

GAC Tutorial

Tab 1: Read Me

GAC: Gene Associations with Clinical **Read Me** Super PC Time to Event Outcome Super PC Continuous Outcome Super PC Binary Outcome Forest Plot Tutorial About Us ▾

Background:

Currently, the Super PC method has been implemented in an R package 'superpc' for time-to-event outcome and a continuous outcome. However, it did not incorporate binary outcome in this R package. Furthermore, it is a programming-based tool which is not user-friendly for clinicians and biomedical researchers with limited programming exposure. To overcome the limitations, we are presenting GAC: Gene Association with Clinical, an interactive web-based application for gene association with different clinical outcomes of interest, developed based on R package 'shiny' and 'superpc'. GAC could perform a SuperPC analysis for three various types of outcome including time-to-event, continuous and binary. Meanwhile, the users could generate a forest plot to visualize the clinical association for a binary outcome with different genetic or clinical variables of interest simultaneously.

Supervised Principal Components Analysis (Super PC)

NOTE: This app provides a one stop shop to carry out clinical association with multiple genes at one time. You can have three different types of outcome, including binary, time to event and continuous outcomes.

a) Tab 2. This is for gene association with a time-to-event outcome of interest.
b) Tab 3. This is for gene association with a continuous outcome of interest.
c) Tab 4. This is for gene association with a binary outcome of interest.

NOTE1: For all supervised principal component analysis, you will be able to upload data, choose number of iterations, number of folds, proportion to subset datasets. You can also choose to replicate the results with existing fold ids or not. To replicate, upload your previously saved fold ids.

NOTE2: For the results, you can find the association between the predicated principal component with a set of selected important genes through plot and summary statistics and analysis. You will also be able to view and download the selected important genes.

Forest Plot

In the fifth Tab, you are able to upload your associations with a binary outcome to generate a forest plot.

Tab 2: Super PC Time to Event Outcome

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Input Time to Event file

Select an example Clinical ds or upload your own with 'Load my own'

Example ds File ▾

Download Example data

Input Expression file

Select an example Expression ds or upload your own with 'Load my own'

Example ds File ▾

Download Example data

Choose Options

Split data:

☐ 70-30
☒ 60-40
☐ 50-50

Number of iterations for cross validation:

☒ 100
☐ 150
☐ 200

Number of folds:

☒ 2
☐ 5
☐ 10

Run analysis

Step 1:

Select example 'Time to event' clinical dataset or upload your own. Uploaded data should be in the same format as example.

To view example data and format, use download button to view .csv file.

Step 2:

Select example 'expression' dataset or upload your own. The patients should be ordered in same order and should be exact same.

To view example data and format, use download button to view .csv file.

Step 3:

Choose data split into training and validation. Default uses 60-40 i.e. data is split into 40 % for training and remaining 60% for validation. You can also choose the number of interactions. For example purposes a smaller number 100 is used.

Also, select number of folds for cross validation. Default is 2.

Step 4:

Hit button to run analysis after each change in option.

Input Fold IDs

Input Fold IDs to Replicate Previous Results:

☐ Yes

☒ No

If Yes, Select input ids for example data or upload your own with 'Load my own'

Example ds File

Download Example data

Step 5 (Optional):

The user can replicate previously generated results by uploading fold-ids (download available below). When running analysis for first time, leave option to 'No'.

Download the List for Important Features or Genes

Download Super PC Results

Step 6 (Optional):

The user can download the tabular results in .csv file.

Download a table with fold ids to upload to replicate results

Download Fold IDs to Replicate

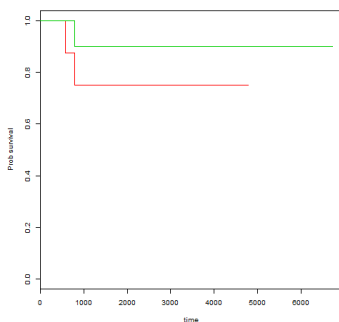
Step 7 (Optional):

The user can download the fold-ids in csv format to replicate results at a later time. These can be uploaded in the input fold id section.

Association between Continuous Predicted Principal Component with Time to Event Outcome

The p-value for the first Principal component is = 0.21536408598728.

