Analysis of nasal & urine with comparisons to blood

DARPA PHD

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A Hero

Dept of EECS

University of Michigan

Analysis summary

I. Facts about the urine and nasal data

- Nasal data (N): 57 pairs at early (pre-inocculation) and late (peak sx) times
- Urine data (U): 57 pairs ....
- Approximately 12% of the 228 data samples were poor (labeled as “<LOW>”)

II. Applied Behrens-Fisher FDR screening to discover sx-asx diff expressed N and U proteins

1. Nasal data had more significant diff expressed (SDE) proteins
2. HRV had no SDE's proteins in either N or U below 50% FDR threshold
3. (RSV,INF) had some SDE's proteins even at 10% FDR

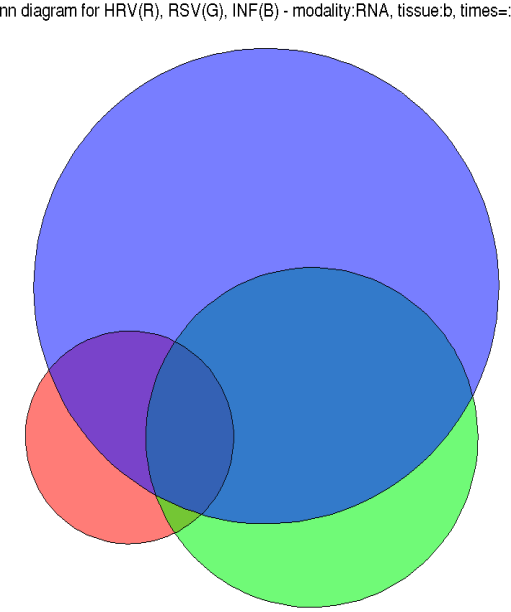
III. Applied regularized linear classifer to classify sx-asx

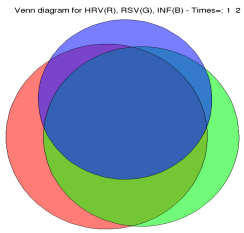
1. trained on all N or all U data
2. all BL and PC samples labeled as asx
3. to mitigate overfitting we used
   * Bolasso variable selection used
   * 3-fold CV performed
4. Insufficient data for implementation of more sophisticated classifier

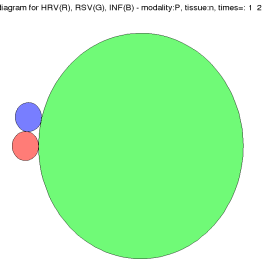
IV. Results of ROC analysis

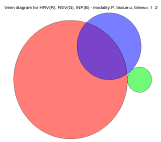
1. Non-blood assays are less discriminating than Blood, significantly less wrt Blood RNA
2. Proteomic assays Blood is best, followed by Nasal and Urine, respectively
3. Nasal and Urine assays are most discriminating for RSV, followed by INF and HRV.

Behrens-Fisher FDR Screening - Platform Comparisons









P blood, q=0.2
16 30 32 6 9 14 5

P nasal: q=0.2
0 60 1 0 0 0 0

P urine: q=0.2
22 0 7 0 4 0 0

RNA blood, q=0.2
781 1986 3893 266 500 1419
243

/home/hero/Hero/Matlab/PHD/HRVRSVINFAnalysis/FDR/All_tissues

Pan-viral screening

Nasal discriminants found (FDR 10%)

RV	RSV	INF	HRVINF	HRVRSV	RSVINF	HRVRSVINF	
0	1	1	0	0	0	0	RSV(1) **Alpha-1 Antitrypsin**, INF(1): **Thrombopoietin**
0	1	1	0	0	28	50	(persistency) (See next slide for list)

Urine discriminants found (FDR 10%)

RV	RSV	INF	HRVINF	HRVRSV	RSVINF	HRVRSVINF	
0	0	3	0	0	0	0	INF(3): **GCF, IL-5, MMP-9**
0	0	3	11	4	3	6	(persistency) (See next slide for list)

Top nasal persistent discriminants (FDR 10%)

RSVINF

'IL-3'
'IL-7'
'ICAM-1'
'Brain-Derived Neurotrophic Factor'
'IL-18'
'MIP-1beta'
'Stem Cell Factor'
'von Willebrand Factor'
'MCP-1'
'IL-5'
'MMP-3'
'Apolipoprotein H'
'IL-8'
'C Reactive Protein'
...
...

