

## 1. What I have done:

(1).

Did multiclass classification on the cancer types with features set as sbs signatures, using the softmax to construct the BPNet to perform the training and testing of the model, and extracted weight of each sbs signatures in each cancer types and gene types. **the result of the classification accuracy of all the fold's validation dataset for cancer is of (5-fold cross validation):**

The 5-fold cross validation has 5 testing result, they are:

[0.8809523809523809, **0.8897243107769424**, 0.8784461152882206, 0.8515037593984962, 0.8602756892230576]

The validation accuracies for 5-fold cross validation are:

[**0.8600723763570567**, 0.850422195416164, 0.8528347406513872, 0.8462002412545235, 0.853437876960193]

The classification report for the classification status of 5 validation sets are shown below:

The first time for the validation set: **86%**, The cancers have 0 accuracy are 6,10,18,30.

	precision	recall	f1-score	support
0	0.83	0.88	0.86	17
1	1.00	0.92	0.96	71
2	0.97	0.79	0.87	168
3	0.98	0.88	0.92	48
4	1.00	0.89	0.94	9
5	1.00	0.96	0.98	69
6	0.00	0.00	0.00	7
7	0.97	0.97	0.97	33
8	0.92	0.94	0.93	65
9	0.92	0.97	0.94	86
10	0.00	0.00	0.00	11
11	1.00	0.86	0.92	56
12	0.98	0.90	0.94	51
13	0.36	0.60	0.45	20
14	0.99	0.99	0.99	85
15	1.00	0.98	0.99	62
16	0.97	0.92	0.94	98
17	1.00	0.98	0.99	85
18	0.00	0.00	0.00	13
19	0.46	1.00	0.63	73
20	0.80	0.67	0.73	30
21	0.55	0.74	0.63	31
22	0.79	0.96	0.87	80
23	0.58	0.96	0.72	26
24	0.64	0.78	0.70	41
25	0.96	1.00	0.98	80
26	0.48	0.48	0.48	25
27	1.00	0.62	0.77	82
28	0.85	0.55	0.67	20
29	1.00	0.99	0.99	89
30	0.00	0.00	0.00	12
31	1.00	0.40	0.57	15
accuracy			0.86	1658
macro avg	0.75	0.74	0.73	1658
weighted avg	0.88	0.86	0.86	1658

The second time: **85%**, The cancers have 0 accuracy are 6,10,18

	precision	recall	f1-score	support
0	0.88	0.82	0.85	17
1	0.92	0.92	0.92	71
2	0.99	0.71	0.83	168
3	0.97	0.81	0.89	48
4	1.00	0.67	0.80	9
5	1.00	0.96	0.98	69
6	0.00	0.00	0.00	7
7	0.97	0.97	0.97	33
8	0.76	0.98	0.86	65
9	0.91	0.97	0.94	86
10	0.00	0.00	0.00	11
11	1.00	0.80	0.89	56
12	0.98	0.92	0.95	51
13	0.36	0.60	0.45	20
14	1.00	0.98	0.99	85
15	1.00	0.98	0.99	62
16	1.00	0.81	0.89	98
17	0.95	0.96	0.96	85
18	0.00	0.00	0.00	13
19	0.88	0.95	0.91	73
20	0.95	0.63	0.76	30
21	0.26	1.00	0.41	31
22	0.84	0.94	0.89	80
23	0.77	0.92	0.84	26
24	0.53	0.90	0.67	41
25	0.99	1.00	0.99	80
26	0.39	0.68	0.49	25
27	0.98	0.62	0.76	82
28	1.00	0.55	0.71	20
29	1.00	0.94	0.97	89
30	1.00	0.67	0.80	12
31	1.00	0.47	0.64	15
accuracy			0.85	1658
macro avg	0.79	0.75	0.75	1658
weighted avg	0.90	0.85	0.86	1658

The third time: **85%**, The cancers have 0 accuracy are 6,10,30.

