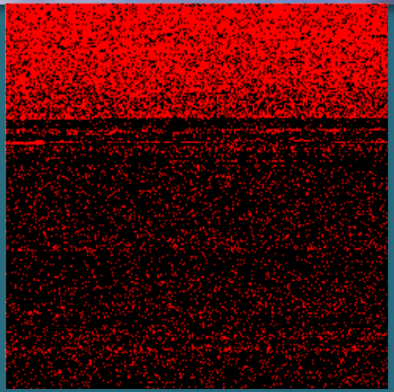
Frederick National Laboratory
for Cancer Research

sponsored by the National Cancer Institute

Cancer Type/Site Classification using Deep-Learning

(Preliminary presentation slides)



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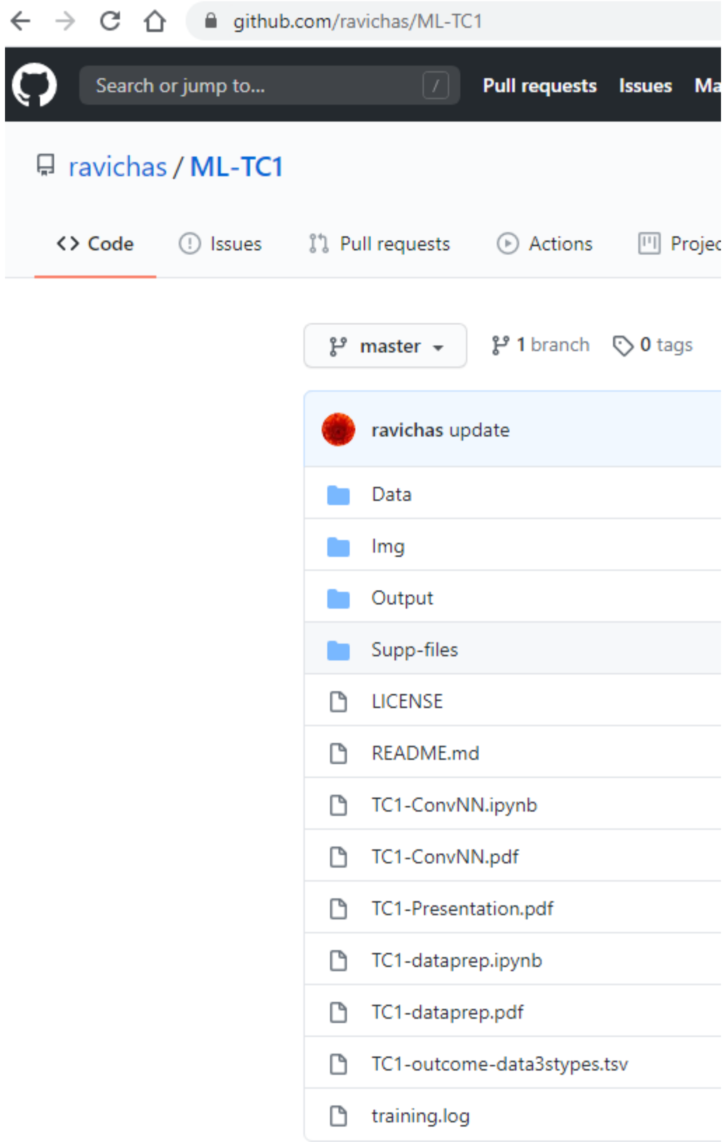
BIDS, FNLCR

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

Frederick National Laboratory is a Federally Funded Research and Development Center operated by Leidos Biomedical Research, Inc., for the National Cancer Institute

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



Data
Img
Output
Supp-files
LICENSE
README.md
TC1-ConvNN.ipynb
TC1-ConvNN.pdf
TC1-Presentation.pdf
TC1-dataprep.ipynb
TC1-dataprep.pdf
TC1-outcome-data3stypes.tsv
training.log

1. **TC1-Presentation.pdf**
   PPT slides in PDF

2. **TC1-dataprep.pdf** and **TC1-ConvNN.pdf** are the pdf versions of the **TC1-dataprep.ipynb** and **TC1-ConvNN.ipynb** Jupyter Notebook

3. **TC1-dataprep.ipynb** and **TC1-ConvNN.ipynb** are the Jupyter notebooks python code

4. **Data** folder will contain the data files

5. **Model** folder will contain Model related weights

Biowulf HPC Batch Job scripts

/data/BIDS-HPC/public/Workshops/Ravi/ML-TC1.tar.gz

Contents of *tar.gz file
Scripts

Python code
SLURM script
Data

- Make sure you read the README.txt file for some preliminary setup

- Files will be available only for few days. So, download them in the next few days.

Acknowledgements

- **NCI-DOE Pilot-1 Team**

- **BIDS**
  - Drs. George Zaki, Andrew Weissman, Mark Jensen and Eric Stahlberg
  - Amar Khalsa, Dr. Deb Hope, Anney Che, Hue Readron, Naomi Ohashi, Dr. Yongmei Zhao
  - Colleagues who reviewed the material

Feel free to follow-along

Github

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

https://datascience.cancer.gov/collaborations/joint-design-advanced-computing

The Joint Design of Advanced Computing Solutions for Cancer (JDACS4C)

Frederick National Laboratory for Cancer Research

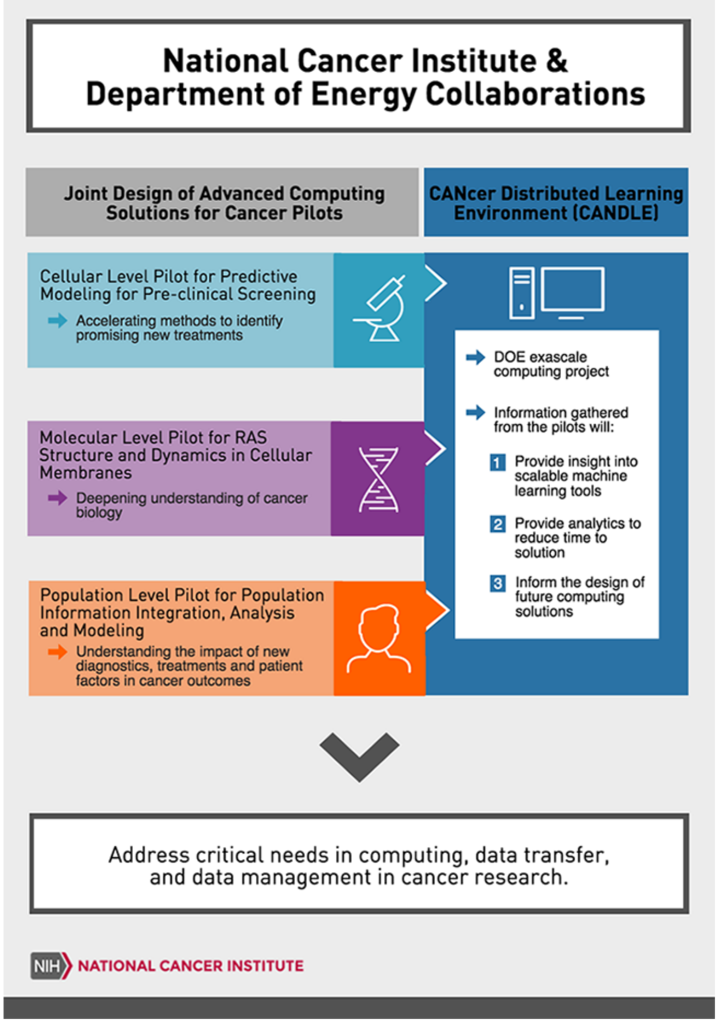
sponsored by the National Cancer Institute

- JDACS4C program was created in 2016 to accelerate cancer research using emerging exascale computing capabilities.
- Part of the Cancer Moonshot
- Cross-agency collaboration between NCI and the DOE
- **Pilot1:**
  - *Focuses on developing predictive models, both computational and experimental, to improve pre-clinical therapeutic drug screening.*
  - https://datascience.cancer.gov/collaborations/joint-design-advanced-computing/cellular-pilot

Pilot1

Pilot2

Pilot3



National Cancer Institute & Department of Energy Collaborations

Joint Design of Advanced Computing Solutions for Cancer Pilots

CANcer Distributed Learning Environment (CANDLE)

Cellular Level Pilot for Predictive Modeling for Pre-clinical Screening

→ Accelerating methods to identify promising new treatments

Molecular Level Pilot for RAS Structure and Dynamics in Cellular Membranes

→ Deepening understanding of cancer biology

Population Level Pilot for Population Information Integration, Analysis and Modeling

→ Understanding the impact of new diagnostics, treatments and patient factors in cancer outcomes

→ DOE exascale computing project

→ Information gathered from the pilots will:

1 Provide insight into scalable machine learning tools

2 Provide analytics to reduce time to solution

3 Inform the design of future computing solutions

Address critical needs in computing, data transfer, and data management in cancer research.

NIH NATIONAL CANCER INSTITUTE

Introduction

- Goal is to share tools/techniques/solutions for cancer related problems
- You would be able to take our test-case (code/scripts) and tune it to your needs
- Deep-Learning is a growing area. This may not address all your questions, but I believe this will be a good starting point
- We want to hear from you, please send us your feed-back

Motivation: Cancer Prediction vs Cancer Detection

- **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 to be used for early cancer detection?**
  - Improving chance of early detection cure/survival?

Hallmarks of cancer: Integral Components of Most Forms of Cancer (Acquired Capabilities)

Hallmarks of Cancer: The Next Generation

src Oncogene mutations

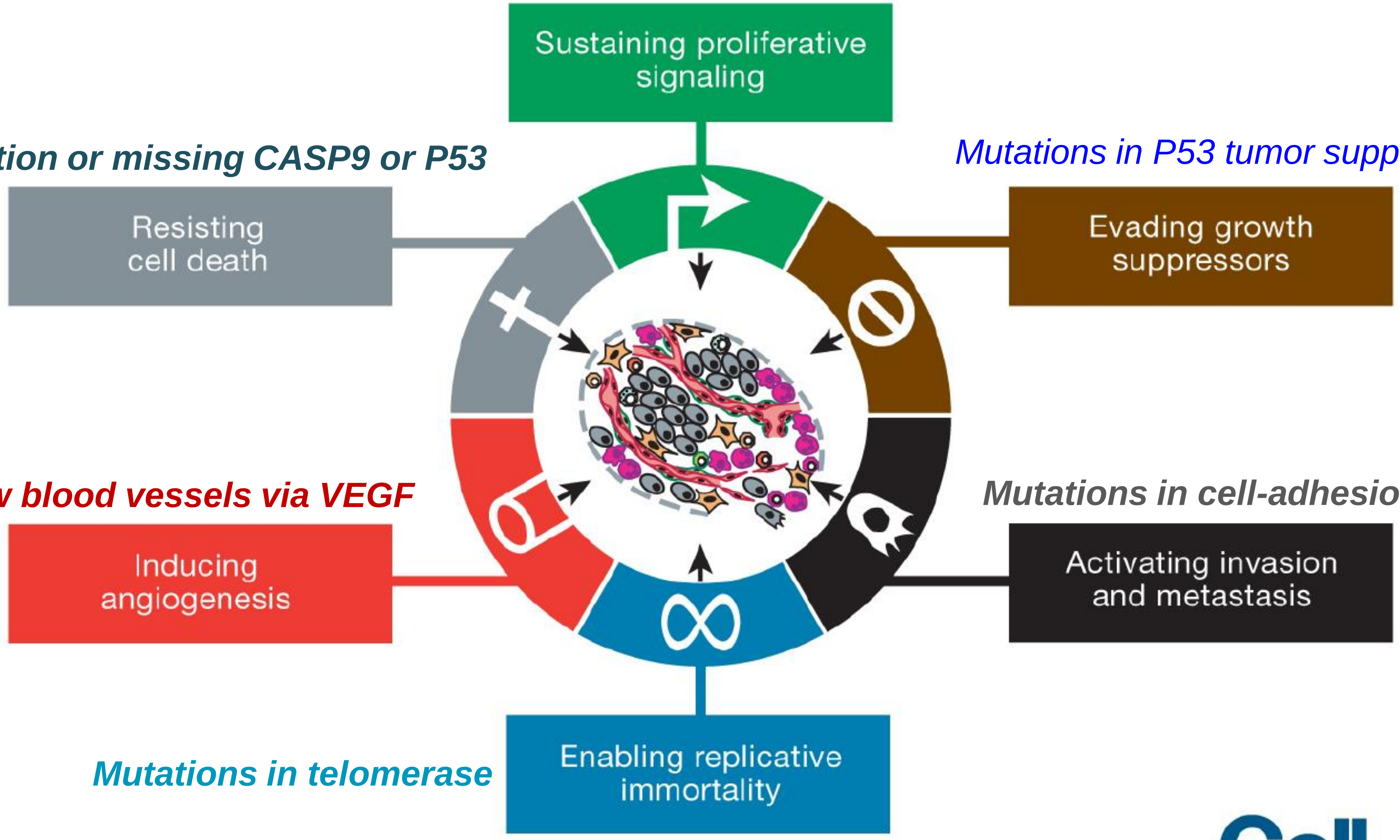
Mutation or missing CASP9 or P53

Mutations in P53 tumor suppressor

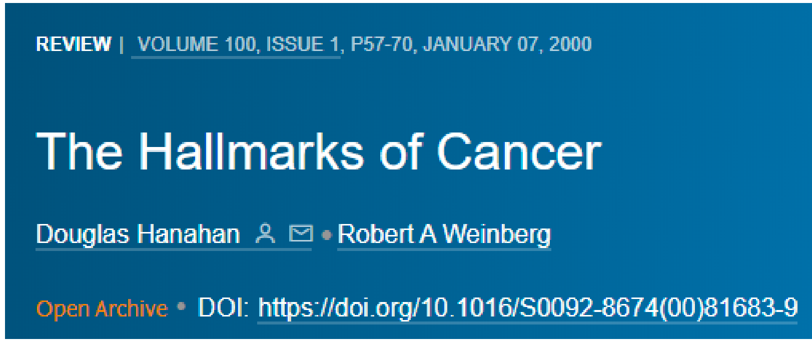
New blood vessels via VEGF

Mutations in cell-adhesion CDH1

Mutations in telomerase


Sustaining proliferative signaling
Resisting cell death
Evading growth suppressors
Inducing angiogenesis
Activating invasion and metastasis
Enabling replicative immortality