KM Plot for Discrete Predicted Principal Component (Cut by Median)



Main panel shows the results from the super PC analysis.

The p-value from 1st supervised PC is reported.

A discrete (categorical) predictor is created by cutting the predictor at its median to form two groups for the Kaplan-Meier analysis.

Important Features Selected

Show 10 entries

Importance-score	Raw-score	Name
184.147	1.468	MUC6.4588
142.24	1.33	YNGA.65266
127.807	1.722	ZNF385B.151126
126.463	1.638	ELOVL2.54898
116.823	1.487	FLT3.2332
112.227	1.497	SORCS1.114815
105.482	1.406	KCNH1.3756
72.727	1.341	KRT32.3882
71.761	1.26	CYP21A2.1589
66.777	1.343	DOC2B.8447

Showing 1 to 10 of 14 entries

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List of all significant genes, in order of decreasing importance score are reported

Tab 3: Super PC Continuous Outcome

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Input Continuous outcome file

Select an example Continuous outcome ds or upload your own with 'Load my own'

Example ds File

Download Example data

Input Expression file

Select an example Expression ds or upload your own with 'Load my own'

Example ds File

Download Example data

Choose Options

Split data:

70-30

60-40

50-50

Number of Iterations for cross validation:

100

150

200

Number of folds:

2

5

10

Predicted Values Type:

Continuous

Discrete

Run analysis

Input Fold IDs

Input Fold IDs to Replicate Previous Results:

Yes

No

If Yes, Select input ids for example data or upload your own with 'Load my own'

Example ds File

Download Example data

Download the List for Important Features or Genes

Download Super PC Results

Download a table with fold ids to upload to replicate results

Download Fold IDs to Replicate

Step 1:

Select example 'continuous' outcome dataset or upload your own. Uploaded data should be in the same format as example.

To view example data and format, use download button to view .csv file.

Step 2:

Select example 'expression' dataset or upload your own. The patients should be ordered in same order and should be exact same.

To view example data and format, use download button to view .csv file.

Step 3:

Choose data split into training and validation. Default uses 60-40 i.e. data is split into 40 % for training and remaining 60% for validation. You can also choose the number of interactions. For example purposes a smaller number 100 is used.

Also, select number of folds for cross validation. Default is 2.

Additionally, choose to display predicted values as scatter plots (for continuous predictors with Pearson correlation's) or boxplot (for binary groups cut off at median with t-test).

Step 4:

Hit button to run analysis after each change in option.

Step 5 (Optional):

The user can replicate previously generated results by uploading fold-ids (download available below). When running analysis for first time, leave option to 'No'.

Step 6 (Optional):

The user can download the tabular results in .csv file.

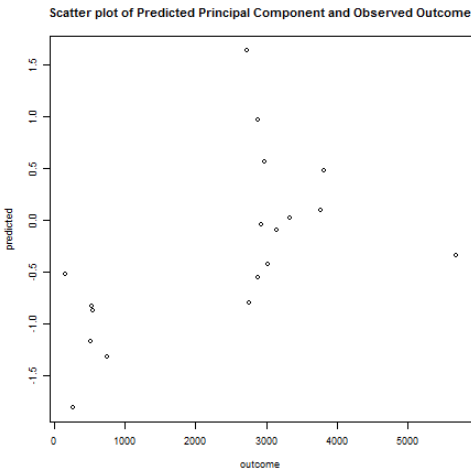
Step 7 (Optional):

The user can download the fold-ids in csv format to replicate results at a later time. These can be uploaded in the input fold id section.

Association between Continuous Predicted Principal Component with Continuous Outcome

The p-value for the first Principal component is = 0.009.

Plot and Tests for Predicted Principal Component



Test statistic	df	P value	Alternative hypothesis	cor
2.75	16	0.01422 *	two.sided	0.5666

Table: Pearson's product-moment correlation: 'outcome' and 'predicted'

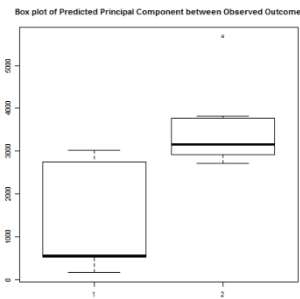
Main panel shows the results from the super PC analysis.