	precision	recall	f1-score	support
0	0.88	0.88	0.88	17
1	0.97	0.93	0.95	71
2	0.98	0.69	0.81	168
3	0.96	0.90	0.92	48
4	1.00	0.67	0.80	9
5	1.00	0.96	0.98	69
6	0.00	0.00	0.00	7
7	1.00	1.00	1.00	33
8	0.76	0.94	0.84	65
9	0.92	0.97	0.94	86
10	0.00	0.00	0.00	11
11	0.98	0.82	0.89	56
12	1.00	0.96	0.98	51
13	0.36	0.60	0.45	20
14	1.00	0.99	0.99	85
15	0.98	0.97	0.98	62
16	0.98	0.92	0.95	98
17	1.00	0.98	0.99	85
18	0.22	0.15	0.18	13
19	0.76	0.97	0.85	73
20	0.80	0.67	0.73	30
21	0.56	0.61	0.58	31
22	0.79	0.94	0.86	80
23	0.83	0.96	0.89	26
24	0.73	0.80	0.77	41
25	0.67	1.00	0.80	80
26	0.27	0.84	0.40	25
27	1.00	0.62	0.77	82
28	1.00	0.55	0.71	20
29	1.00	0.97	0.98	89
30	0.00	0.00	0.00	12
31	1.00	0.47	0.64	15
accuracy			0.85	1658
macro avg	0.76	0.74	0.74	1658
weighted avg	0.88	0.85	0.85	1658

The fourth time: **85%**, The cancers have 0 accuracy are 6,10,18,30.

	precision	recall	f1-score	support
0	0.88	0.88	0.88	17
1	1.00	0.92	0.96	71
2	1.00	0.68	0.81	168
3	0.98	0.83	0.90	48
4	1.00	0.89	0.94	9
5	1.00	0.97	0.99	69
6	0.00	0.00	0.00	7
7	0.97	0.97	0.97	33
8	0.76	0.97	0.85	65
9	0.94	0.95	0.95	86
10	0.00	0.00	0.00	11
11	1.00	0.75	0.86	56
12	0.98	0.92	0.95	51
13	0.36	0.60	0.45	20
14	1.00	0.99	0.99	85
15	0.95	1.00	0.98	62
16	0.99	0.90	0.94	98
17	0.99	0.98	0.98	85
18	0.00	0.00	0.00	13
19	0.62	1.00	0.77	73
20	0.44	0.83	0.57	30
21	0.57	0.55	0.56	31
22	1.00	0.90	0.95	80
23	0.69	0.96	0.81	26
24	0.70	0.76	0.73	41
25	0.98	0.99	0.98	80
26	0.19	0.76	0.31	25
27	1.00	0.62	0.77	82
28	1.00	0.55	0.71	20
29	1.00	0.99	0.99	89
30	0.00	0.00	0.00	12
31	1.00	0.47	0.64	15
accuracy				0.85 1658
macro avg				0.75 0.74 0.72 1658
weighted avg				0.89 0.85 0.85 1658

The fifth time: **85%**, The cancers have 0 accuracy are 6,10, 30.

	precision	recall	f1-score	support
0	0.88	0.88	0.88	17
1	1.00	0.93	0.96	71
2	0.94	0.81	0.87	168
3	0.95	0.85	0.90	48
4	0.89	0.89	0.89	9
5	1.00	0.96	0.98	69
6	0.00	0.00	0.00	7
7	1.00	0.97	0.98	33
8	0.95	0.88	0.91	65
9	0.92	0.98	0.95	86
10	0.00	0.00	0.00	11
11	1.00	0.82	0.90	56
12	1.00	0.92	0.96	51
13	0.39	0.60	0.47	20
14	1.00	0.99	0.99	85
15	0.97	0.98	0.98	62
16	0.98	0.91	0.94	98
17	1.00	0.98	0.99	85
18	0.40	0.15	0.22	13
19	0.37	1.00	0.54	73
20	0.82	0.60	0.69	30
21	0.82	0.29	0.43	31
22	0.85	0.94	0.89	80
23	0.61	0.96	0.75	26
24	0.70	0.78	0.74	41
25	0.99	0.99	0.99	80
26	0.50	0.68	0.58	25
27	1.00	0.65	0.79	82
28	1.00	0.55	0.71	20
29	1.00	0.98	0.99	89
30	0.00	0.00	0.00	12
31	0.88	0.47	0.61	15
accuracy				0.85 1658
macro avg				0.77 0.73 0.73 1658
weighted avg				0.89 0.85 0.86 1658