Hanahan and Weinberg, 2011


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

The Hallmarks of Cancer

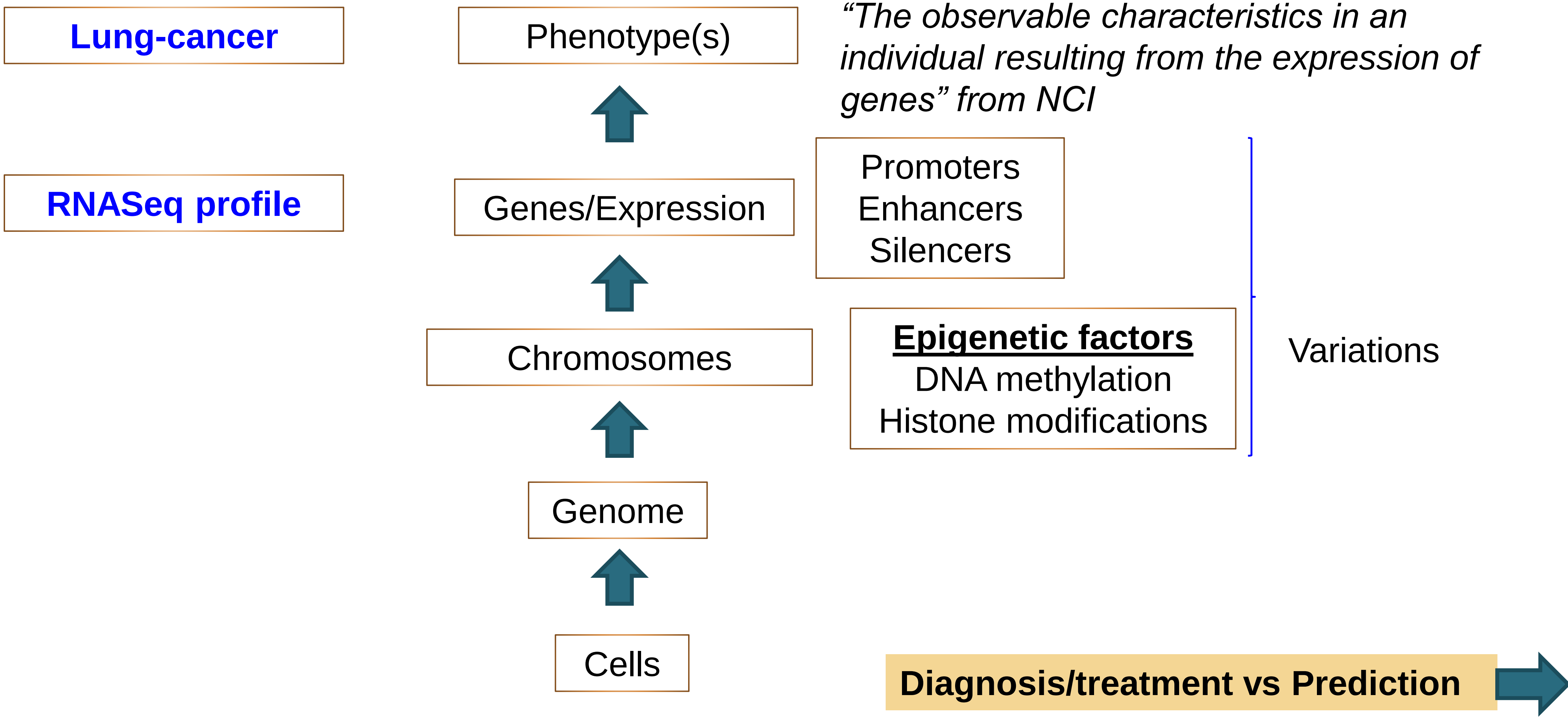
Douglas Hanahan • Robert A Weinberg

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

Overview of Genotype/phenotypes?

Influence of genomic features on phenotypes: An overview

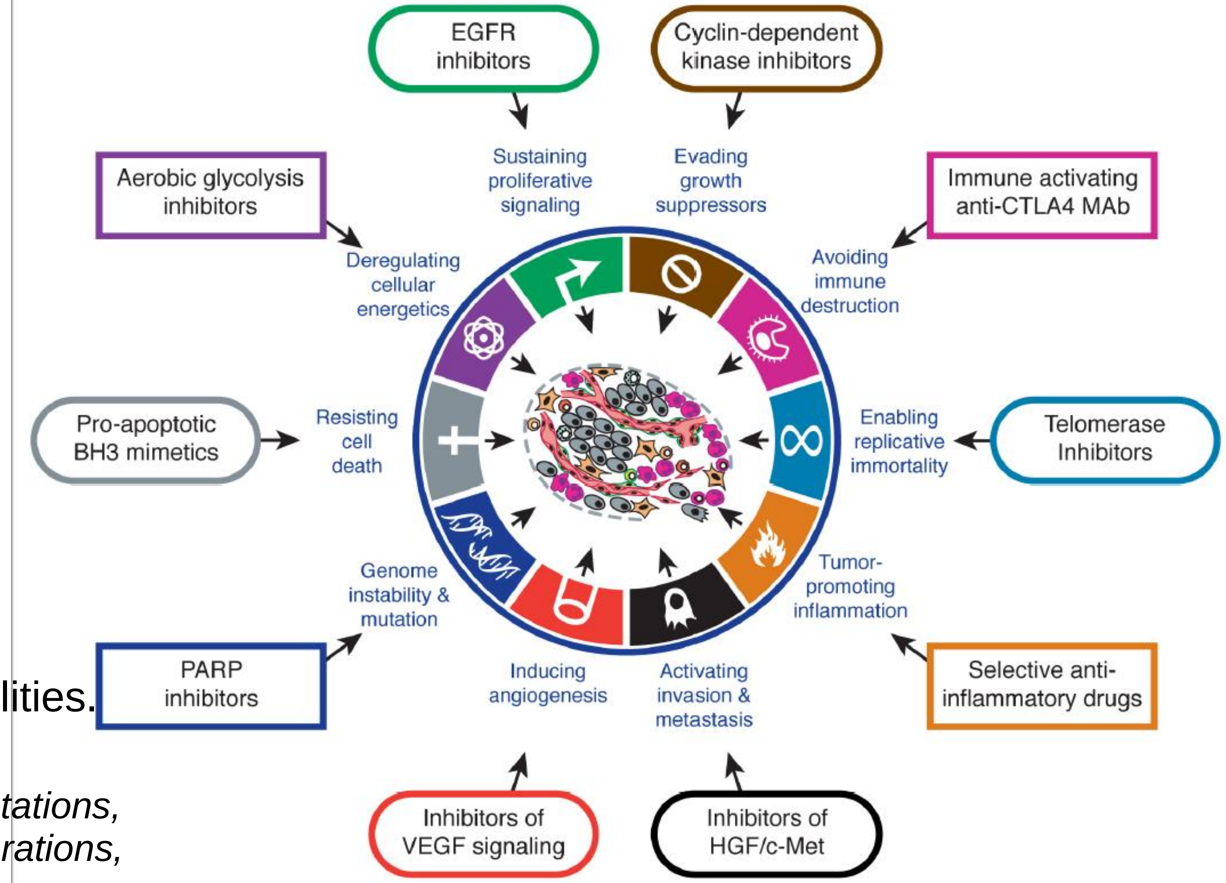
“The observable characteristics in an individual resulting from the expression of genes” from NCI



Treatment vs Type-Prediction

- **Treatment**
  - Gene-centric (or a slice of pathway)
  - Disease:
    - Tumor is called a gastrointestinal stromal tumor, or GIST
    - Medicine/inhibitor: Imatinib targeting BCR/KIT

- **Detecting Type**
  - Genomic instability in Cancer Cells → Random mutations → rare genetic changes that can orchestrate hallmark capabilities. *(Hanahan and Weinberg 2011)*
  - *"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
  - https://pubmed.ncbi.nlm.nih.gov/26963104/ (PLOS, 2016)

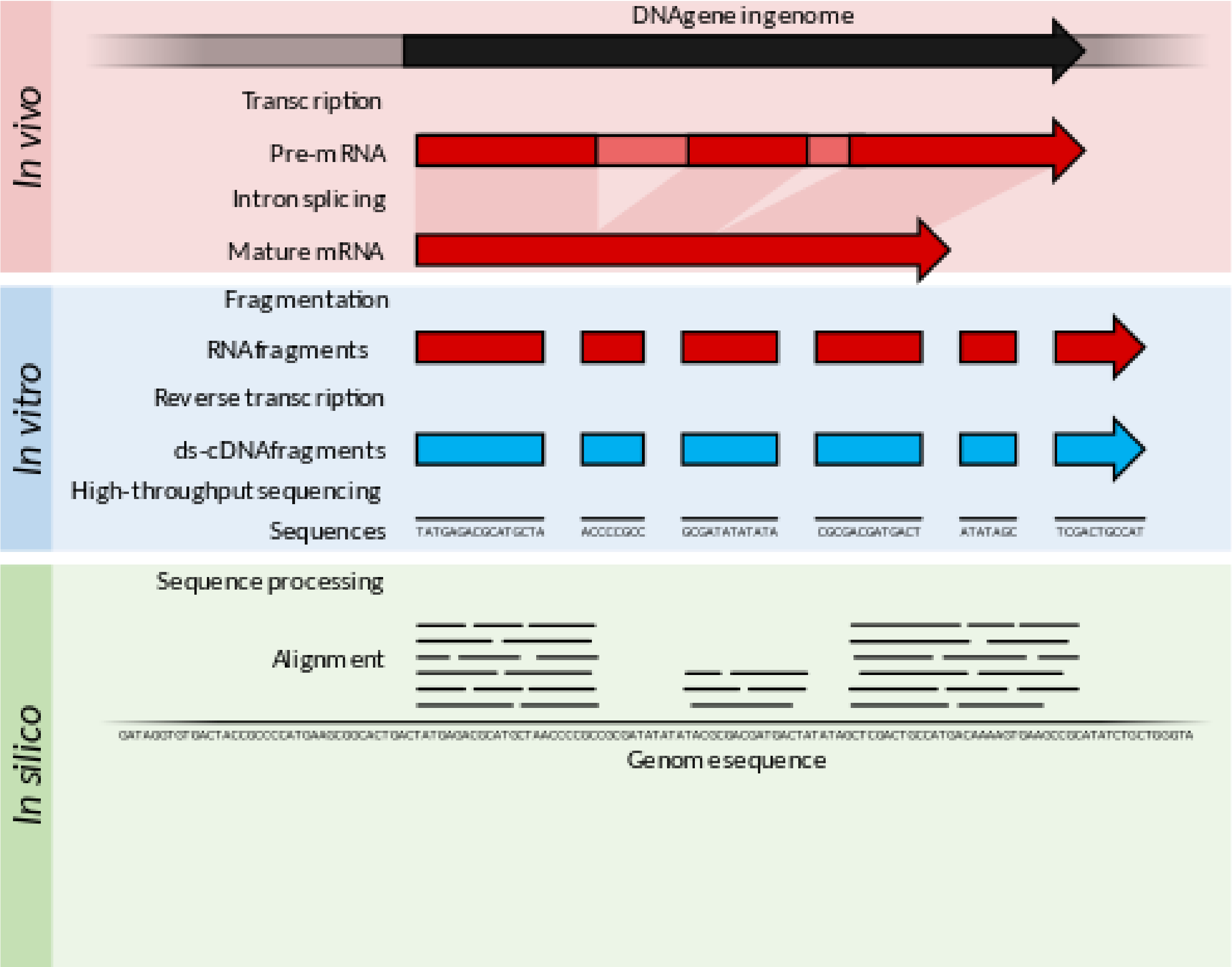

EGFR inhibitors
Cyclin-dependent kinase inhibitors
Aerobic glycolysis inhibitors
Sustaining proliferative signaling
Evading growth suppressors
Immune activating anti-CTLA4 MAb
Deregulating cellular energetics
Avoiding immune destruction
Pro-apoptotic BH3 mimetics
Resisting cell death
Enabling replicative immortality
Telomerase Inhibitors
Genome instability & mutation
Tumor-promoting inflammation
PARP inhibitors
Inducing angiogenesis
Activating invasion & metastasis
Selective anti-inflammatory drugs
Inhibitors of VEGF signaling
Inhibitors of HGF/c-Met

Hanahan and Weinberg, 2011

Expression data

NGS

NGS



Spliced to become mature mRNA

mRNA is extracted

mRNA captured/fragmented/copied into stable ds-cDNA

Sequenced

Reference Genome

Data source: The Cancer Genome Atlas (TCGA)

Frederick National Laboratory for Cancer Research

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- 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

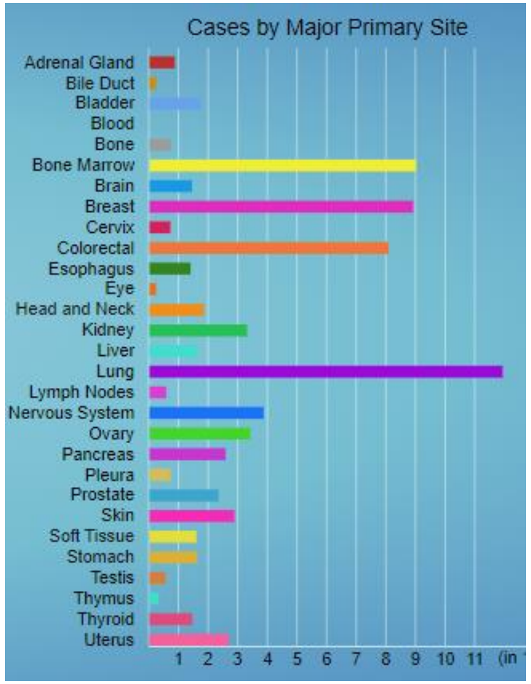
https://www.cancer.gov/about-nci/organization/ccg/research/structural-genomics/tcga

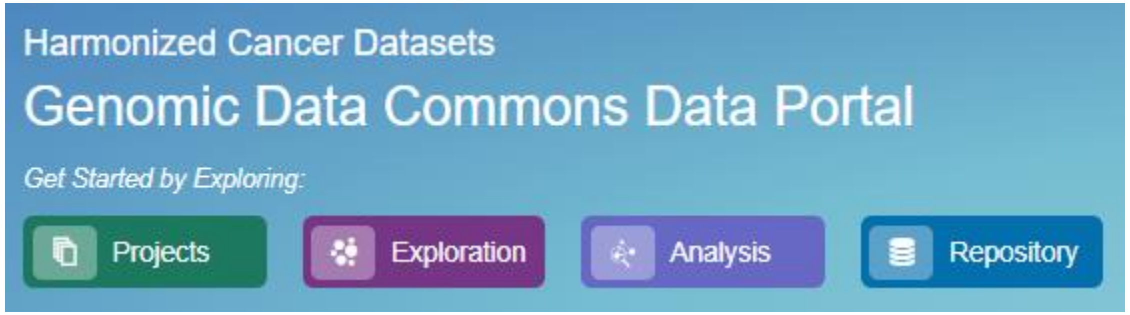
Data Harmonization: GDC (https://gdc.cancer.gov/)