HRVRSVINF

'MMP-3'
'Stem Cell Factor'
'ENA-78'
'MIP-1alpha'
'SHBG'
'IL-7'
'IFN-gamma'
'Brain-Derived Neurotrophic Factor'
'IL-18'
'IL-8'
'EN-RAGE'
'TIMP-1'
'VCAM-1'
'Lipoprotein (a)'
'CD40'
...
...

Urine persistent discriminants (FDR 10%)

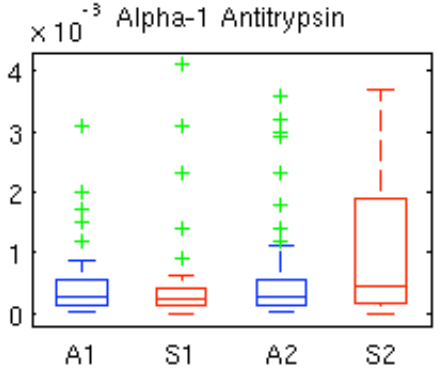
RSVINF

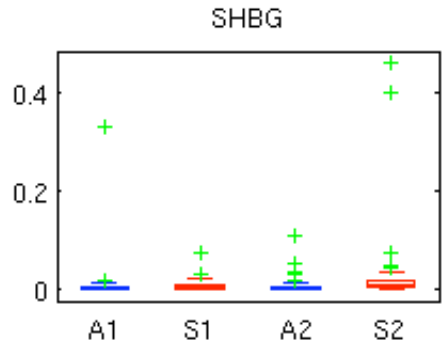
'IgE'
'Insulin'
'Erythropoietin'

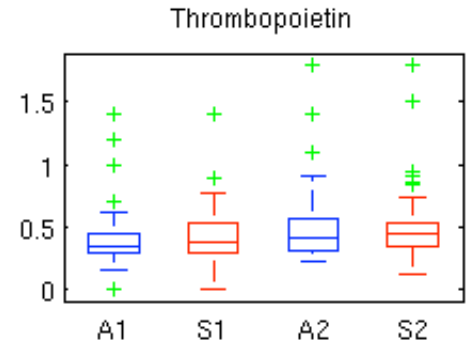
HRVRSVINF

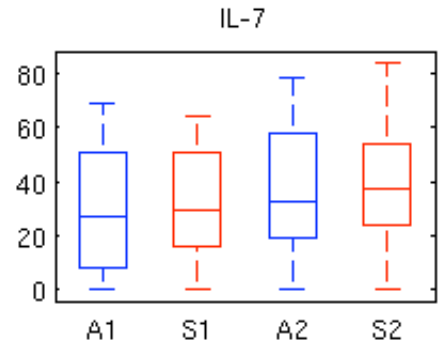
'IgE'
'C Reactive Protein'
'IL-16'
'Stem Cell Factor'
'CD40 Ligand'
'Brain-Derived Neurotrophic Factor'

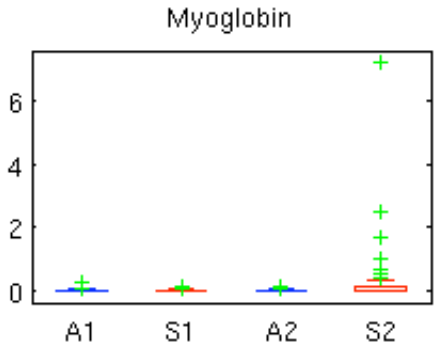
Top 4 RSV/INF discriminants (ranked by Behren's Fisher pv)