As we can see from the graph above, the overall accuracy is good as the average of them are 85 % and there are still some classes that have the 0 accuracy, there are 2 possible reasons:

1. The 6<sup>th</sup> cancer ('DLBC') has number of patients of 7 in each set ,10<sup>th</sup> ('HNSC') cancer has number of patients of 11 in each set, 18<sup>th</sup> cancer('LUSC') has number of patients of 13 in each set and 30<sup>th</sup> ('UCS') has number of patients of 12 in each set.as we can observe from the distribution, those are the cancer types that are minors in the whole data set and therefore, the classification accuracy of theirs are low. The solution would be reducing the batch size to try to help with training or getting more data set, which is time consuming.
2. Those cancers are similar to other cancers in the whole dataset and therefore their classification accuracies are interfered by other classes of cancers. The solution would be trying to classify on lesser cancer types and keep those type of cancers to see the accuracy performance of them afterwards.

Except for that, the performance of multiclass classification is pretty good, and the model is generally tested on each 6-fold and get the close results, also. The validation accuracies are also stable and close to the best trained model's testing accuracy.

**The precision:** In an imbalanced classification problem with more than two classes, the precision of each class is calculated as the sum of true positives across that classes divided by the sum of true positives and false positives across that classes. Number of identified items are relevant.

**The Recall** = TP / (TP+FN) (number of relevant items are identified)

**The F1-score:** The F-score or F-measure is a measure of a test's accuracy. indicating how perfect is the recall and precision.

**Support:** number of samples in that class

**Accuracy:** how many items identified are the relevant element.

**Marco Average:** macro averaging reduces the problem to multiple one-vs-all comparisons. The truth and estimate columns are recoded such that the only two levels are A and other, and then precision is calculated based on those recoded columns. The results of Marco of each class are then weighted together. The **Pr1** is the precision of class 1.its same for recall and f1-score.

$$Pr_{macro} = \frac{Pr_1 + Pr_2 + \dots + Pr_k}{k} = Pr_1 \frac{1}{k} + Pr_2 \frac{1}{k} + \dots + Pr_k \frac{1}{k}$$

**Weighted Average:** weighted avg is the total number TP (true positive of all classes)/total number of objects in all classes. It's the same for recall and f1-score.

**the result of the classification accuracy of all the fold's validation dataset for cancer is of (5-fold cross validation):**

The 5-fold cross validation has 5 testing result, they are:

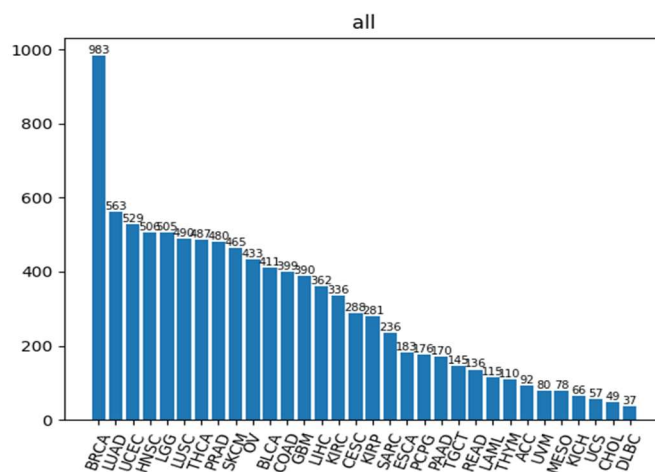
[0.993734335839599, 0.9931077694235589, 0.9906015037593985, 0.9862155388471178, 0.9874686716791979]