- 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



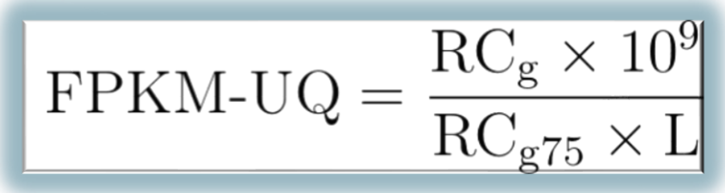

Harmonized Cancer Datasets

Genomic Data Commons Data Portal

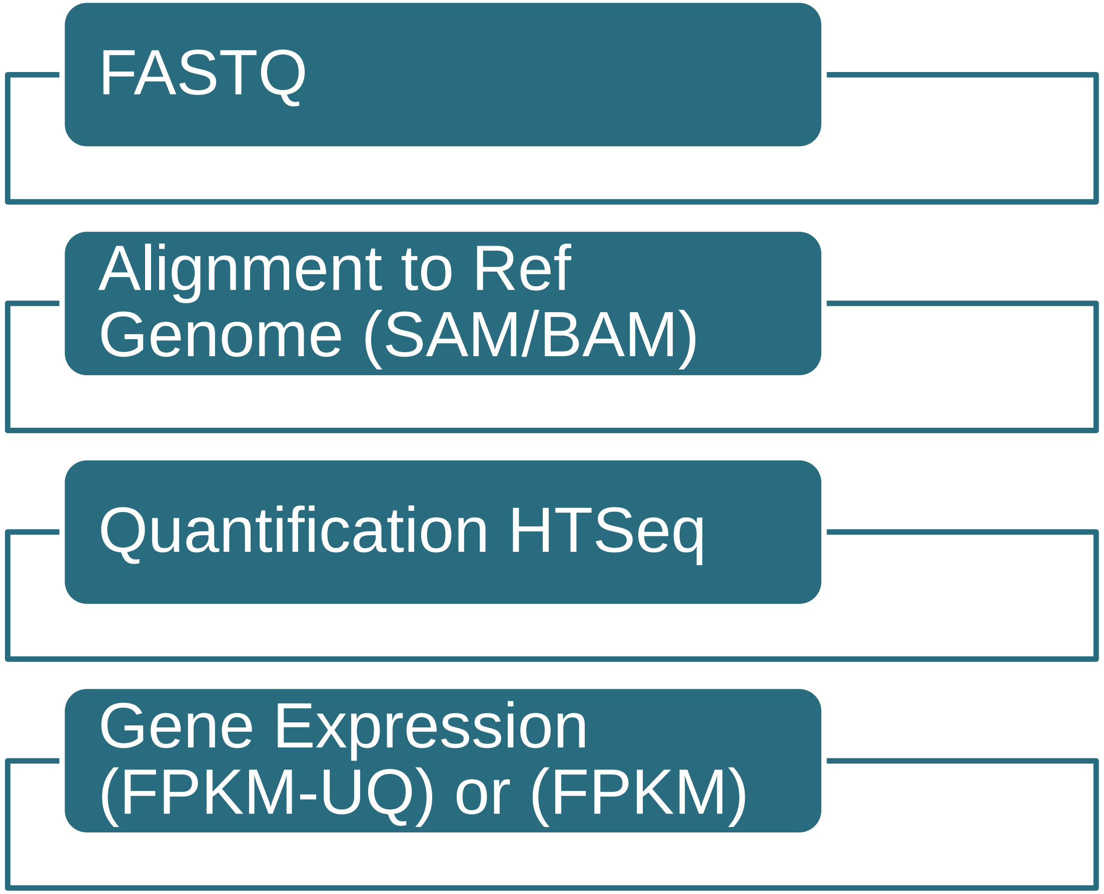
Get Started by Exploring:

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**

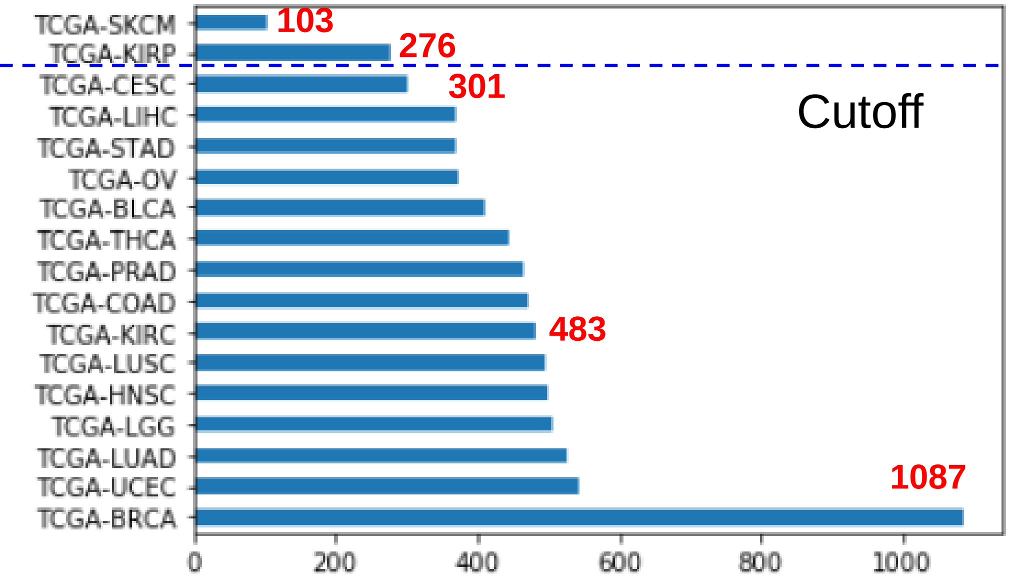


$$\mathrm{FPKM\text{-}UQ} = \frac{\mathrm{RC_g} \times 10^9}{\mathrm{RC_{g75}} \times \mathrm{L}}$$


FASTQ
Alignment to Ref Genome (SAM/BAM)
Quantification HTSeq
Gene Expression (FPKM-UQ) or (FPKM)

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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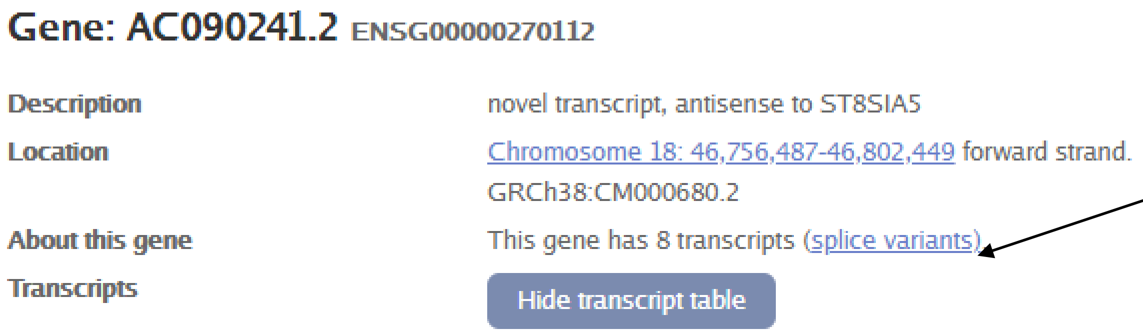


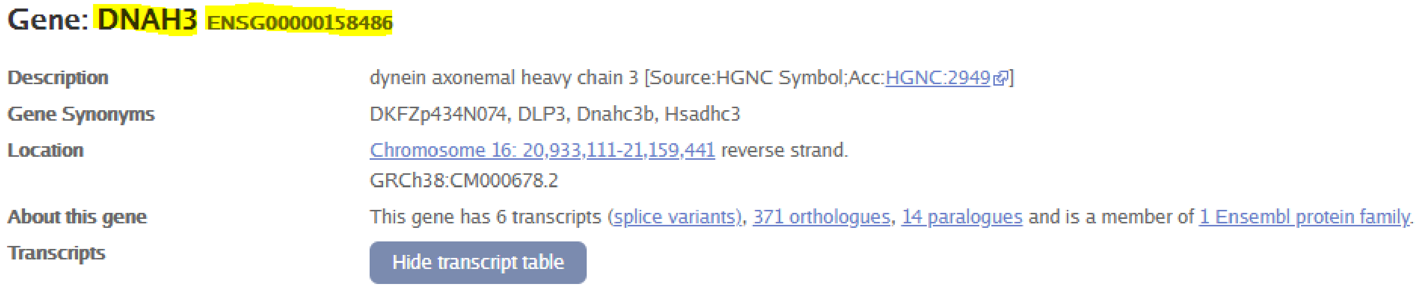
Gene: AC090241.2 ENSG00000270112

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



Gene: DNAH3 ENSG00000158486

Description dynein axonemal heavy chain 3 [Source:HGNC Symbol;Acc:HGNC:2949]

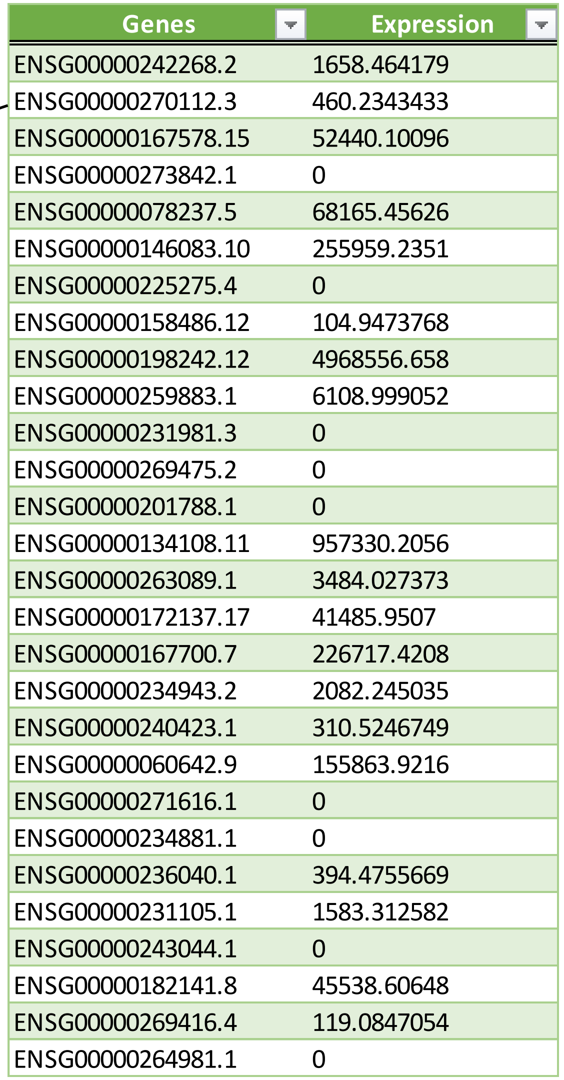
Gene Synonyms DKFZp434N074, DLP3, Dnahc3b, Hsadhc3

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

TCGA-BRCA



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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

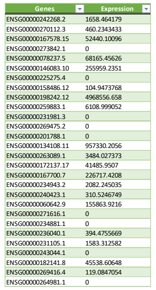
60,483 transcripts

Data Preparation

Breast Cancer

60,484 transcripts

Sample1



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ENSG00000259883.1	6108.999052
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ENSG00000269475.2	0
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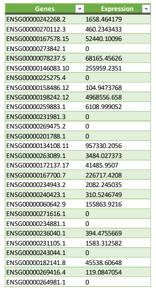
Sample2



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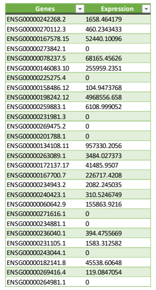
Sample3



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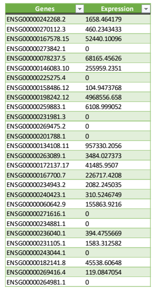
Sample4



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ENSG00000225275.4	0
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ENSG00000269475.2	0
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ENSG00000243044.1	0
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ENSG00000264981.1	0

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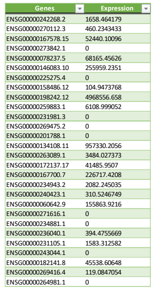
Sample297



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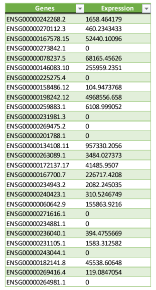
Sample298



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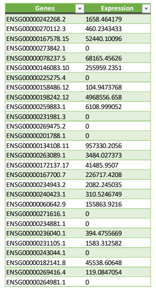
Sample299



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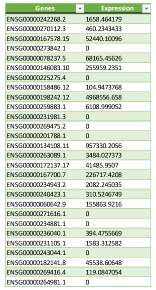
Sample300



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Data Preparation

Frederick National Laboratory for Cancer Research

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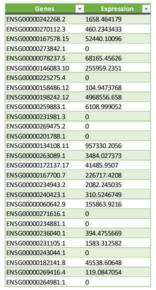
Sample1 Sample2 Sample3 Sample4 Sample297 Sample298 Sample299 Sample300

Breast Cancer



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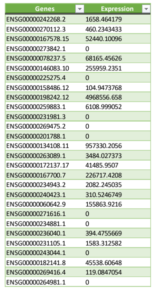

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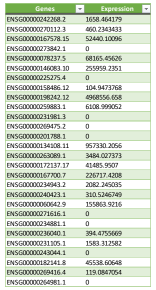

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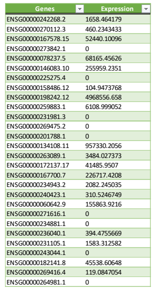

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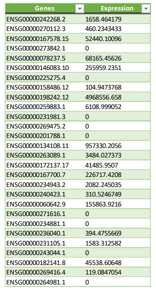

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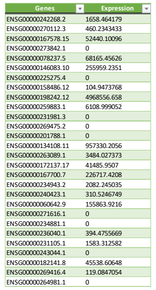

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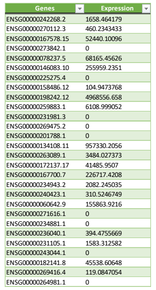

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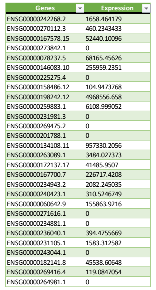

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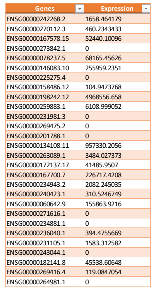
Lung Cancer



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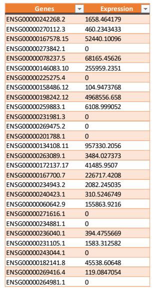