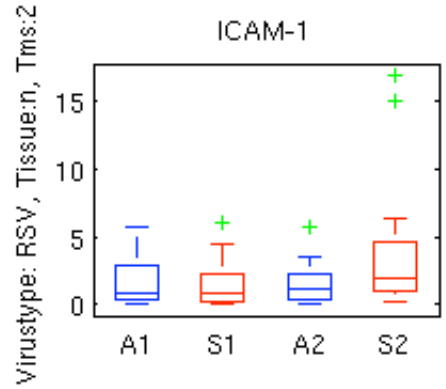


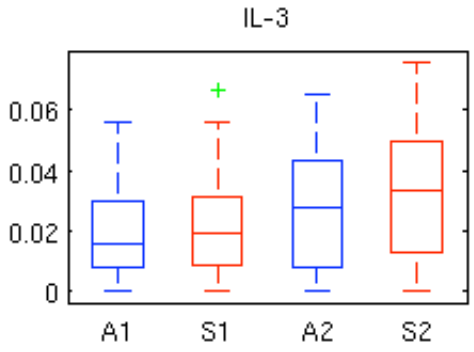


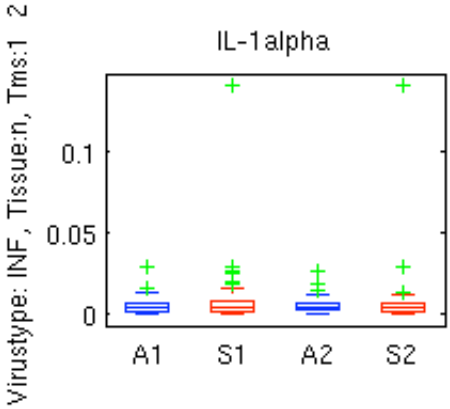








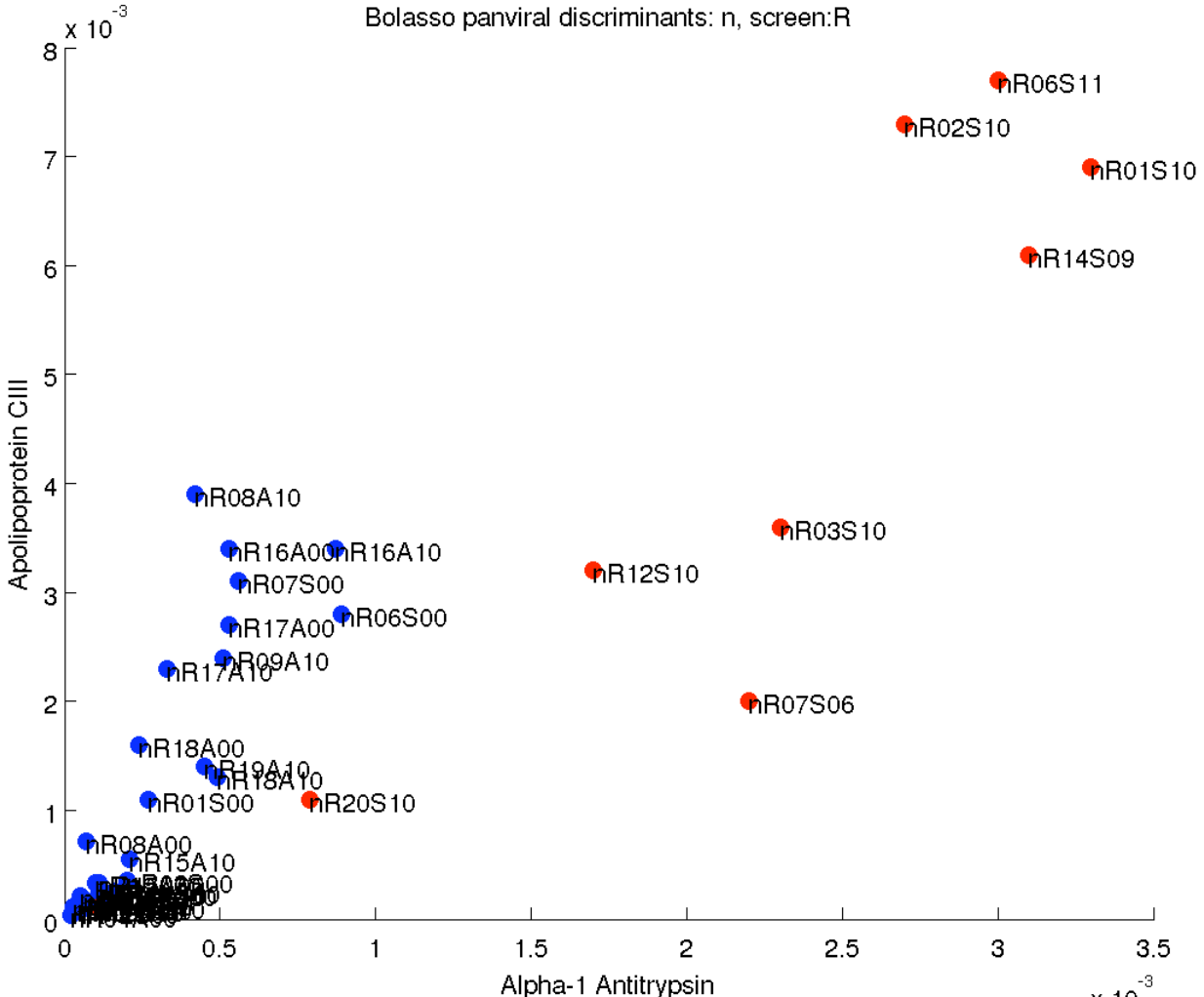




