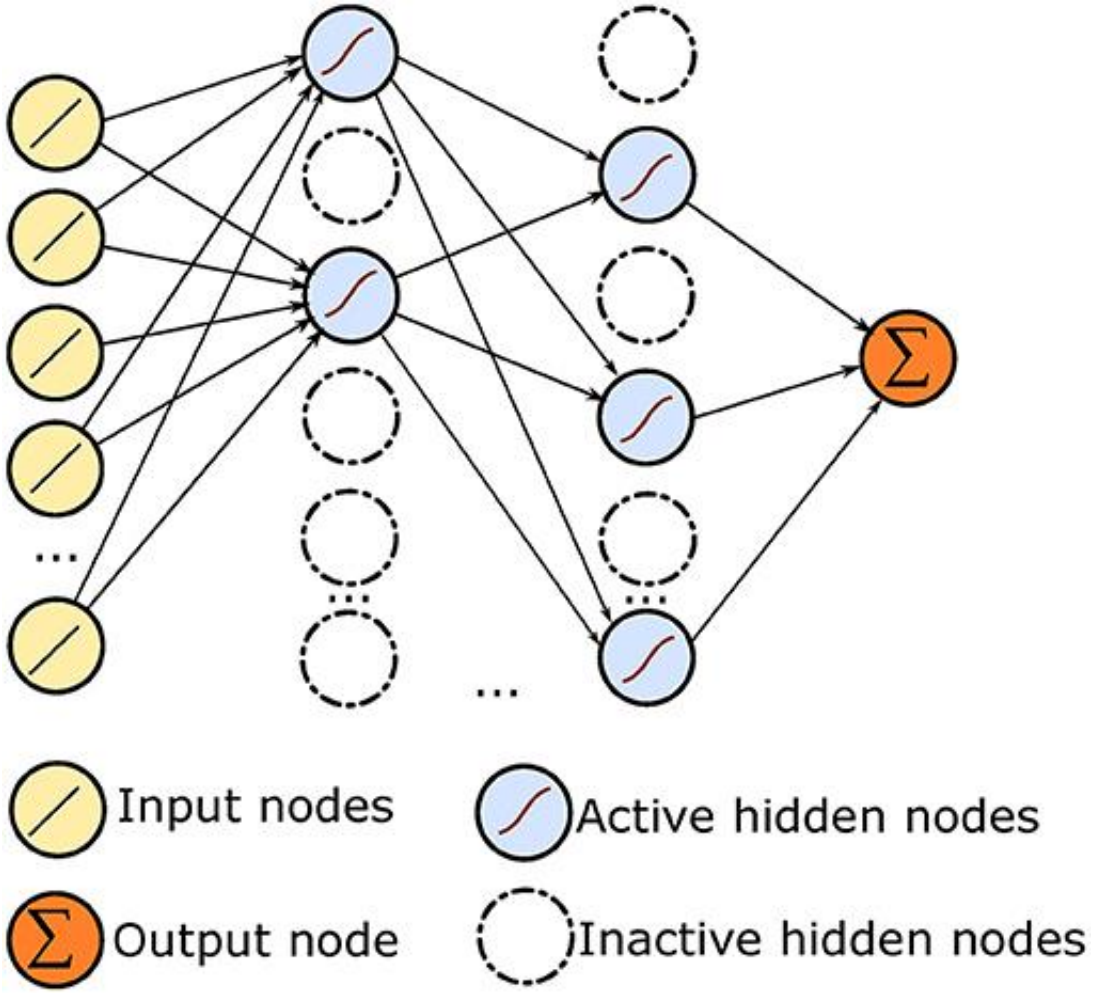


5. Dense

Each neuron receives input from all the neurons in the previous layer (densely connected)