The p-value from 1st supervised PC is reported.

Scatter plot showing correlation of continuous predictor with outcome using Pearson correlation is reported. Discrete predictors are created by cutting the predictor at its median to form two groups and reported as boxplots.

Predicted Values Type:

- ☐ Continuous
- ☒ Discrete



Test statistic	df	P value	Alternative hypothesis
-4.331	14.8	0.0006114 * * *	two.sided

Table: Welch Two Sample t-test: 'dat\$outcome' by 'dat\$pred.discrete' (continued below)

mean in group 1	mean in group 2
1270	3472

Important Features Selected

Show [10 / 75] entries

Importance-score	Raw-score	Name
97.196	0.623	CYP4F8.11283
76.61	0.591	NOPH1.30010
69.261	0.773	AFP.174
63.632	0.703	V5IG2.23564
63.19	0.67	TNFRSF13B.23495
61.456	1.131	NNAT.4826
59.825	0.579	LOC389633.389933
55.884	0.726	GPIAT2.150793
55.516	0.884	TNN.63923
55.036	1.163	DNASE1L3.1776

Showing 1 to 10 of 75 entries

Previous 1 2 3 4 5 ... 6 Next

List of all significant genes, in order of decreasing importance score are reported

Tab 4: Super PC Binary Outcome

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Input Expression with Binary Outcome file

Select an example ds or upload your own with 'Load my own'

Example ds File

Download Example data

Step 1:

Select example 'expression with binary outcome indicator' dataset or upload your own. Uploaded dataset format should be same as example.

To view example data and format, use download button to view .csv file.

Choose Options

Split data:

- ☐ 70-30
☒ 60-40
☐ 50-50

Number of Iterations for cross validation:

- ☒ 100
☐ 150
☐ 200

Number of folds:

- ☒ 2
☐ 5
☐ 10

Predicted Values Type:

- ☒ Continuous
☐ Discrete

Run analysis

Step 2:

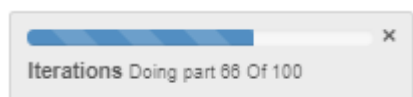
Choose data split into training and validation. Default uses 60-40 i.e. data is split into 40 % for training and remaining 60% for validation. You can also choose the number of interactions. For example purposes a smaller number 100 is used.

Also, select number of folds for cross validation. Default is 2.

Additionally, choose to display predicted values as boxplots (for continuous predictors with t-test) or bar plot (for discrete groups cut off at median with chisq test).

Step 3:

Hit button to run analysis after each change in option. A progress indicator may appear to the right corner of the page.



Input Fold IDs

Input Fold IDs to Replicate Previous Results:

- ☐ Yes
☒ No

If Yes, Select input ids for example data or upload your own with 'Load my own'

Example ds File

Download Example data

Step 4 (Optional):

The user can replicate previously generated results by uploading fold-ids (download available below). When running analysis for first time, leave option to 'No'.

Download the List for Important Features or Genes

Download Super PC Results

Step 5 (Optional):

The user can download the tabular results in .csv file.

Download a table with fold ids to upload to replicate results

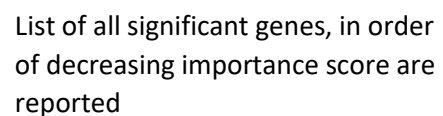
Download Fold IDs to Replicate

Step 6 (Optional):

The user can download the fold-ids in csv format to replicate results at a later time. These can be uploaded in the input fold id section.

The p-value for the most significant Principal component is = 0.013.

Box plot of Predicted Principal Component between Observed groups



Tab 4: Forest Plot

GAC: Gene Associations with Clinical

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Super PC Continuous Outcome

Super PC Binary Outcome

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Input your file

Select an example ds or upload your own with 'Load my own'

Example ds File

Download Example data

Cosmetic Changes

Font size:

0 8 10

Left_text_label

Longer Overall Survival

Right_text_label

Shorter Overall Survival

Text label Font size:

0 4 10

Scale data

0.2,0.6,0.8,1,1.2,1.8,5

Gene location slider (L-R):

-20 0.25 10

Color for good group

Color for intermediate group

Color for bad group

Step 1:

Select example dataset or upload your own.