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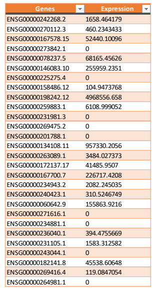

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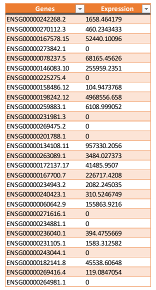

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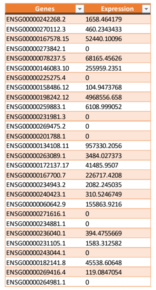

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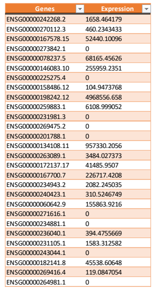

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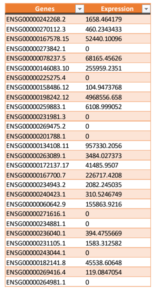

Genes	Expression
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ENSG00000263089.1	3484.027373
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ENSG00000240423.1	310.5246749
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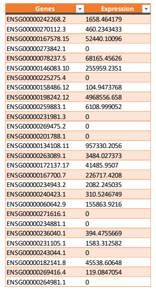

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ENSG00000225275.4	0
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ENSG00000167700.7	226717.4208
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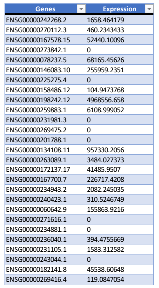
ENSG00000269416.4	119.0847054
ENSG00000264981.1	0

Kidney Cancer



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ENSG00000225275.4	0
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ENSG00000271616.1	0
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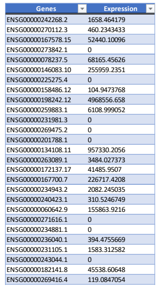

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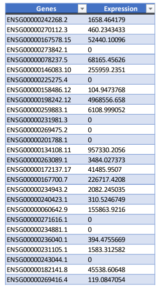

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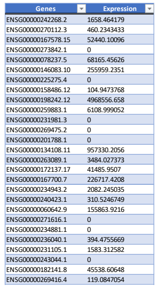

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ENSG00000234881.1	0
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ENSG00000231105.1	1583.312582
ENSG00000243044.1	0
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ENSG00000269416.4	119.0847054

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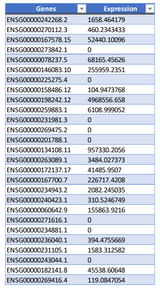

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ENSG00000231981.3	0
ENSG00000269475.2	0
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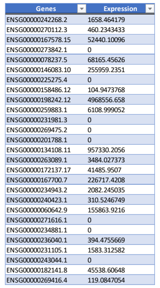

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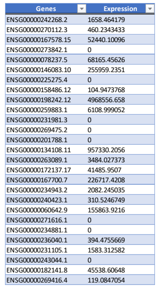

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ENSG00000263089.1	3484.027373
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ENSG00000167700.7	226717.4208
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ENSG00000240423.1	310.5246749
ENSG00000060642.9	155863.9216
ENSG00000271616.1	0
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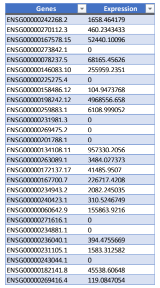

Genes	Expression
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ENSG00000231105.1	1583.312582
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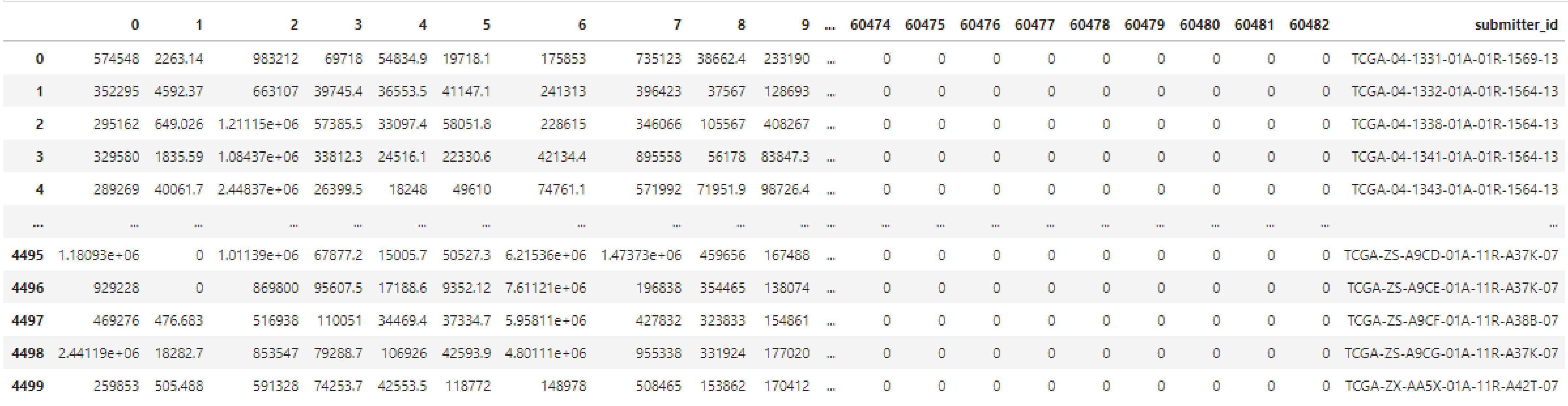
ENSG00000269416.4	119.0847054

Merged Sample Expression Data

Genes

SAMPLES



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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
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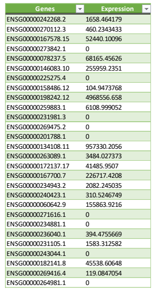
4499	259853	505.488	591328	74253.7	42553.5	118772	148978	508465	153862	170412	...	0	0	0	0	0	0	0	0	0	TCGA-ZX-AA5X-01A-11R-A42T-07

4500 rows × 60484 columns

Transpose and add as a row



Genes	Expression
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ENSG00000078237.5	68165.45626
ENSG00000146083.10	255959.2351
ENSG00000225275.4	0
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ENSG00000198242.12	4968556.658
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ENSG00000231105.1	1583.312582
ENSG00000243044.1	0
ENSG00000182141.8	45538.60648
ENSG00000269416.4	119.0847054
ENSG00000264981.1	0

Quantifying mRNA abundance and Scaling

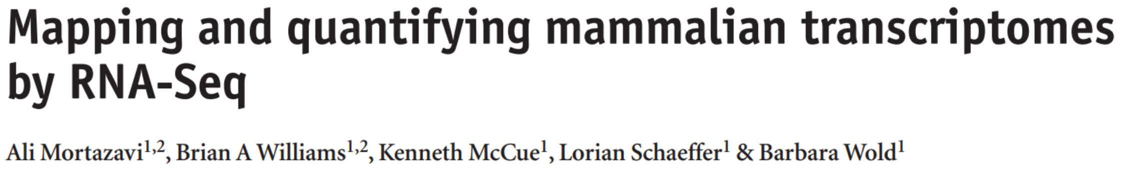
- **Use GDC harmonization expression data (X = FPKM or FPKM-UQ)**
- **FPKM-UQ or FPKM is rescaled to TPM using the following formula.**

Thanks to Andrew for his help in simplifying the scaling slides

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

- **TPM has nice mathematical properties and a stable entity and can be compared across samples**

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

TCGA-CESC
TCGA-LIHC
TCGA-STAD
TCGA-OV
TCGA-BLCA
TCGA-THCA
TCGA-PRAD
TCGA-COAD
TCGA-KIRC
TCGA-LUSC
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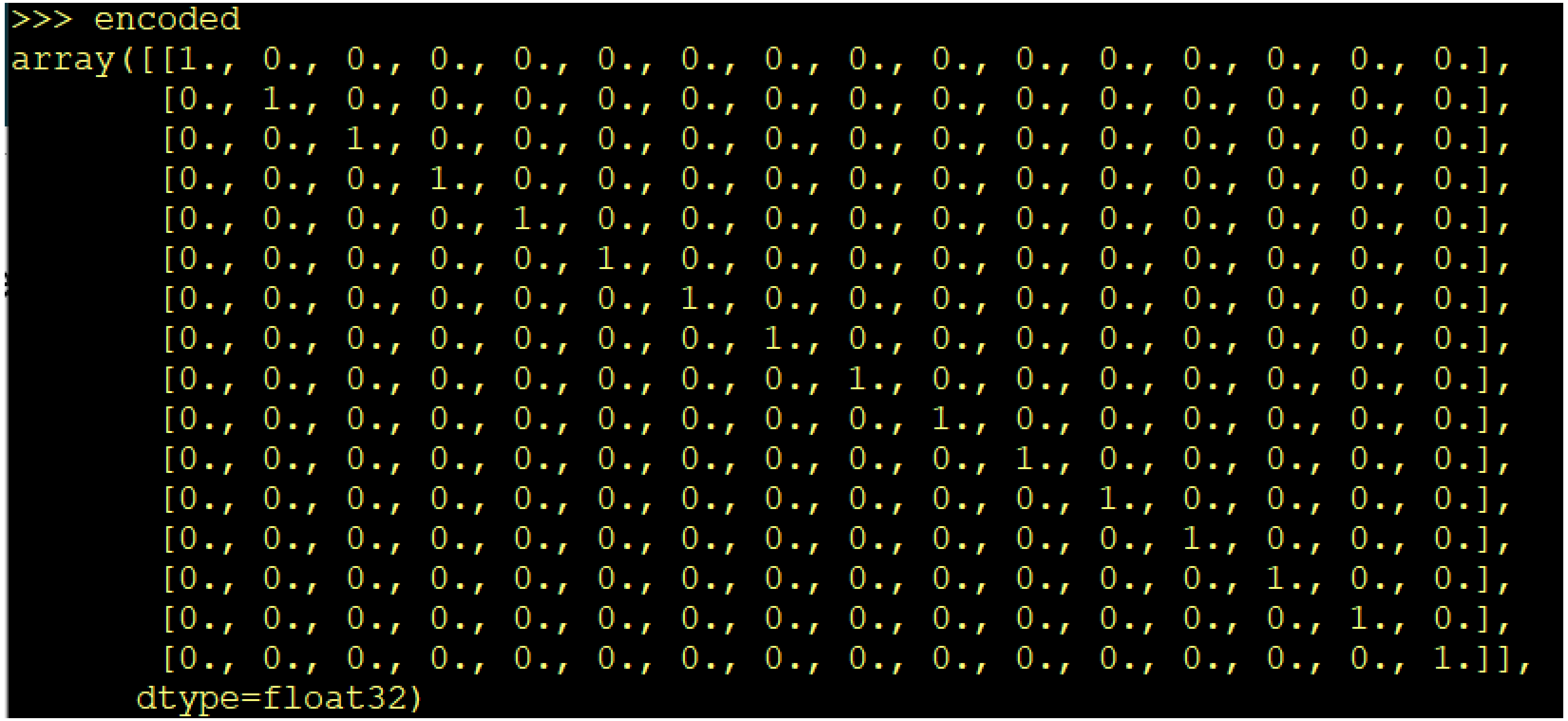
TCGA-LUAD
TCGA-UCEC
TCGA-BRCA



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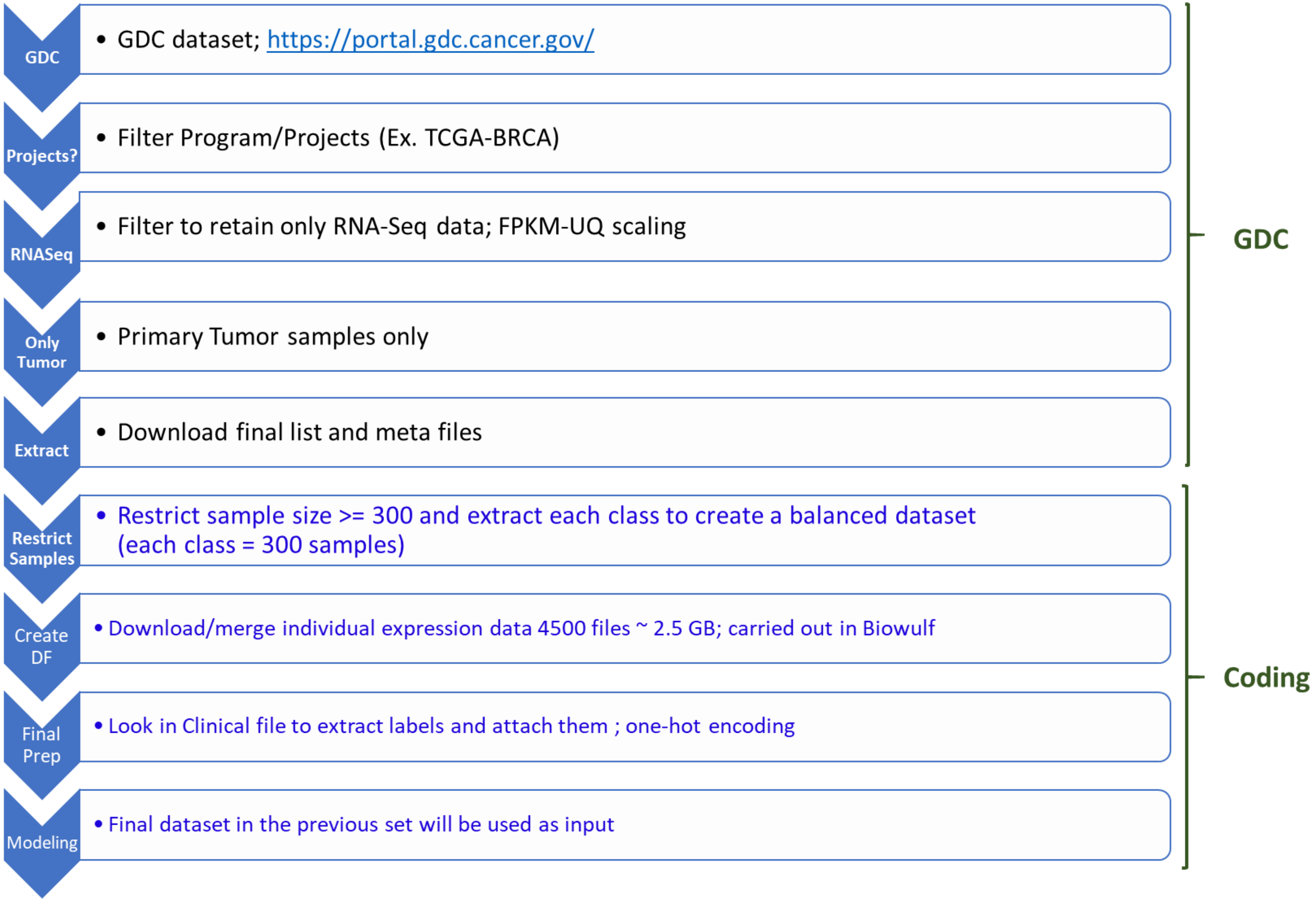
Data preparation steps summary