6. Dropout

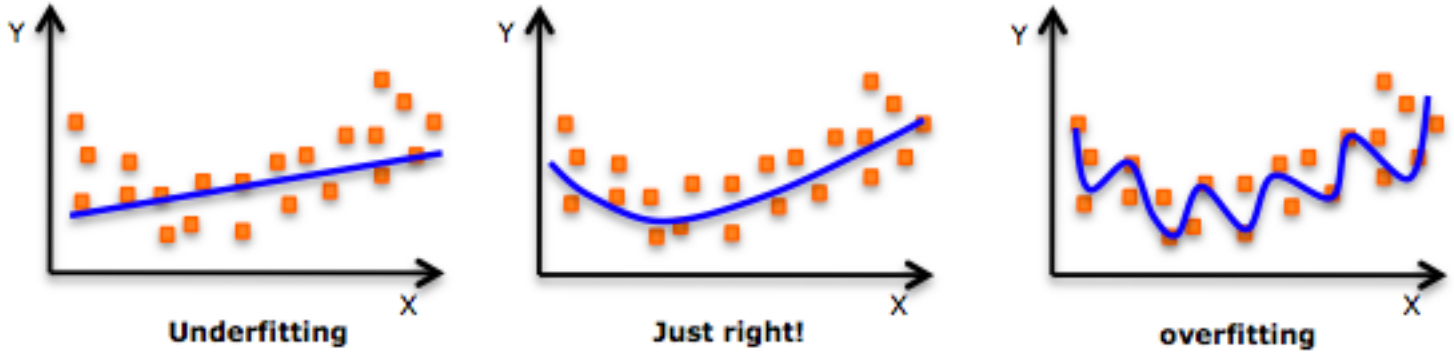


Imbalance in the weights among the nodes can lead to some node weights not contributing to the learning

One solution:
Remove a random proportion of selection of neurons in a neural network during training

Can help weak learners become strong learners

6. Dropout



Model Summary

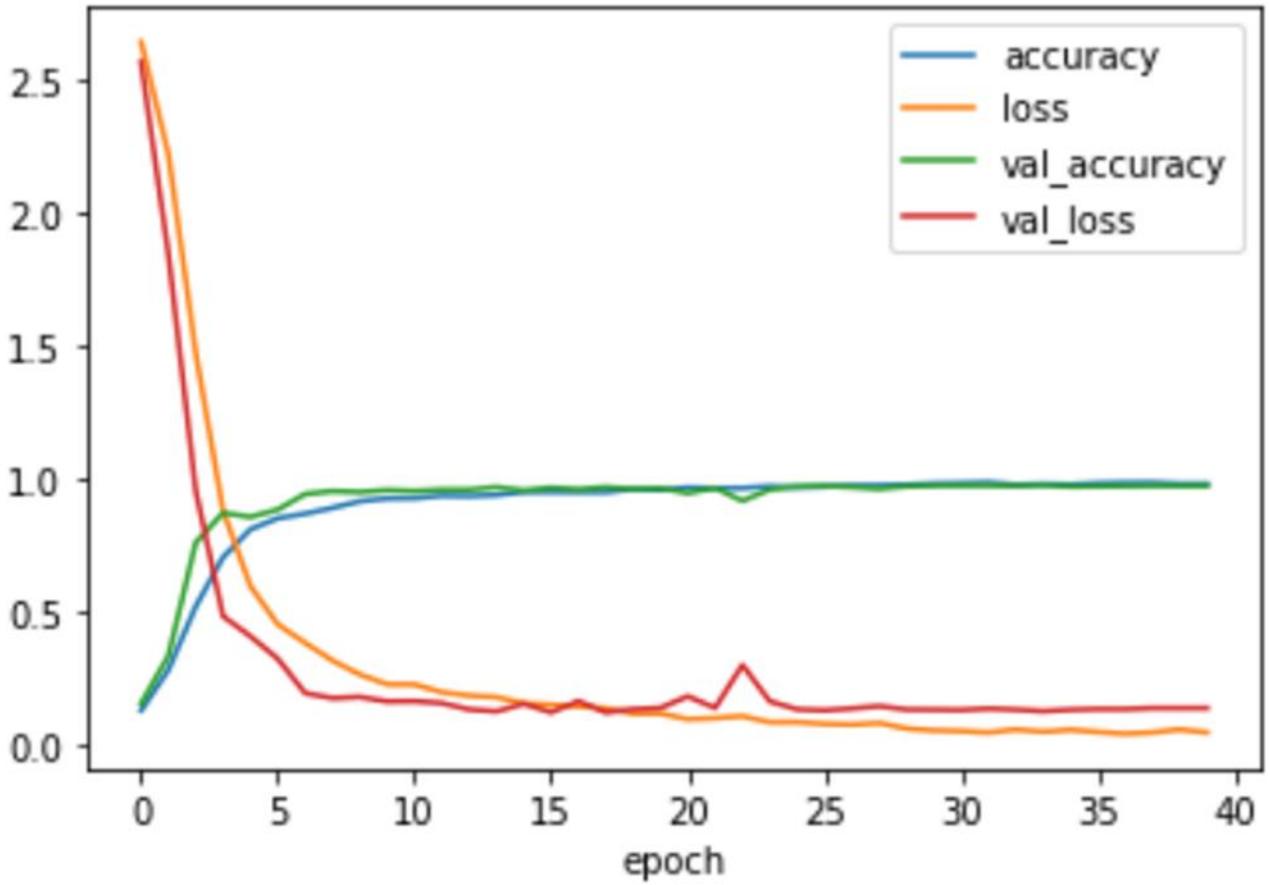

```
1.0 128 10 1
Model: "sequential_1"
_________________________________________________________________
Layer (type)                 Output Shape              Param #
=================================================================
conv1d_1 (Conv1D)            (None, 60464, 128)        2688
_________________________________________________________________
activation_1 (Activation)    (None, 60464, 128)        0
_________________________________________________________________
max_pooling1d_1 (MaxPooling1 (None, 60464, 128)        0
_________________________________________________________________
conv1d_2 (Conv1D)            (None, 60455, 128)        163968
_________________________________________________________________
activation_2 (Activation)    (None, 60455, 128)        0
_________________________________________________________________
max_pooling1d_2 (MaxPooling1 (None, 6045, 128)         0
_________________________________________________________________
flatten_1 (Flatten)          (None, 773760)            0
_________________________________________________________________
dense_1 (Dense)              (None, 200)               154752200
_________________________________________________________________
activation_3 (Activation)    (None, 200)               0
_________________________________________________________________
dropout_1 (Dropout)          (None, 200)               0
_________________________________________________________________
dense_2 (Dense)              (None, 20)                4020
_________________________________________________________________
activation_4 (Activation)    (None, 20)                0
_________________________________________________________________
dropout_2 (Dropout)          (None, 20)                0
_________________________________________________________________
dense_3 (Dense)              (None, 15)                315
_________________________________________________________________
activation_5 (Activation)    (None, 15)                0
=================================================================
Total params: 154,923,191
Trainable params: 154,923,191
Non-trainable params: 0
```