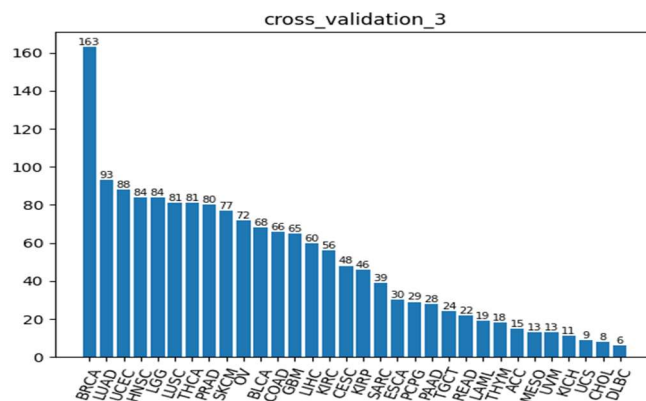
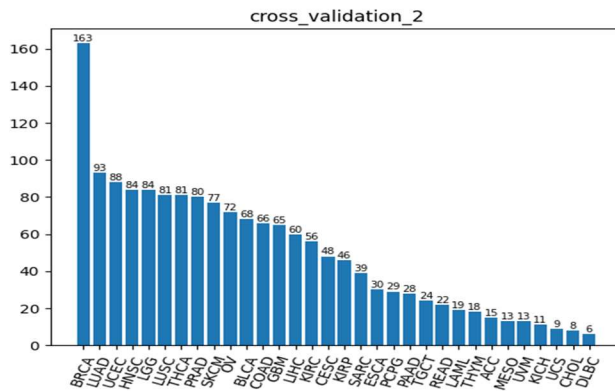
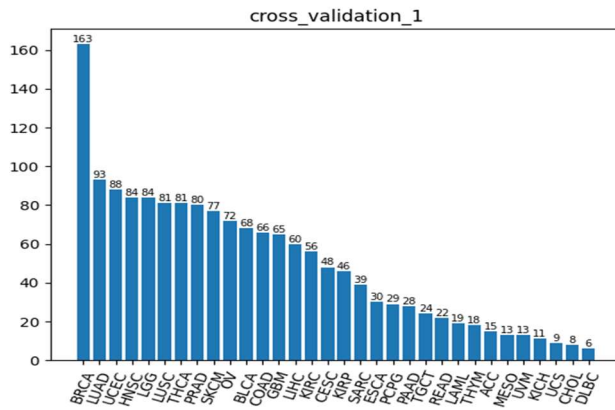
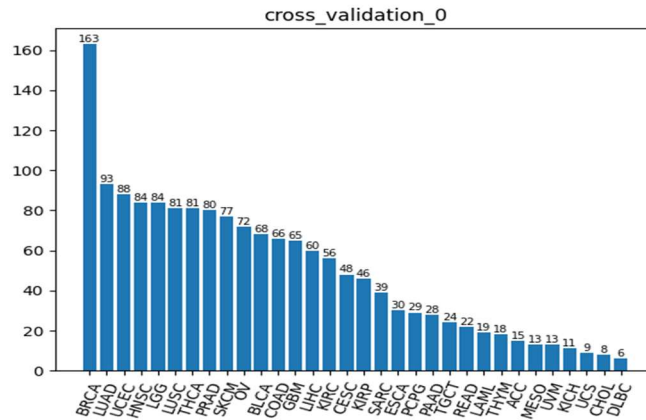
The validation accuracies for 5-fold cross validation are:

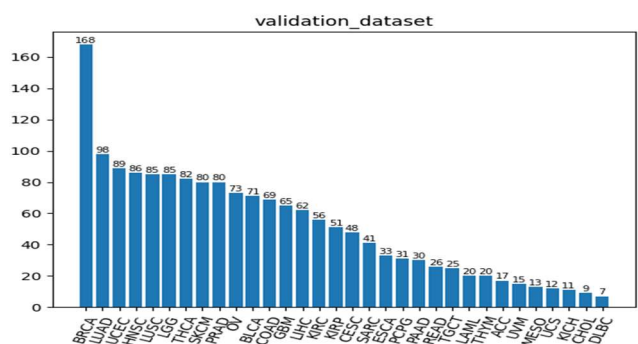
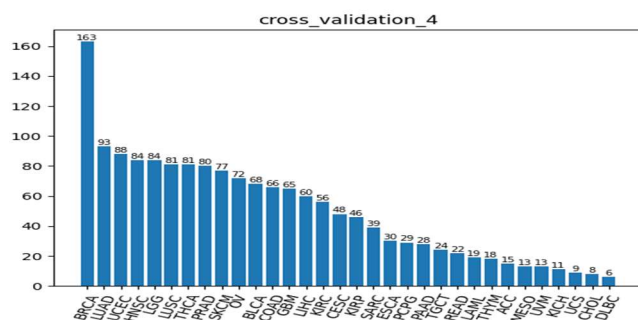
[0.9927623642943305, **0.9939686369119421**, 0.9909529553679132, 0.9891435464414958, 0.9909529553679132]