GDC
- GDC dataset; https://portal.gdc.cancer.gov/

Projects?
- Filter Program/Projects (Ex. TCGA-BRCA)

RNASeq
- Filter to retain only RNA-Seq data; FPKM-UQ scaling

Only Tumor
- Primary Tumor samples only

Extract
- Download final list and meta files

Restrict Samples
- Restrict sample size >= 300 and extract each class to create a balanced dataset (each class = 300 samples)

Create DF
- Download/merge individual expression data 4500 files ~ 2.5 GB; carried out in Biowulf

Final Prep
- Look in Clinical file to extract labels and attach them ; one-hot encoding

Modeling
- Final dataset in the previous set will be used as input

GDC

Coding

Before we break for hands-on

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

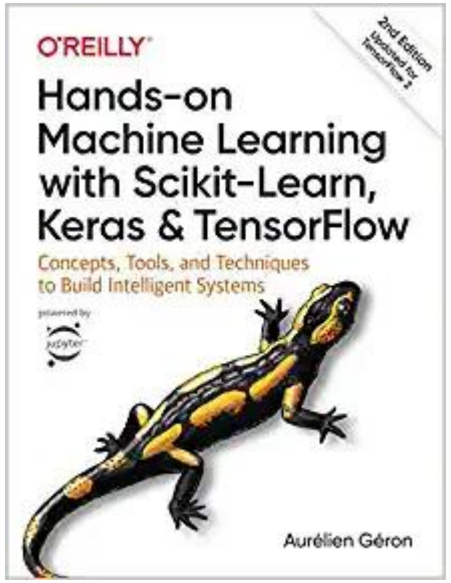
- **Will use Jupyter Notebook for sharing the code**
  - With little effort one can convert the Python code into R and still use Jupyter Notebook

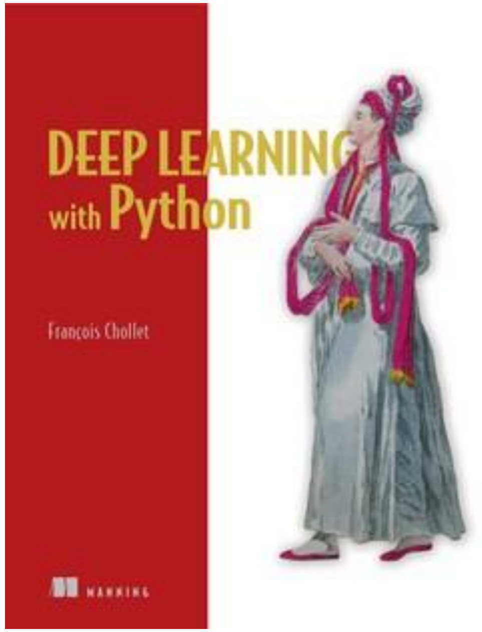
To be continued after hands-on

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

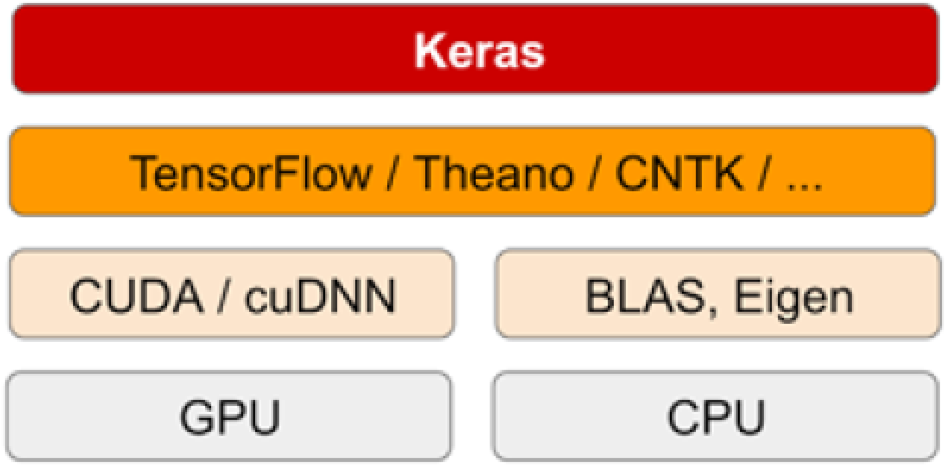
Before we begin the modeling section …

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


O'REILLY
2nd Edition Updated for TensorFlow 2
Hands-on Machine Learning with Scikit-Learn, Keras & TensorFlow
Concepts, Tools, and Techniques to Build Intelligent Systems
powered by jupyter
Aurélien Géron



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



Keras

TensorFlow / Theano / CNTK / ...

CUDA / cuDNN

BLAS, Eigen

GPU

CPU

These are good books for beginners and up

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

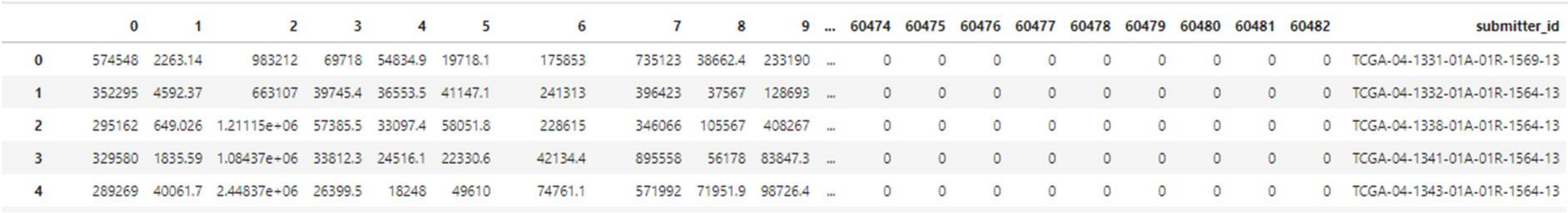
- Train a machine learning
  - Model refers to learning its parameters (for an Architecture), which typically involves minimizing a loss function on training data with the aim of making accurate predictions on unseen (test) data

Supervised Learning:

Data: (x,y) ; where x is the genomic expression profile ; y is the cancer classes

Goal? Learn the function that maps
x → y

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**

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(x):
    y = 2.0 + 5.0 * x
    return(y)
```

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

```
Model ← lm( y ~ x)
```

- Neural Network using the data learn the algorithm.

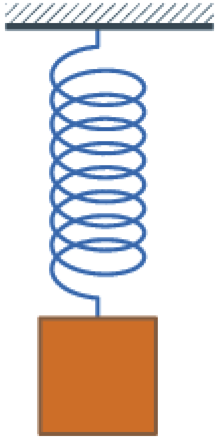
INPUT

ALGORITHM

OUTPUT

A Simple Network

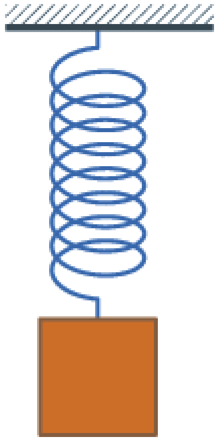
Input: Mass or M (kg)
Output: Length or L (m)



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



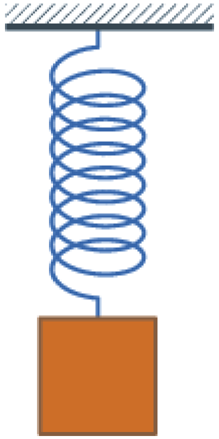
M	L
0.125	0.39
0.25	0.40
0.5	0.43
1	0.48
2	0.58
3	0.68

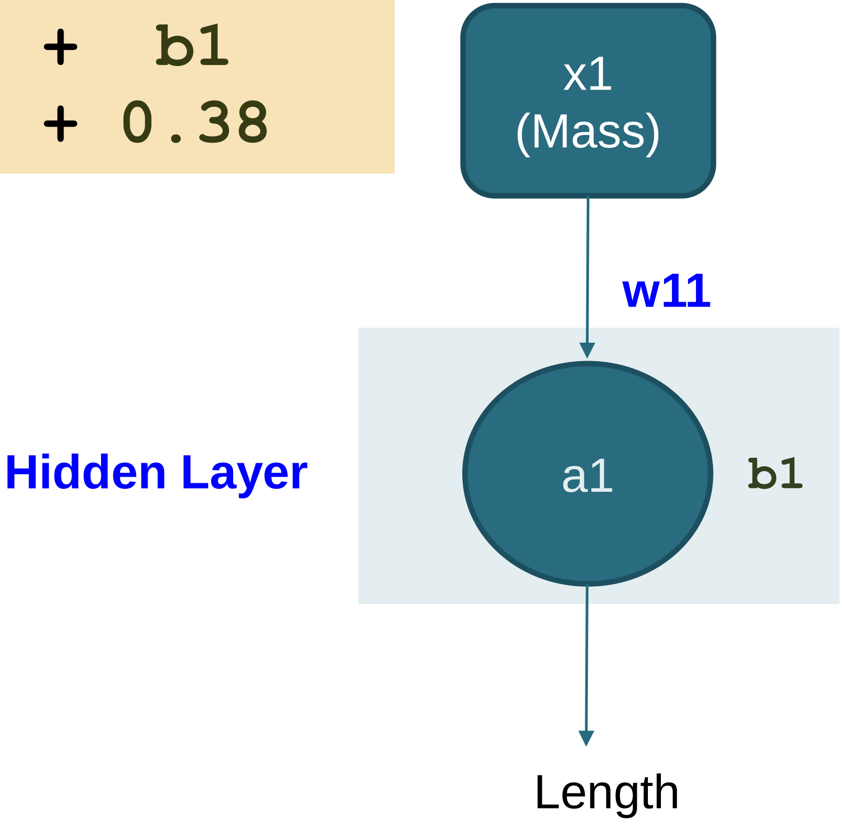
$$L = 0.1 * Mass + 0.38$$

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

A Simple Network

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





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)]
```

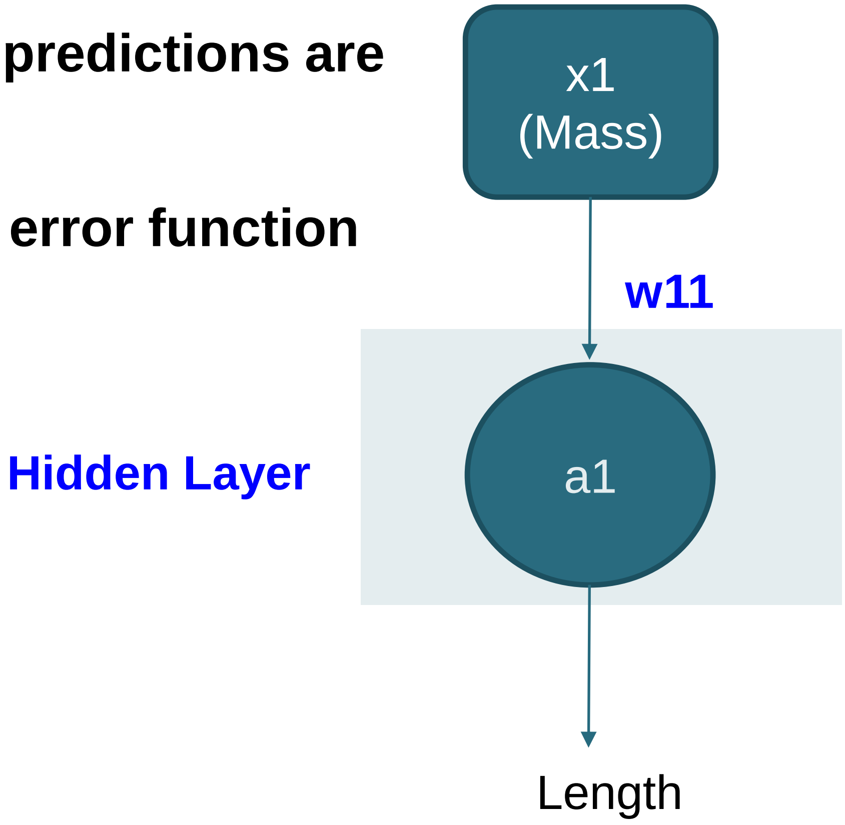
Based on Mary Attenborough, in Mathematics for Electrical Engineering and Computing, 2003

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 want to pick a set of w that minimizes the error function**