To view example data and format, use download button to view .csv file.

Step 2:

Change font size for the IDs (genes) displayed to the left of forest plot.

Step 3:

Change label for text to be displayed above the horizontal line to the left and right of the HR= 1 dotted line.

A slider bar to change font size for these labels is also available.

Step 4:

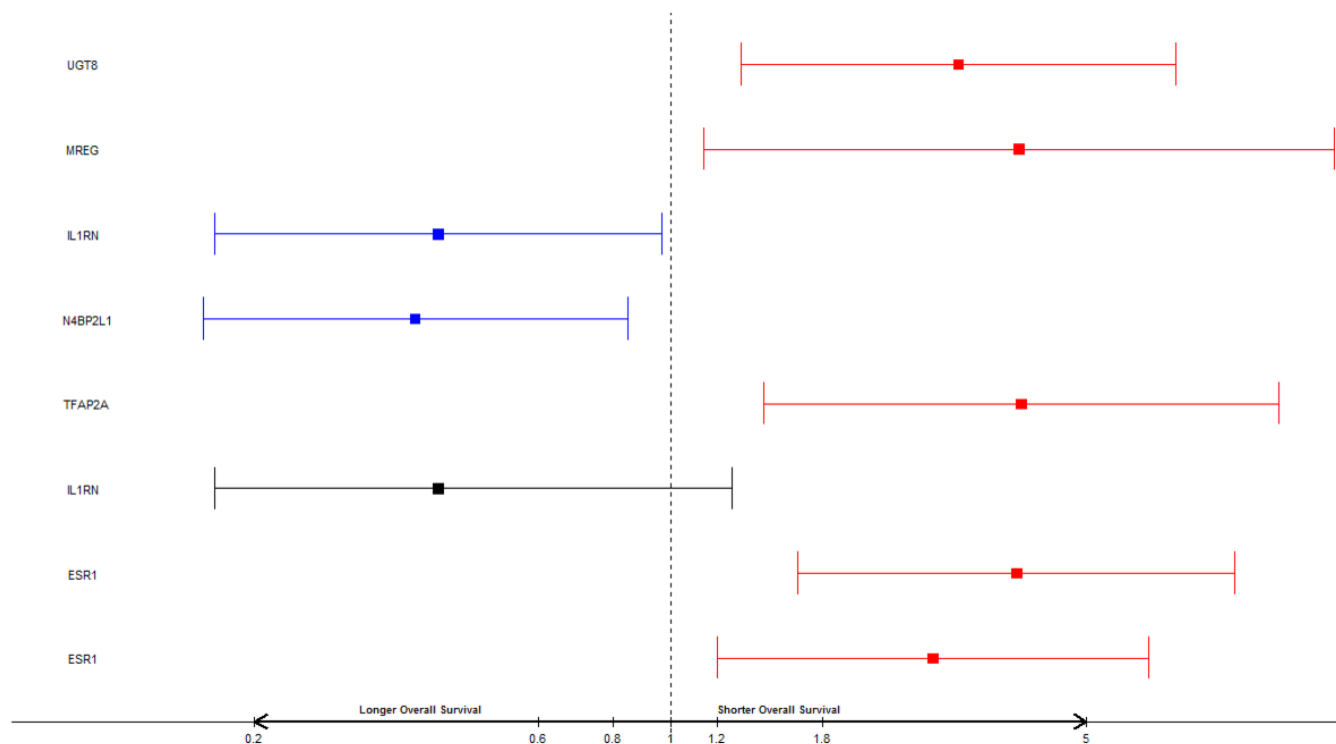
Choose x ticks to display below the horizontal line depending on dataset.

Step 7:

Move IDs (genes) slightly to right or left to avoid overlap with the forest plot.

Step 8:

Change color of outcomes. Genes with HR and their 95% CI below 1 are coded blue (good group), overlapping 1 are coded black (the intermediate group) and those over 1 are coded red (the bad group).



Reporting results from super PC analysis through forest plot. Genes with HR < 1 are coded in blue, those overlapping 1 are coded black and those greater than 1 are coded red.