**(2).**

Finished the evaluation stage of making the new cross validation strategy to test on generalization of the model and using the stratified sampling method to ensure the cancer distribution in each cancer types in each folds are the same, here is the cancer distribution in each of the folds. **(Please notice that if you find out that the number of sample in a class is different than the support shown in the above validation classification report is because I have changed the data to test different performance.)**







The detailed algorithm used for stratified sampling is shown below:

### 1. The stratified sampling

1. choose k for fold numbers.
2. use pandas data frame to group the data by cancer types

Cancer type	Sbs1	Sbs2	Gene1	Sample_id
ACC	32.12	45.76	1	0
ACC	34.12	0	1	1
ACC	33.12	40	1	2
...	...	...	1	...
BLCA	56	98	0	50
BLCA	67	99	0	51
...	...	...	0	...
BRCA	23	34	1	100
...	...	...	1	...

3. for each cancer type and the data in that cancer type:  
[reset index of each cancer type's data with indices as length of data in each cancer types](#)

**Eg.**

ACC's indexes would be [0,1,2,3,...49]

BLCA's indexes would be [0,1,2,3,...49]

BRCA's indexes would be [0,1,2,3,...49]

...

[We shuffle the index in each data of each cancer types](#)

**Eg.**

ACC's indexes would now be [0,3,2,40,1,49...]

BLCA's indexes would now be [0,2,1,48,36,...]

BRCA's indexes would now be [0,32,1,18,...]

...

[Then ,we append those indexes in each cancers and their number of pieces to be put in each fold into indexe\\_list](#)

**Eg.**

The list contains:

ACC: ([0,3,2,40,1,49...], 50/k)

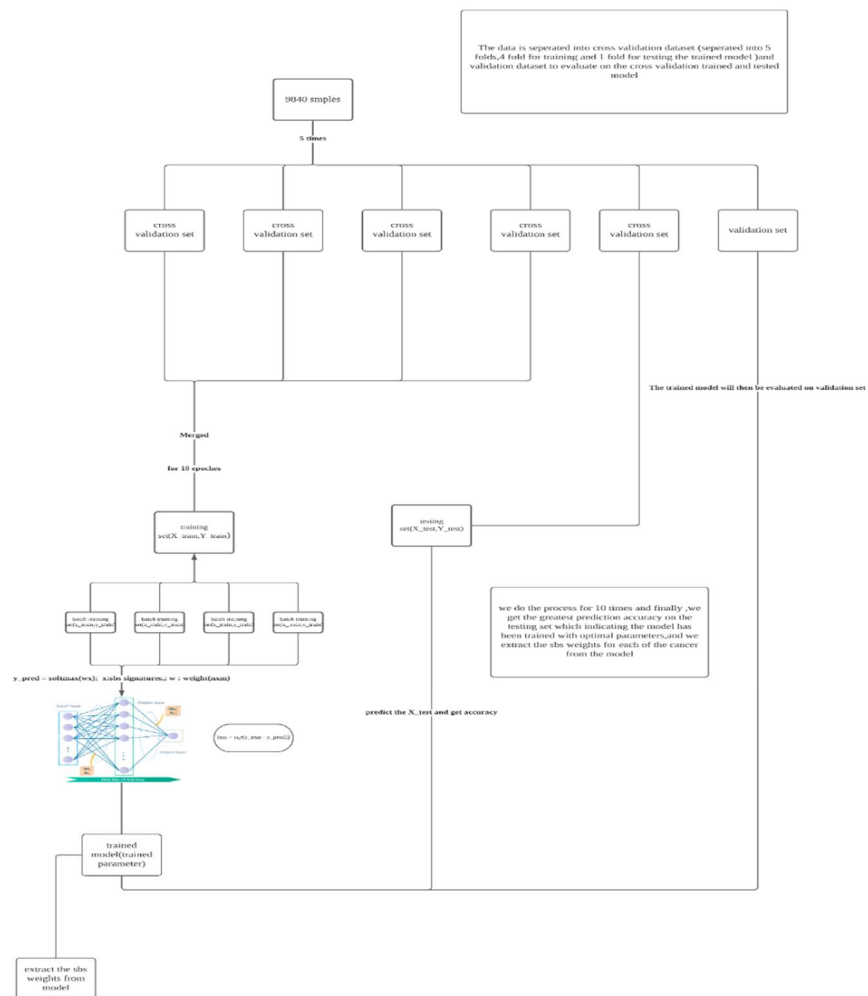
BLCA: ([0,2,1,48,36,...], 50/k)