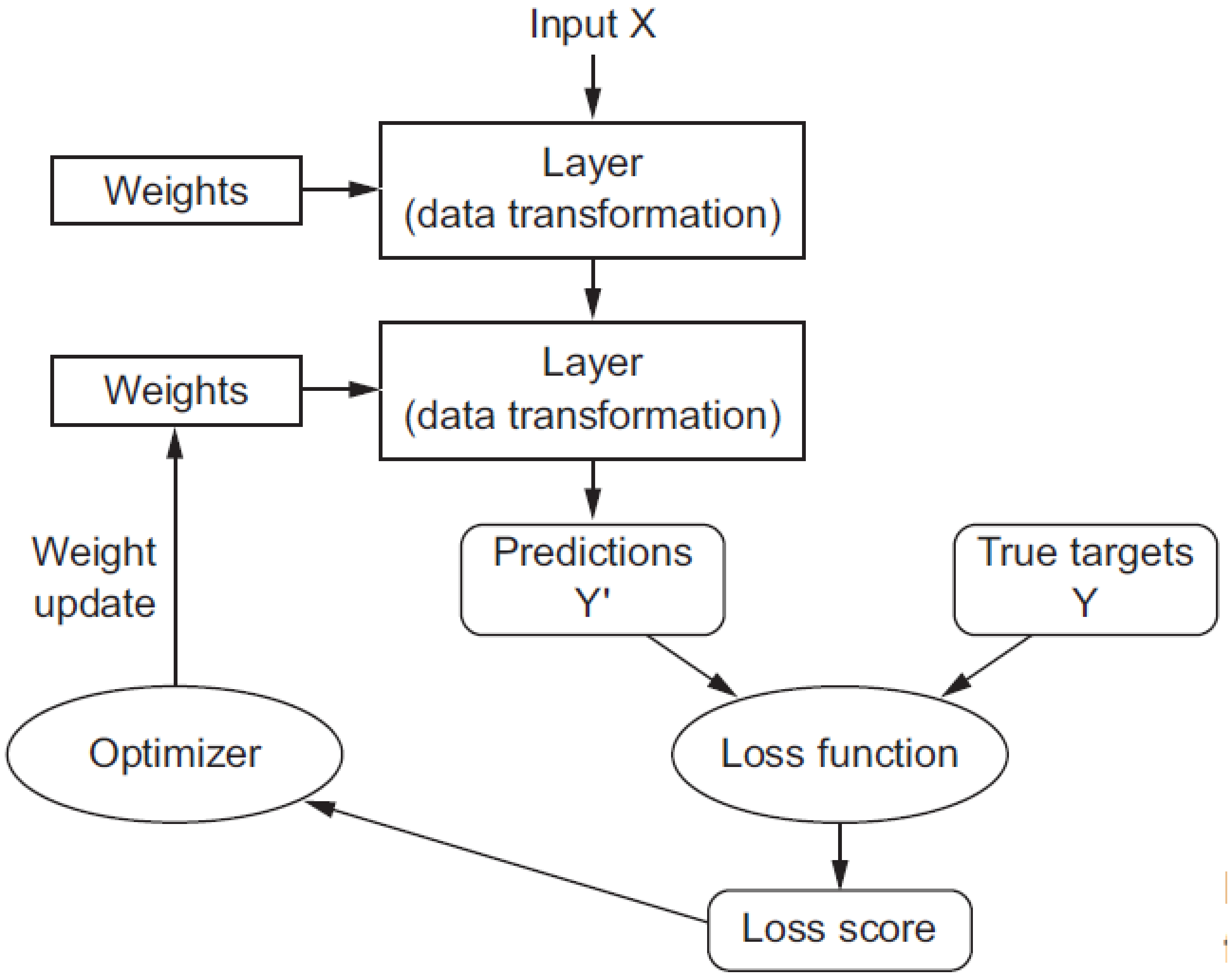


Deep Learning Procedure

Frederick National Laboratory for Cancer Research

sponsored by the National Cancer Institute

Taken from Deep Learning with Keras book



Vanilla network

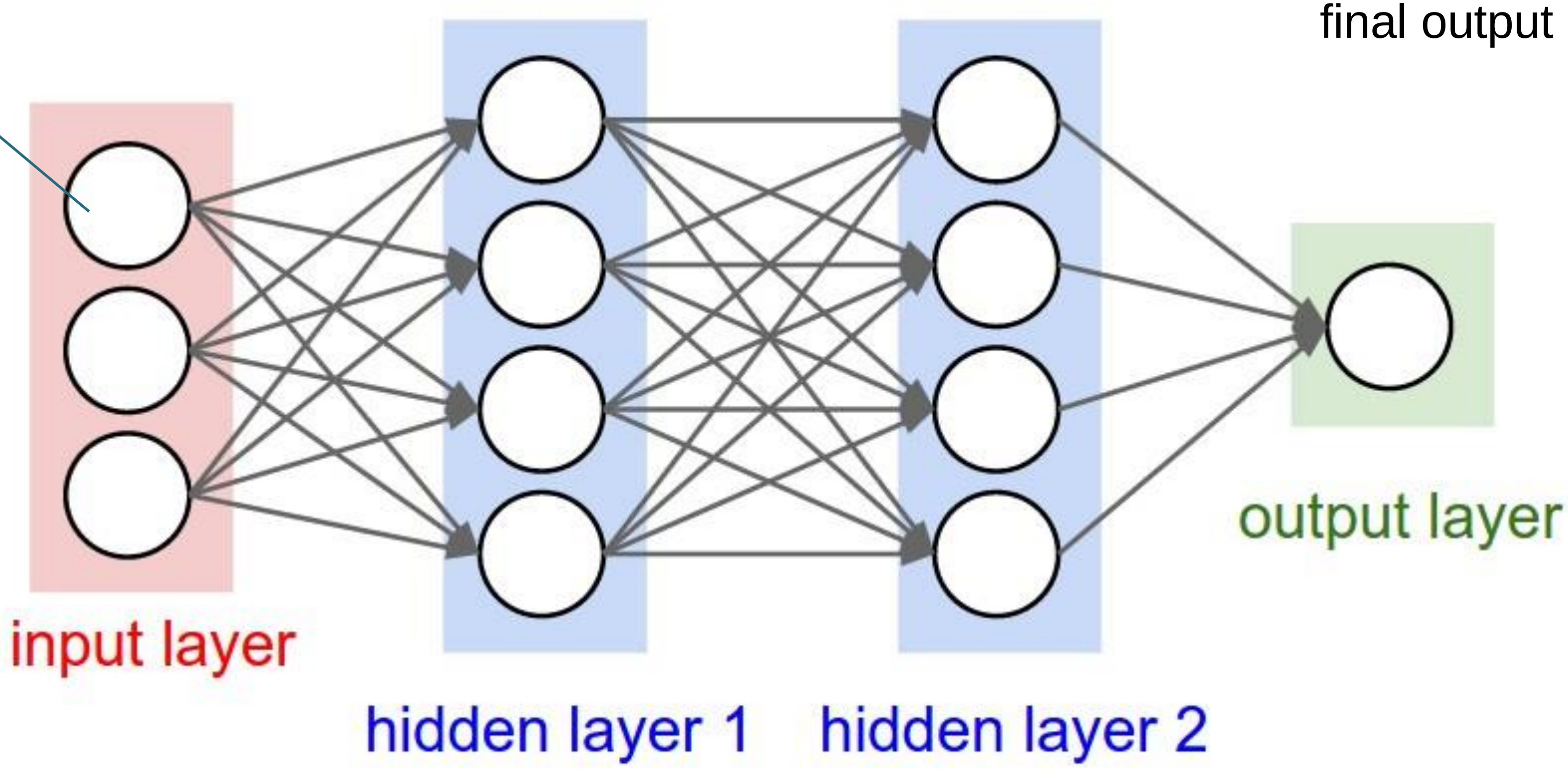
Each neuron receives input from all the neurons in the previous layer (densely connected)

Neuron: a unit that holds a number

representations

representations

representations
final output



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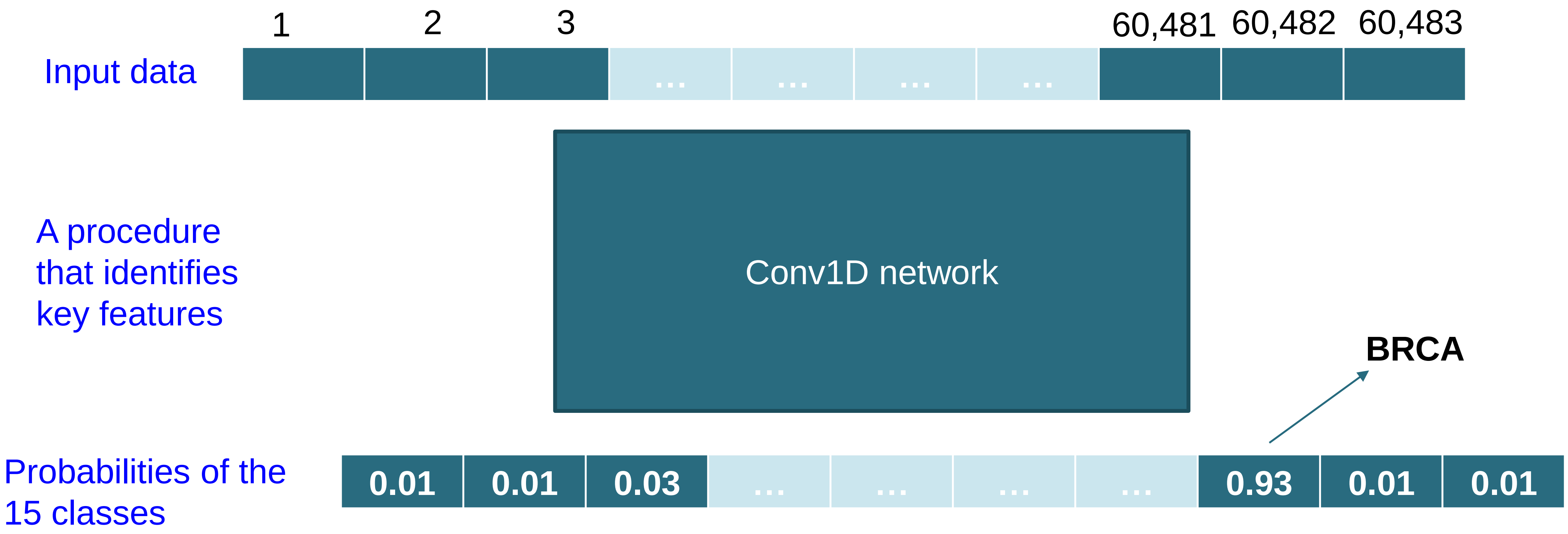
Convolutional Neural Network

- **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**



Input data

1 | 2 | 3 | … | … | … | … | 60,481 | 60,482 | 60,483

A procedure that identifies key features

Conv1D network

BRCA

Probabilities of the 15 classes

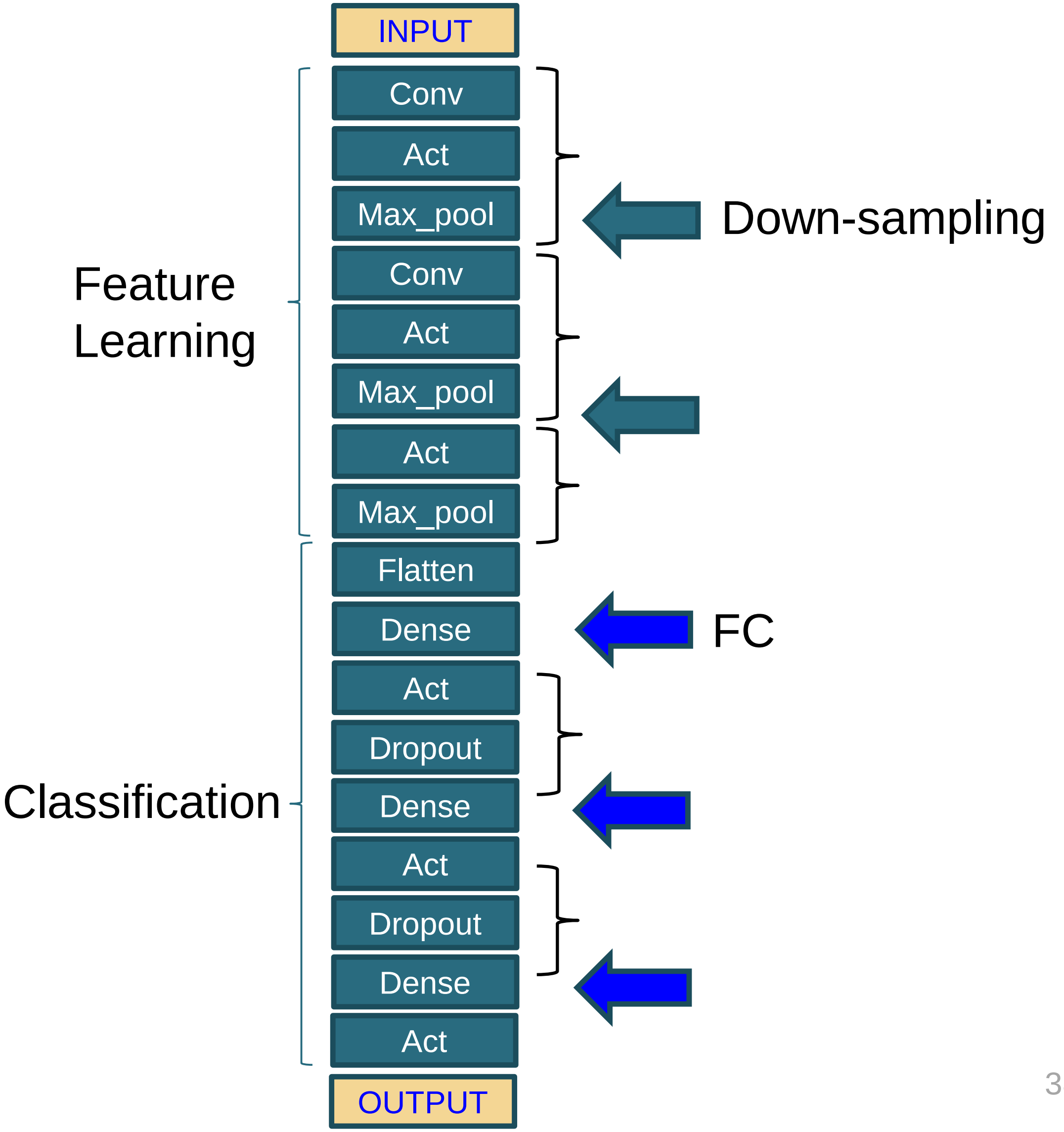
0.01 | 0.01 | 0.03 | … | … | … | … | 0.93 | 0.01 | 0.01

Components of conv1D

1. **Act: Activation**
2. **Conv: Convolution**
3. **Max_pool: Maxpooling**
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 (& domain knowledge).