~ 154 M parameters

Code execution and progress


```
Epoch 00001: val_loss improved from inf to 2.56791, saving model to Pilot1.h5

Epoch 2/400
3375/3375 [==============================] - 228s 68ms/step - loss: 2.2202 - acc: 0.2821 - val_loss: 1.8444 - val_acc:
Epoch 00002: val_loss improved from 2.56791 to 1.84441, saving model to Pmodel.h5

Epoch 3/400
3375/3375 [==============================] - 228s 68ms/step - loss: 1.4736 - accuracy: 0.5206 - val_loss: 0.9554 - val_acc:
Epoch 00003: val_loss improved from 1.84441 to 0.95540, saving model to Pmodel.h5

Epoch 4/400
3375/3375 [==============================] - 228s 68ms/step - loss: 0.8795 - accuracy: 0.7058 - val_loss: 0.4835 - val_acc:
Epoch 00004: val_loss improved from 0.95540 to 0.48347, saving model to Pmodel.h5

Epoch 5/400
3375/3375 [==============================] - 228s 68ms/step - loss: 0.5968 - accuracy: 0.8107 - val_loss: 0.4083 - val_acc:
Epoch 00005: val_loss improved from 0.48347 to 0.40829, saving model to Pmodel.h5

Epoch 6/400
3375/3375 [==============================] - 228s 68ms/step - loss: 0.4529 - accuracy: 0.8519 - val_loss: 0.3236 - val_acc:
Epoch 00006: val_loss improved from 0.40829 to 0.32363, saving model to Pmodel.h5

Epoch 7/400
3375/3375 [==============================] - 228s 68ms/step - loss: 0.3835 - accuracy: 0.8690 - val_loss: 0.1944 - val_acc:
Epoch 00007: val_loss improved from 0.32363 to 0.19439, saving model to Pmodel.h5

Epoch 8/400
3375/3375 [==============================] - 228s 68ms/step - loss: 0.3170 - accuracy: 0.8910 - val_loss: 0.1754 - val_acc:
Epoch 00008: val_loss improved from 0.19439 to 0.17536, saving model to Pmodel.h5

Epoch 9/400
3375/3375 [==============================] - 228s 67ms/step - loss: 0.2647 - accuracy: 0.9156 - val_loss: 0.1800 - val_acc:
Epoch 00009: val_loss did not improve from 0.17536

Epoch 10/400
3375/3375 [==============================] - 228s 68ms/step - loss: 0.2276 - accuracy: 0.9265 - val_loss: 0.1632 - val_acc:
Epoch 00010: val_loss improved from 0.17536 to 0.16323, saving model to Pmodel.h5
```