BRCA: ([0,32,1,18,...], 50/k)

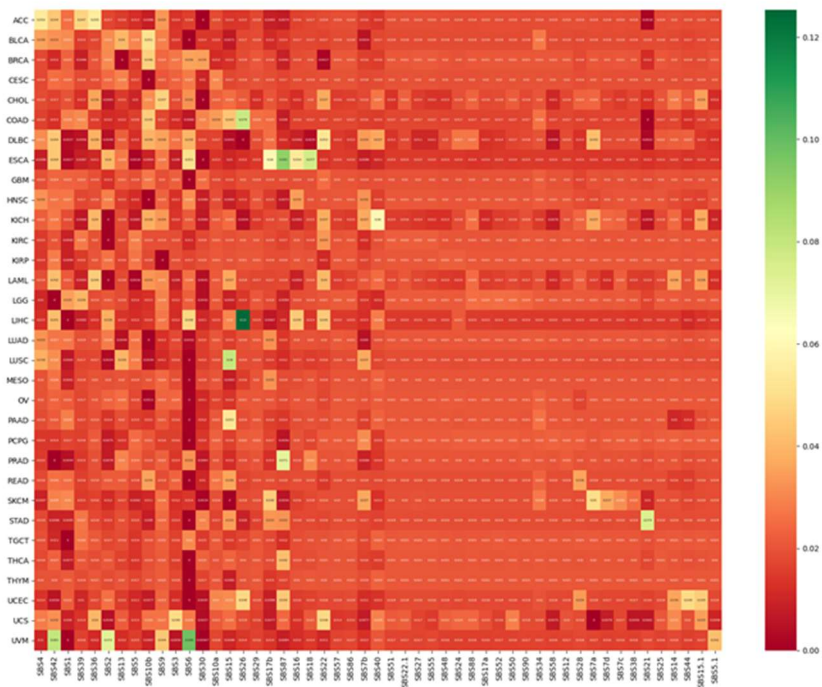


The graph below shows the classification working flow for both models.

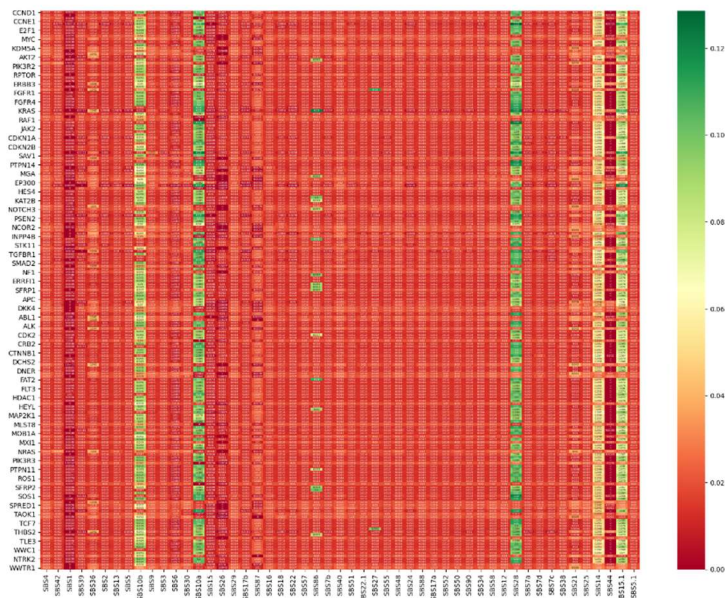
The approach is to separate the whole data into 6 datasets (5 cross validation dataset and 1 validation dataset) in each iteration of 5 iterations, we select the  $i$ th dataset in 5 cross validation datasets as testing set and rest as training set using the BPnet and at each iteration, when evaluate the best trained model on the evaluation set.