ConvNets Architecture

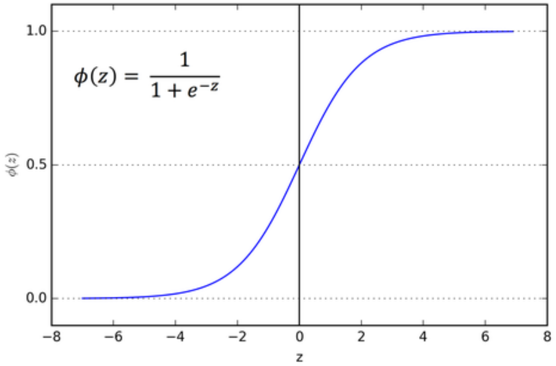
- **Depends on the problem**
- **Try that worked for a similar problem before you try new options**
- **[(CONV-RELU) * N - POOL?] * M - (FC-RELU)*K, SOFTMAX**
  - N is usually up to ~5
  - M is large
  - 0 <= K <= 2.
- **Trend is to use smaller filter and deeper architectures**
    - *Fei-Fei Li & Justin Johnson & Serena Yeung Lecture notes*

1. Activation Function

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

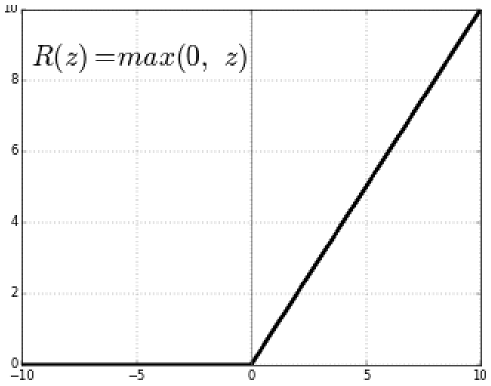
- **Sigmoid**
- **ReLU**
- **Leaky ReLU**
- **ELU**
- **Maxout**
- **Tanh**

Sigmoid

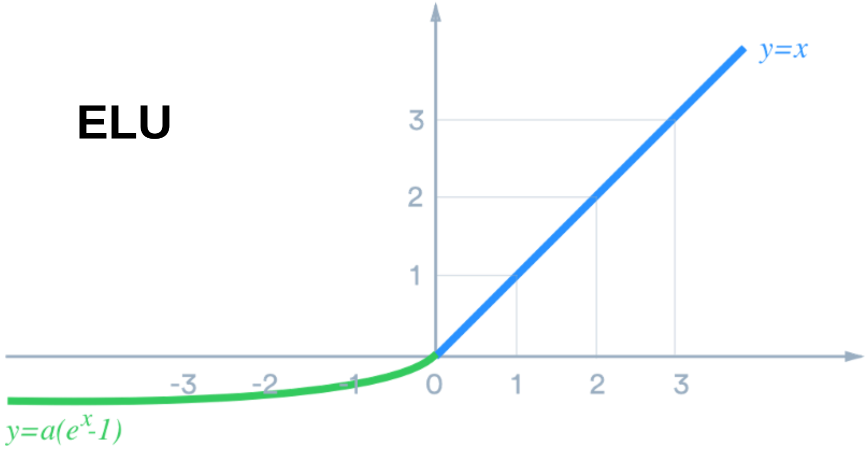


Squashes the #s to [0, 1]

ReLU

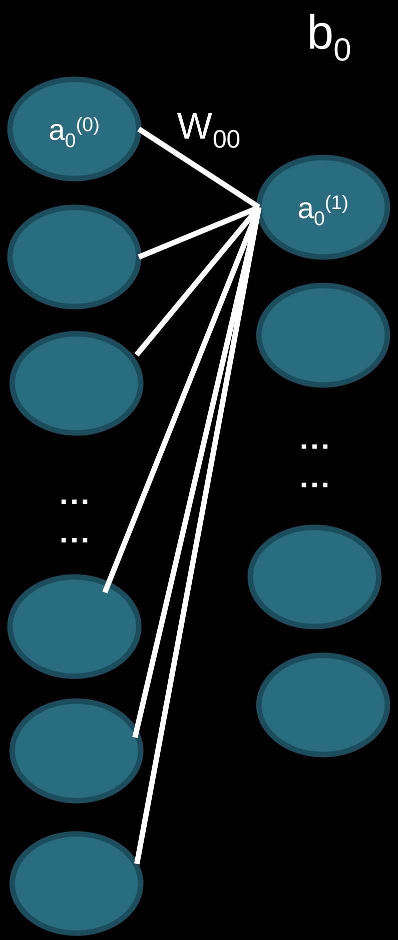


ELU



1. Activation function

$$a^{(L)} = \mathrm{ReLU}(\, w^{(L)} a^{(L-1)} - b^{(L)} \,)$$



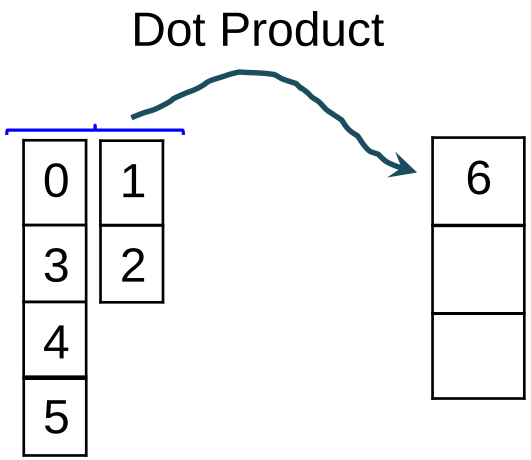
$$\mathrm{ReLU}\left(\begin{bmatrix} W_{0,0} & W_{0,1} & \cdots & W_{0,n} \\ W_{1,0} & W_{1,1} & \cdots & W_{1,n} \\ . & . & . & . \\ . & . & . & . \\ . & . & . & . \\ W_{k,0} & W_{k,1} & \cdots & W_{k,n} \end{bmatrix} \begin{bmatrix} a_0^{(0)} \\ a_1^{(0)} \\ . \\ . \\ . \\ a_n^{(0)} \end{bmatrix} + \begin{bmatrix} b_0 \\ b_1 \\ . \\ . \\ . \\ b_n \end{bmatrix}\right)$$

$$a_0^{(1)} = \mathrm{ReLU}(\, W_{00}a_0^{(0)} + W_{0,1}a_1^{(0)} + \ldots\, W_{0,n}a_n^{(0)} - b_0)\,)$$

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



2. Convolution

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

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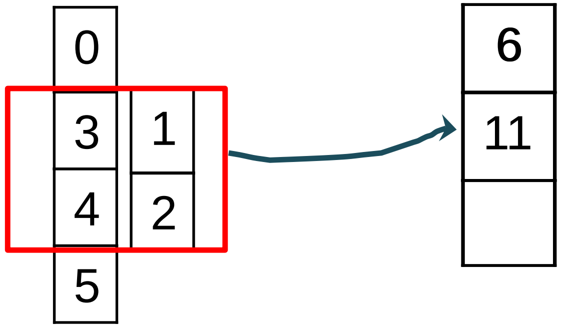
Dot Product



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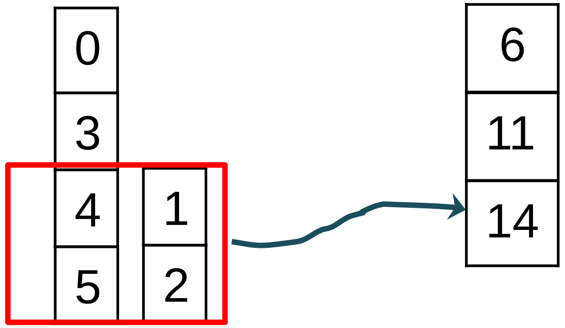
Dot Product



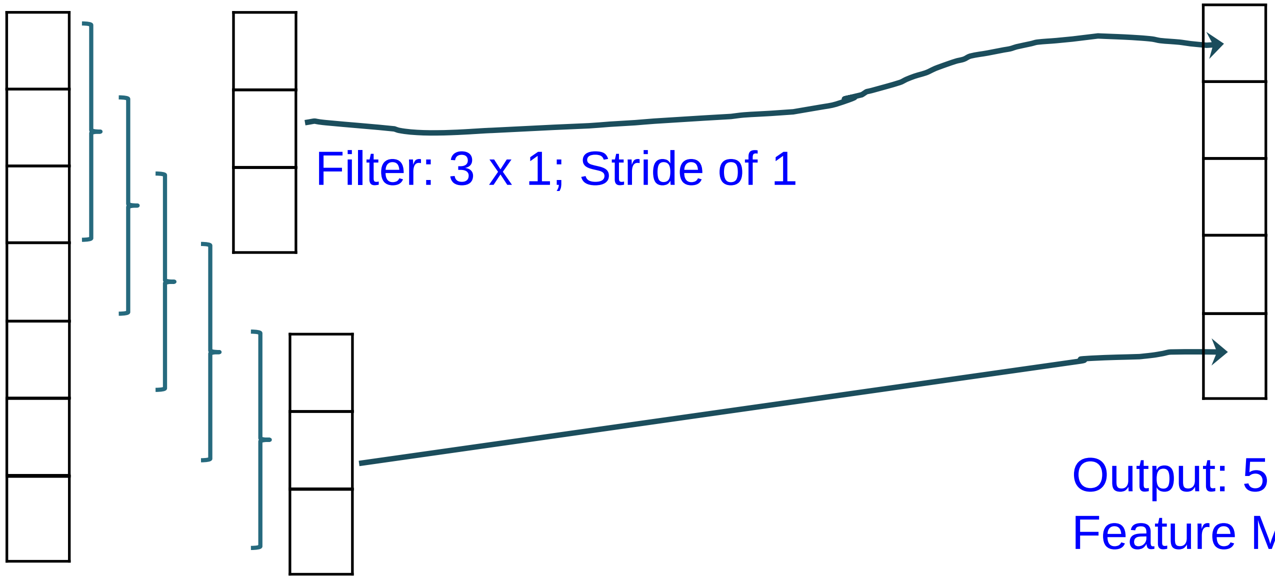
2. Convolution

Process of applying filter (<u>kernel</u>) 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

Dot product

Activation Map: 3 x 1



Filter: 3 x 1; Stride of 1

Output: 5 x 1
Feature Map

Data: 7 x 1

((N-F)/stride) + 1 will be the size after filtering

(7-3)/1+1 = 5 ;
zero padding on the border

2. Convolution

- **Summary**
- **Common settings**
  - Number of filters (K): Chosen in powers of 2 (ex. 32, 64, etc.)
  - Spatial Extent (F): 3 or 5
  - Stride (S): 1 or 2
  - Zero padding (P): 0, 1, 2

2. Convolution

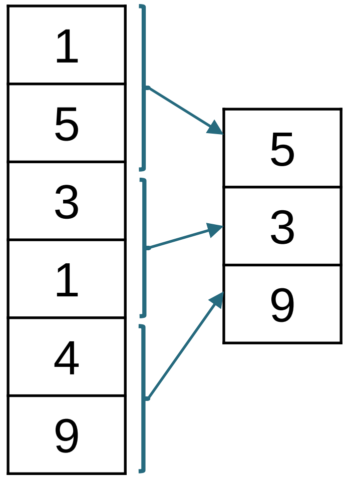
- **Convolution Layer**
  - Hyperparameters
    - Number of filters
    - Spatial extent
    - Stride
    - Amount of zero padding

Andrew, an expert in CANDLE, can help you with Hyperparameter optimization.

andrew.weisman@nih.gov

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

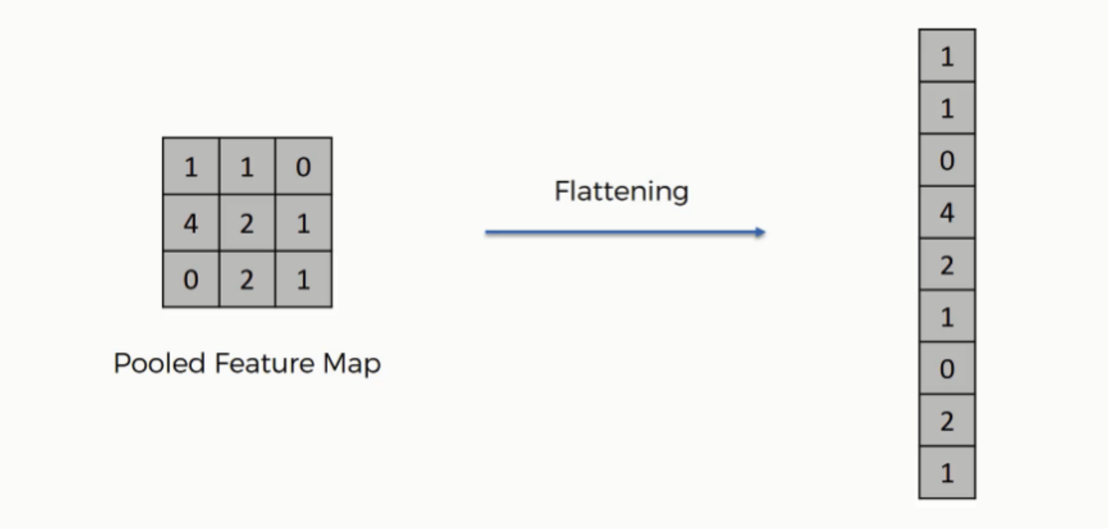
Each of these are activation and we are looking for

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

Common setting for filter 2 or 3

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)