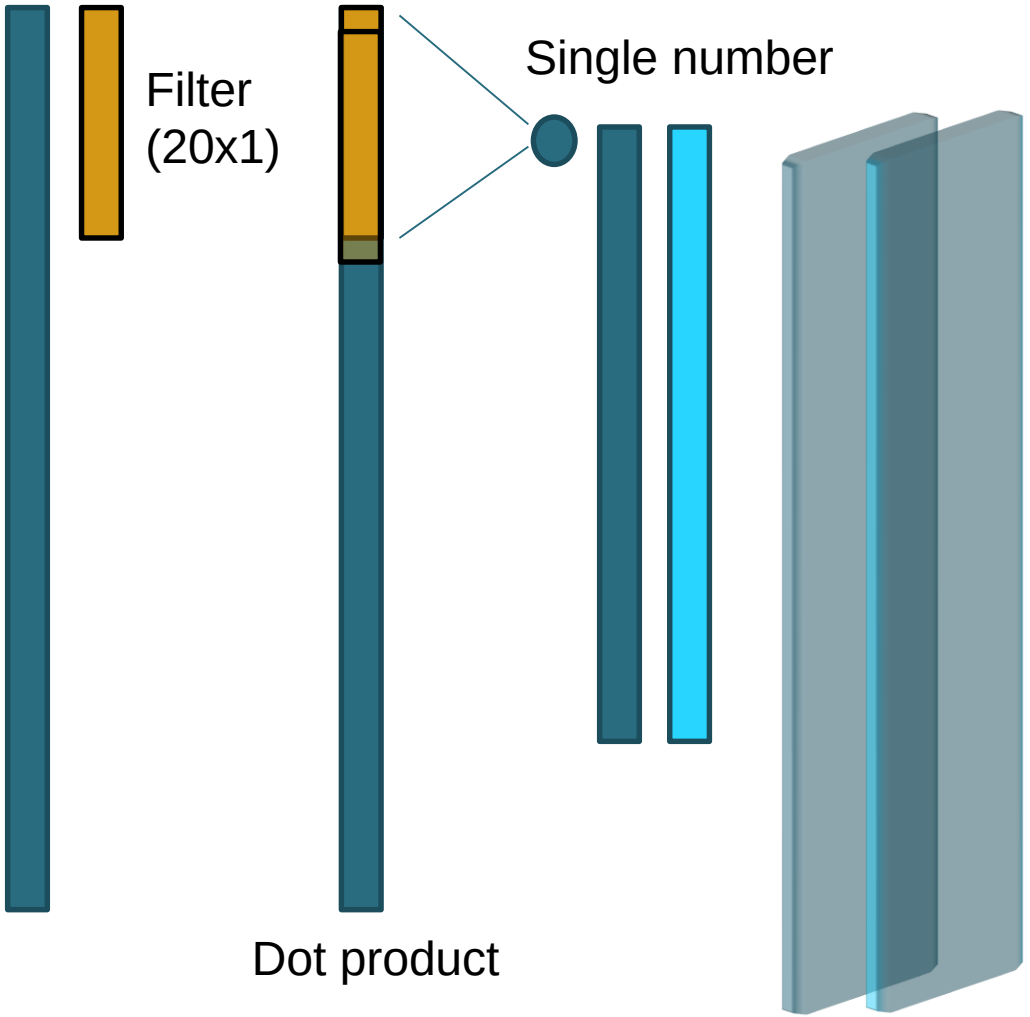
Model Performance



Thanks

S. Ravichandran

4. Convolution Layer



$$w^T x + b$$

Convolution activation maps

Pooling layer

- **We will be using**

Down-sampling

CONV	ACT RELU	M.Pooling	Conv	ACT RELU	Max Pooling	FC
						BRCA (0.88)
						LUAD (0.02)
						…
						..