This is for the weight of the sbs signature in each cancer types.



This is for the sbs weight in each gene.



(3).

found the heavier weight of sbs in each cancer type and heavier weight of each sbs in each gene and taken the length of the intersection set of those sbs signatures and divided by length of total sbs signatures to find the intersection (cancer type & gene set) that has most of the sbs signatures covered, which means that this gene's mutation has most likely caused the occurrence of heavier sbs signatures used to identify the cancer type. thus, found the top 10 most determinable genes (the activity of those gene might cause the specific cancer) in each cancer types. The graph below shows the top 10 genes in each cancer types. This is for the future for building the recommender system based on those top 10 genes

cancer type	genes								
ACC	CCND1 CCND2 CCNE1 CDK4 CDK6 E2F1 E2F3 MYCN ARRDC1 PIK3R2								
BLCA	IGF1R RAC1 STK11 ACVR2A CSNK1D CUL1 SOS1 STK4 CCND1 CCND2								
BRCA	IGF1R RAC1 STK11 ACVR2A CSNK1D CUL1 SOS1 STK4 CCND1 CCND2								
CESC	CCND1 CDK4 CDK6 E2F1 E2F3 ARRDC1 RHEB RICTOR EGFR FGFR1								
CHOL	CCND2 IGF1R RAC1 STK11 ACVR2A CSNK1D CUL1 SOS1 STK4 CCND1								
COAD	MYCN IGF1R RAC1 LATS2 NOV PTEN STK11 TGFB2 ACVR2A CSNK1D								
DLBC	IGF1R RAC1 NOV STK11 ACVR2A CSNK1D CUL1 SOS1 STK4 CCND1								
ESCA	CCND1 CCND2 CDK4 CDK6 E2F1 E2F3 ARRDC1 PIK3CA RHEB RICTOR								
GBM	IGF1R RAC1 STK11 ACVR2A CSNK1D CUL1 SOS1 STK4 CCND1 CCND2								
HNSC	CCND1 CDK4 CDK6 E2F1 E2F3 ARRDC1 RHEB RICTOR EGFR FGFR1								
KICH	CCND2 IGF1R RAC1 NOV STK11 ACVR2A CSNK1D CUL1 SOS1 STK4								
KIRC	IGF1R RAC1 STK11 ACVR2A CSNK1D CUL1 SOS1 STK4 CCND1 CCND2								
KIRP	IGF1R RAC1 RB1 STK11 ACVR2A CSNK1D CUL1 SOS1 STK4 CCND1								
LAML	CCND2 IGF1R RAC1 STK11 ACVR2A CSNK1D CUL1 SOS1 STK4 CCND1								
LGG	CCND2 IGF1R RAC1 STK11 ACVR2A CSNK1D CUL1 SOS1 STK4 CCND1								
LIHC	CCND1 CCND2 CCNE1 CDK4 CDK6 E2F1 E2F3 MYCN ARRDC1 PIK3CA								
LUAD	CCND1 CDK4 CDK6 E2F1 E2F3 ARRDC1 RHEB RICTOR EGFR FGFR1								
LUSC	CCND1 CDK4 CDK6 E2F1 E2F3 ARRDC1 RHEB RICTOR EGFR FGFR1								
MESO	IGF1R RAC1 STK11 ACVR2A CSNK1D CUL1 SOS1 STK4 CCND1 CCND2								
OV	CCND1 CDK4 CDK6 E2F1 E2F3 ARRDC1 RHEB RICTOR EGFR FGFR1								
PAAD	IGF1R RAC1 STK11 ACVR2A CSNK1D CUL1 SOS1 STK4 CCND1 CCND2								
PCPG	IGF1R RAC1 STK11 ACVR2A CSNK1D CUL1 SOS1 STK4 CCND1 CCND2								
PRAD	CCND2 IGF1R RAC1 STK11 ACVR2A CSNK1D CUL1 SOS1 STK4 CCND1								
READ	IGF1R RAC1 STK11 ACVR2A CSNK1D CUL1 SOS1 STK4 CCND1 CCND2								
SKCM	CCND2 MYCN IGF1R RAC1 MDM2 LATS2 PTEN STK11 TGFB2 ACVR2A								
STAD	CCND1 CDK4 CDK6 E2F1 E2F3 ARRDC1 RHEB RICTOR EGFR FGFR1								
TGCT	IGF1R RAC1 STK11 ACVR2A CSNK1D CUL1 SOS1 STK4 CCND1 CCND2								
THCA	IGF1R RAC1 STK11 ACVR2A CSNK1D CUL1 SOS1 STK4 CCND1 CCND2								
THYM	IGF1R RAC1 STK11 ACVR2A CSNK1D CUL1 SOS1 STK4 CCND1 CCND2								
UCEC	CCND1 CCND2 CDK4 CDK6 E2F1 E2F3 ARRDC1 RHEB RICTOR EGFR								
UCS	CCND2 IGF1R RAC1 NOV STK11 ACVR2A CSNK1D CUL1 SOS1 STK4								
UVM	CCND1 CCND2 CCNE1 CDK4 CDK6 E2F1 E2F3 MYCN ARRDC1 PIK3CA								