RSV

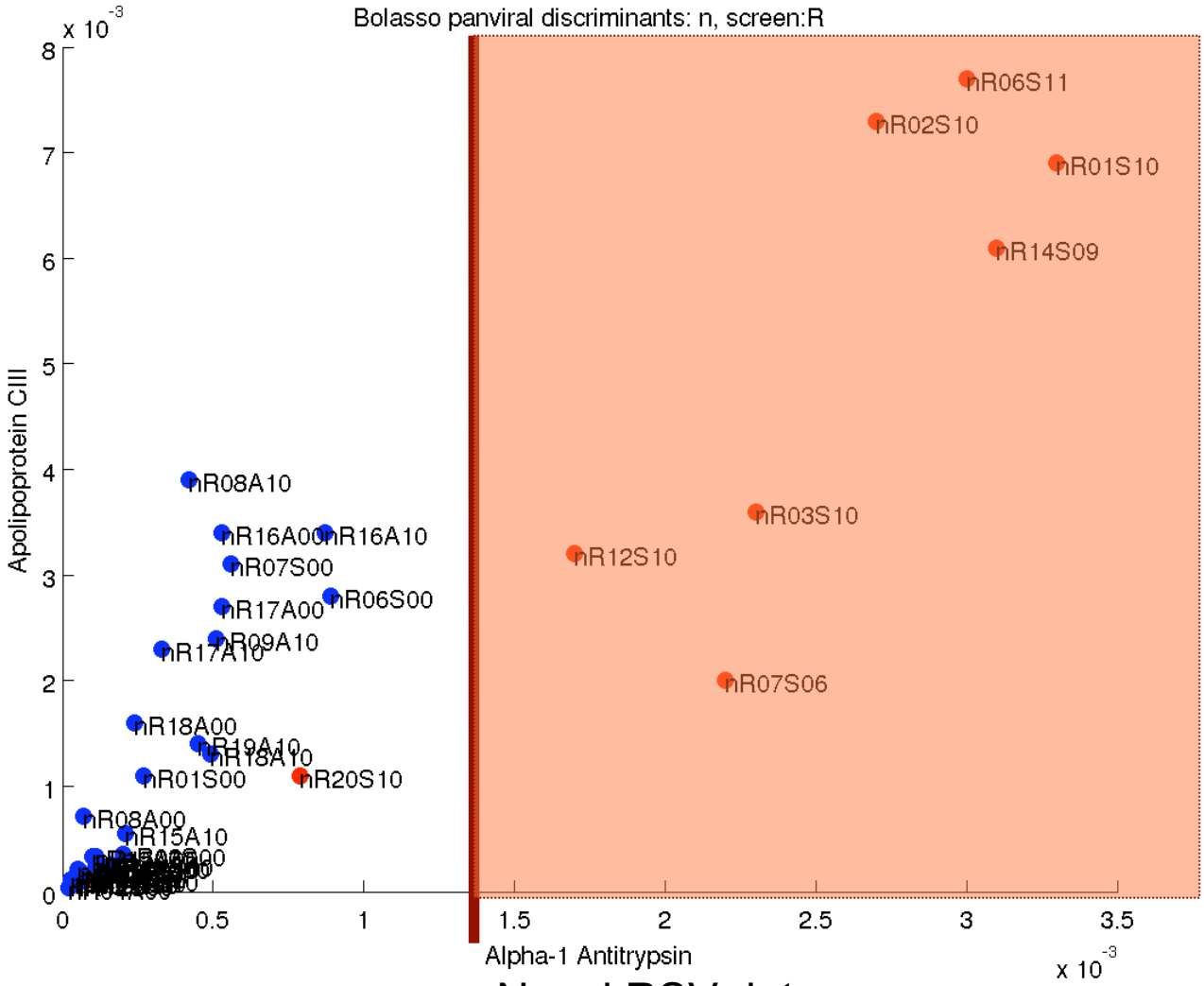
INF

Nasal RSV Bolasso variable selection



Nasal RSV data

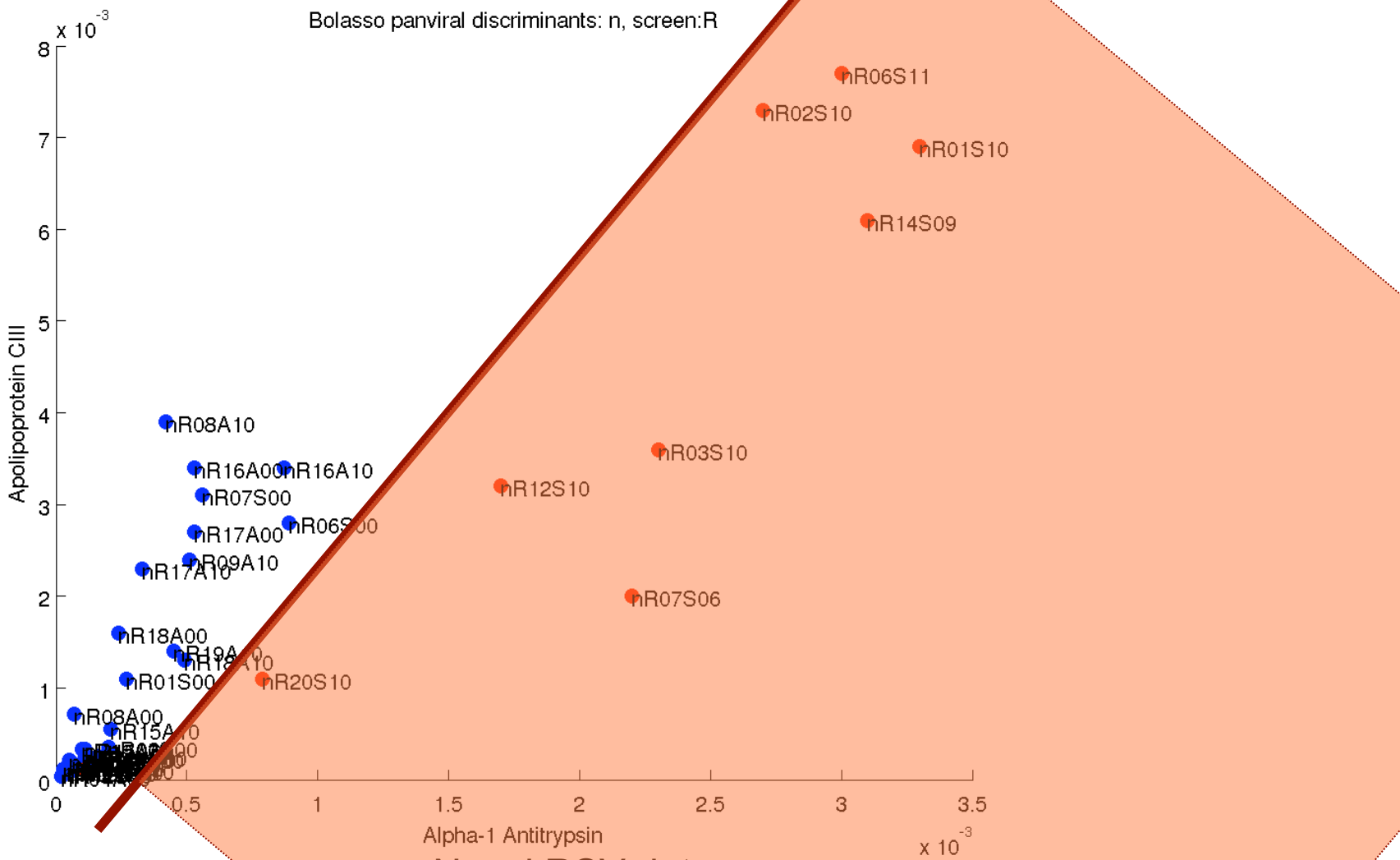
1D Nasal RSV linear discriminant