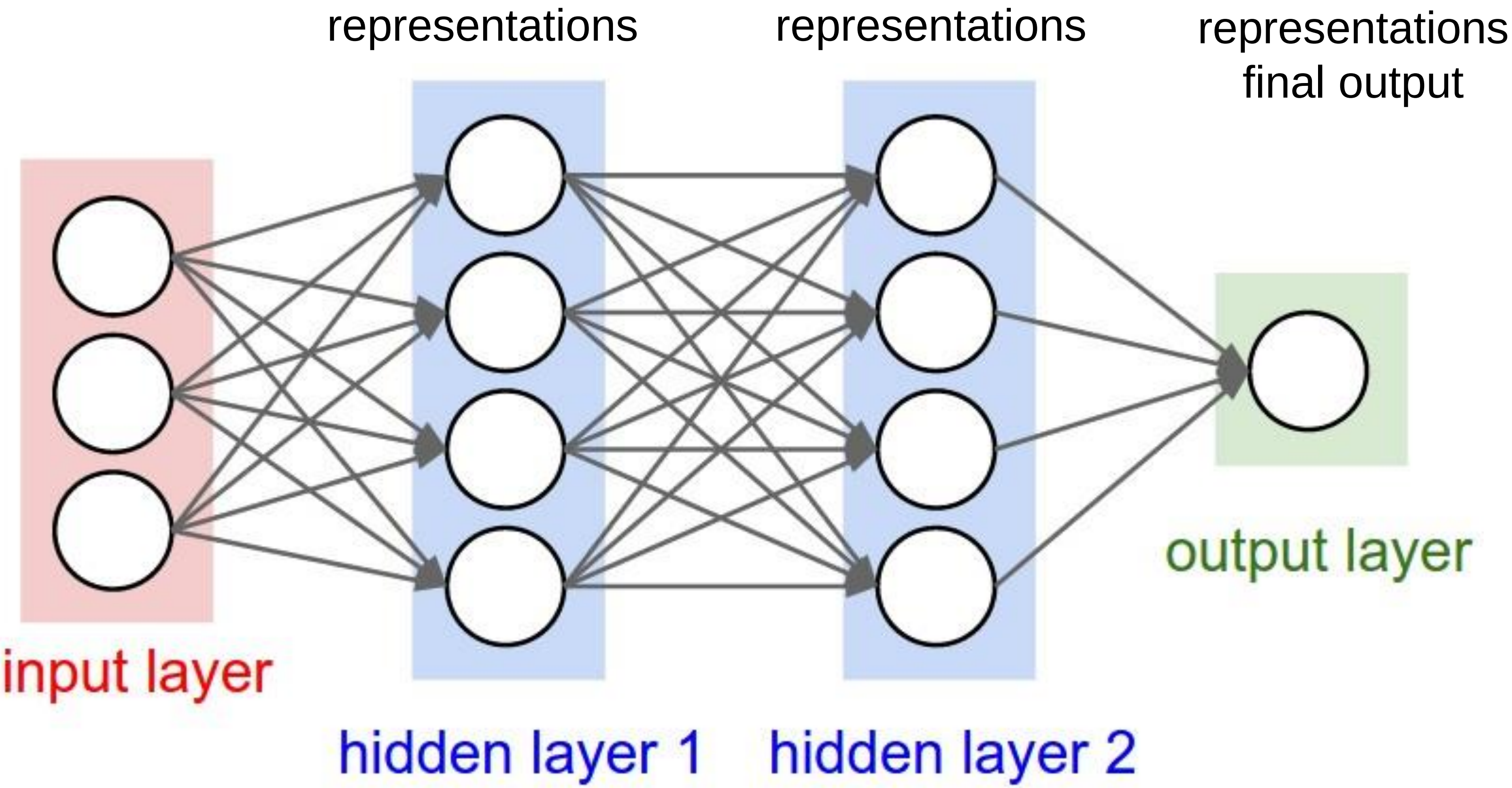


1	1	0
4	2	1
0	2	1

1
1
0
4
2
1
0
2
1

5. Dense

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



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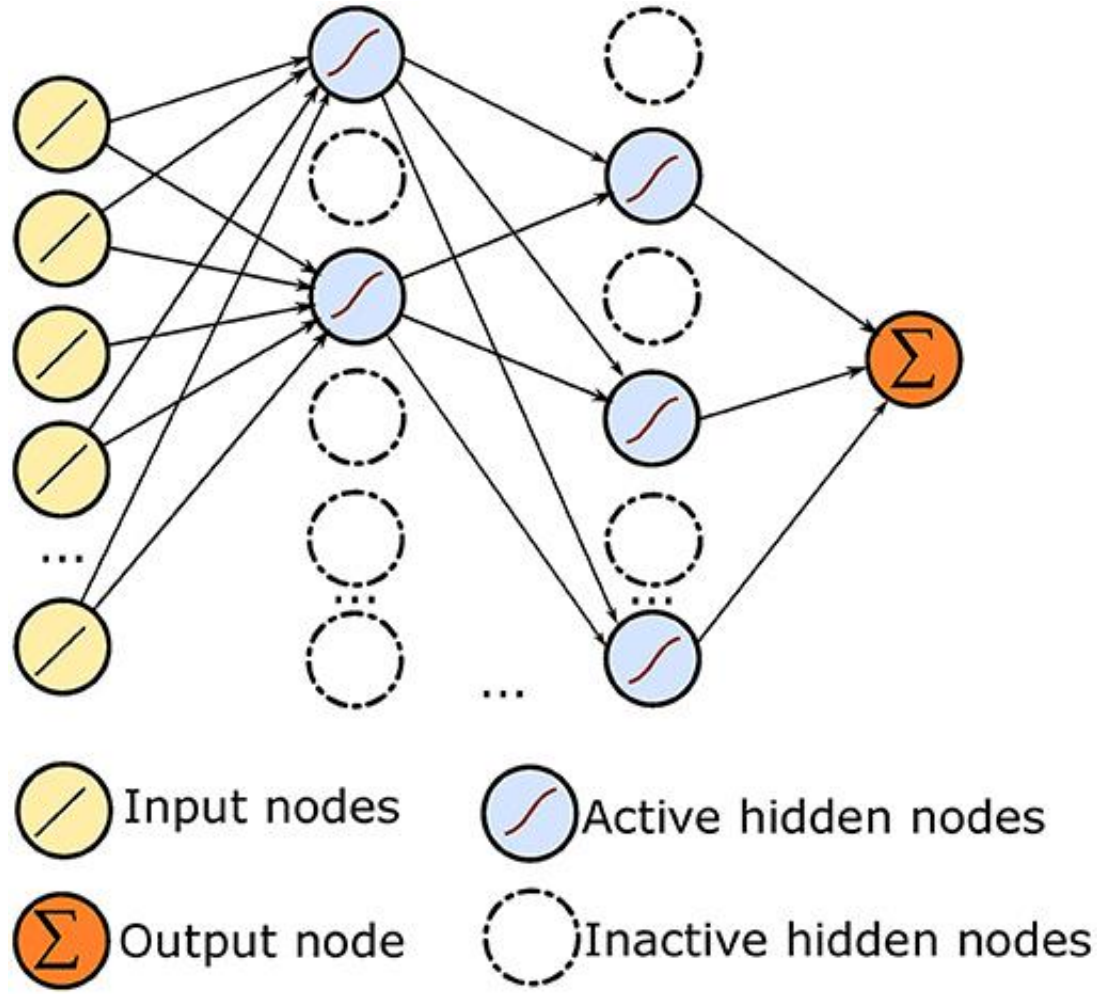
6. Dropout



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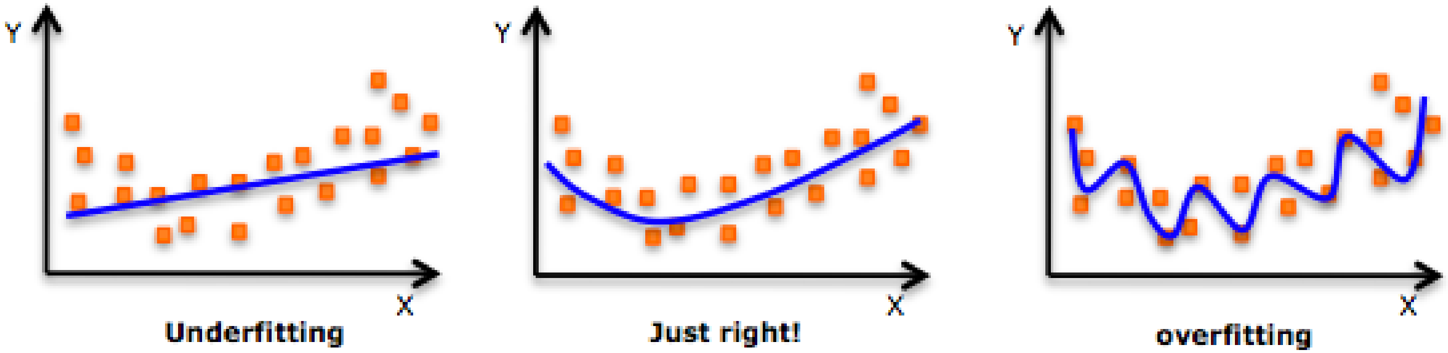
Imbalance in the weights among the nodes can lead to some node weights not contributing to the learning

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



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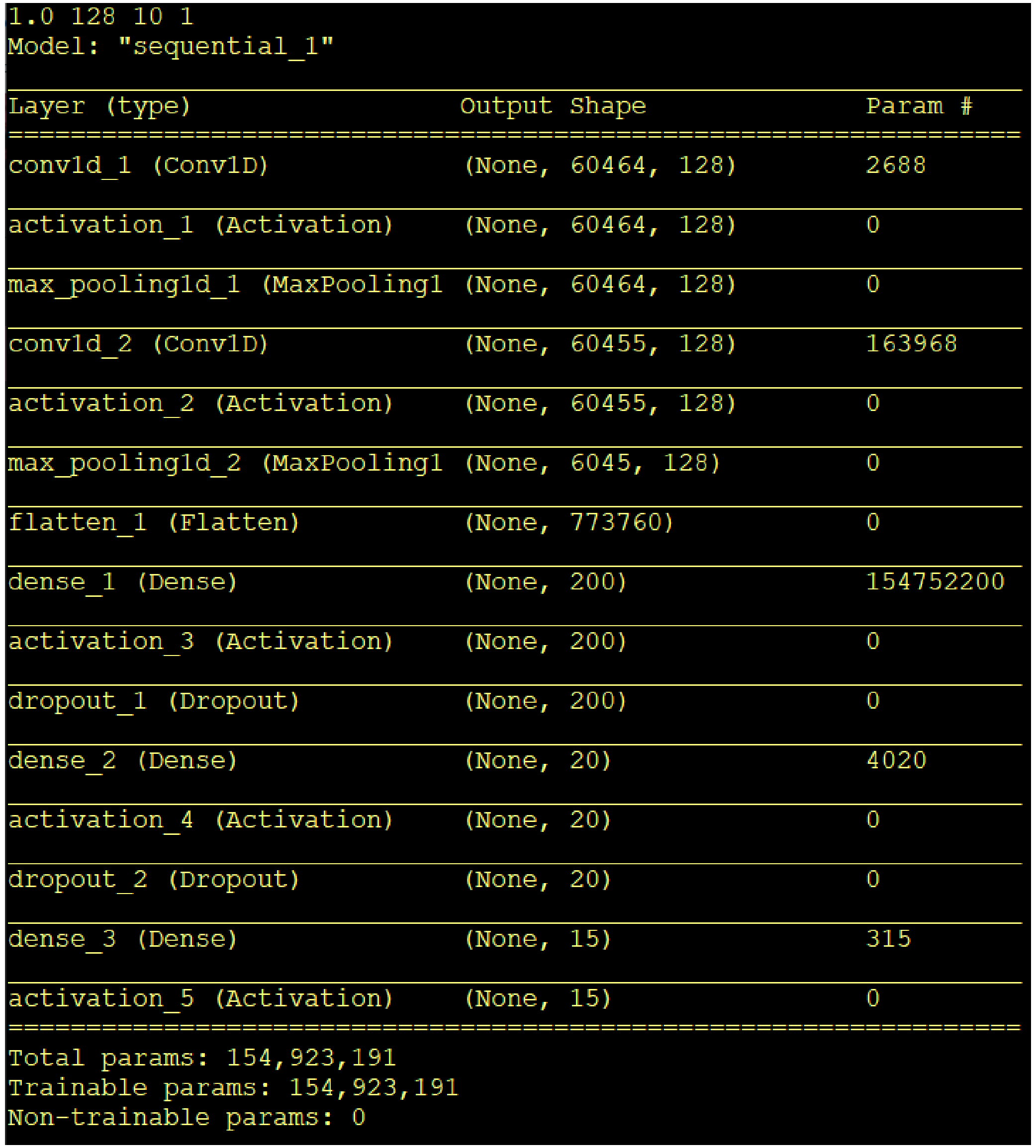
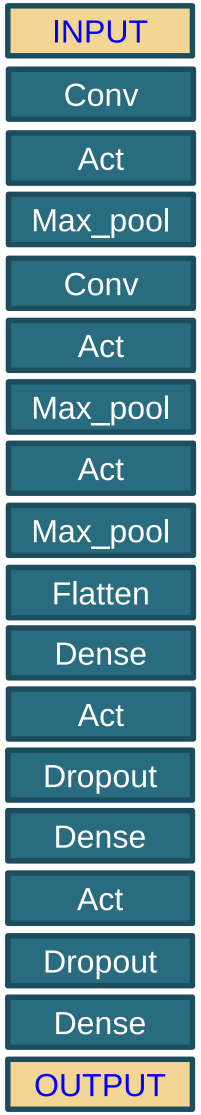
Model Summary

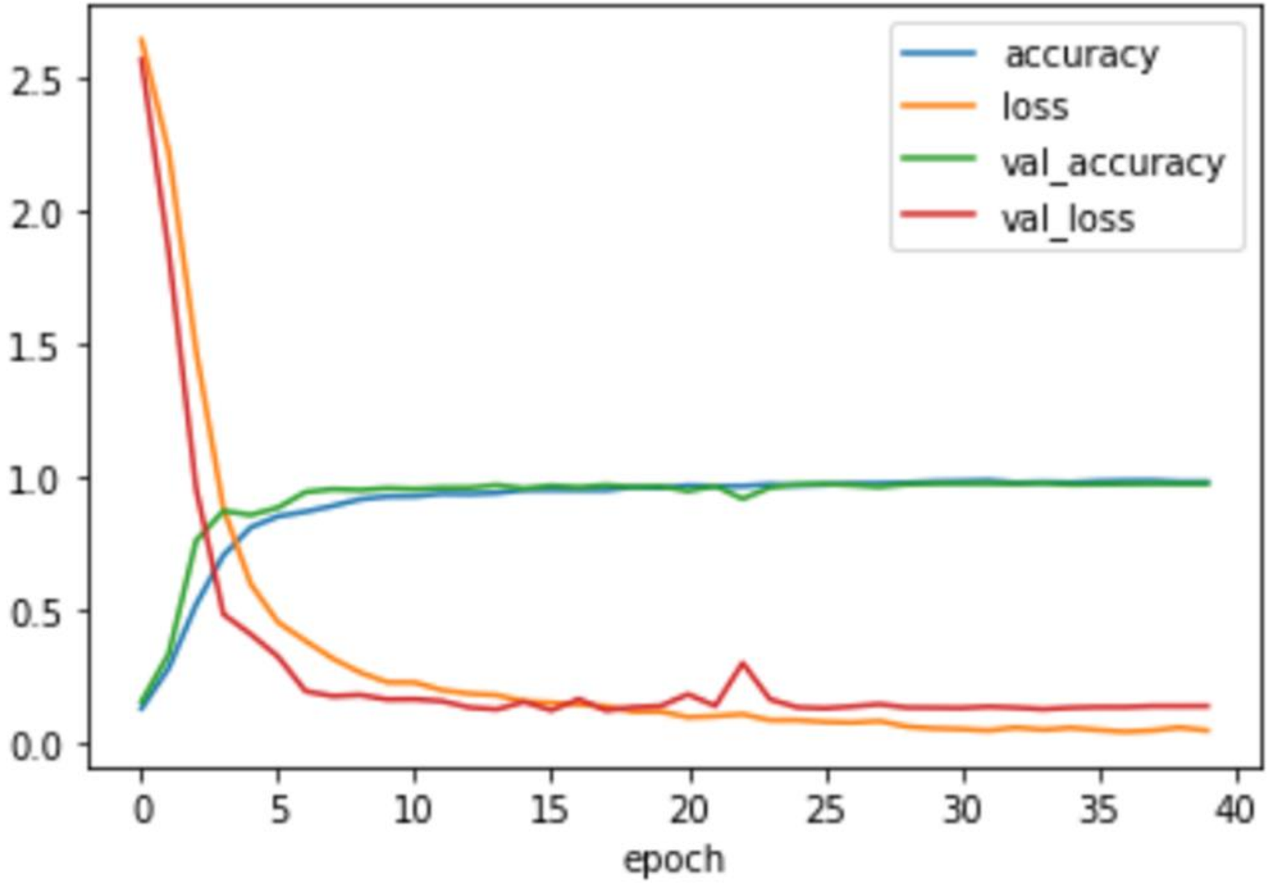


```
1.0 128 10 1
Model: "sequential_1"
_________________________________________________________________
Layer (type)                 Output Shape              Param #
=================================================================
conv1d_1 (Conv1D)            (None, 60464, 128)        2688
_________________________________________________________________
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

Model Performance



Inference

- **Key points to note**
  - Obvious points about dataset
  - Same dimension (feature) as the input data
    - Keras: Make sure the shape is the same as the training data
  - Ssame scaling as the training data

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Questions/Comments

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ravichandrans@mail.nih.gov