So, the graph of explaining what did I do in finding the relationship between gene and cancer types is presented here:

The most weighted sbs signatures for different cancer types

ACC	Sbs1	Sbs2	Sbs3	Sbs4	Sbs5	Sbs6	Sbs7	Sbs8
LGG	Sbs2	Sbs3	Sbs4	Sbs5	Sbs6	Sbs7	Sbs8	Sbs9
UVM	Sbs17	Sbs67	Sbs89	Sbs90	Sbs2	Sbs5	Sbs7	Sbs8

The most weighted sbs signatures for different genes

Gene1	Sbs1	Sbs2	Sbs3	Sbs4	Sbs5	Sbs6		
Gene2	Sbs1	Sbs2						

So, the common set for ACC and gene1 would be sbs1,2,3,4,5,6, assuming there's 52 sbs signatures in total, we calculate the gene in cancer as

Relation of ACC and gene1 :  $\text{num}(\text{sbs1,2,3,4,5,6})/\text{len}(\text{all sbs}) = 6/52$

Relation of ACC and gene2 :  $\text{num}(\text{sbs1,2})/\text{len}(\text{all sbs}) = 2/52$

Then, the relationship between gene1 and ACC is much denser than that of gene2 and ACC. we list top 10 of the genes in each of the cancers an relate them.

#### (4).

Solved the class distance problem mentioned earlier by supervisor , I changed the loss calculation from finding error on the class label to finding the error from the vector representation

#### (5).

Wrote the data and data preprocessing part of dissertation, need to find the reference to make sure the reason why it's using sbs as features is explained. And worked on part of the classification method part.

## **2.The problems:**

1. The gene of some of the patients in the cancer type may have mutated and the same gene may not be mutated in other patients in the same cancer type.so. the top 10 gene may not be indicative in this senario.

The solution that I have thought about is to find the number of patients that have that specific gene mutated in their body and total number of patients have that gene recorded and we divide it to get the percentage of the patients that have the gene mutated and we sort the 187 genes based on this and strippe out lower occuraced genes to ensure those genes are frequently mutated in the patients of that cancers,then we calculate the weight of those genes in cancer and recommend those top 10 genes are the most related to this cancer.

## **3.The plan**

- (1). Solve the problem of weighted genes in each cancer.
- (3). working on method part of the dissertation