Nasal RSV data

tpr, fpr	1.0000	0
fnr tnr	0.2222	0.7778

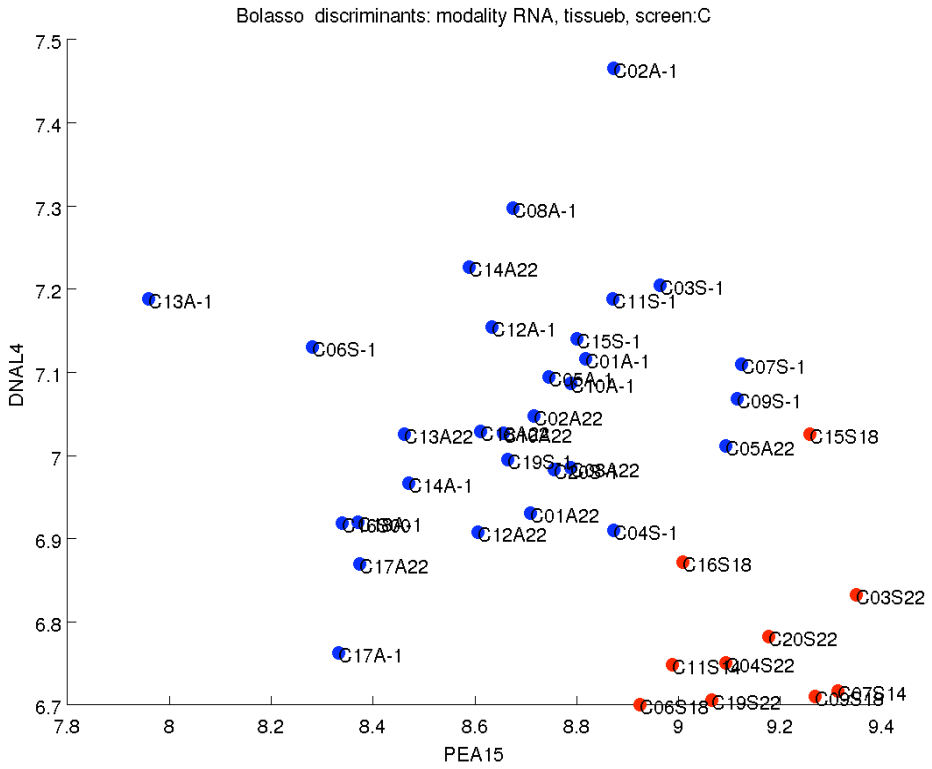
N RSV linear discriminant in 2D

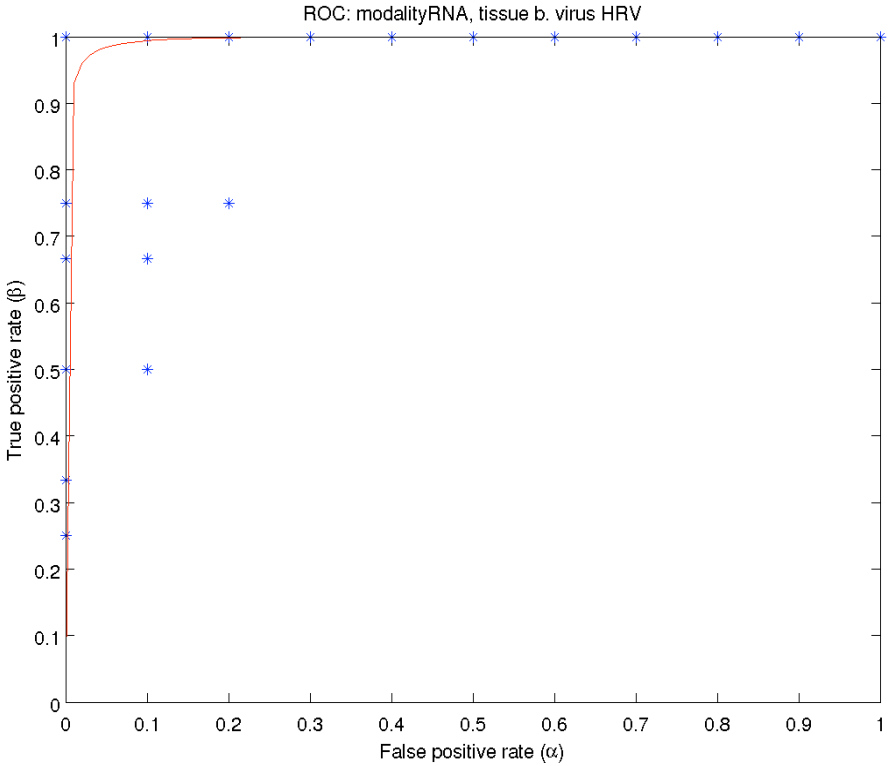


Nasal RSV data

tpr, fpr	1.0000	0
fnr tnr	0.1111	0.8889

ROC analysis: Linear classifier – RNA blood HRV





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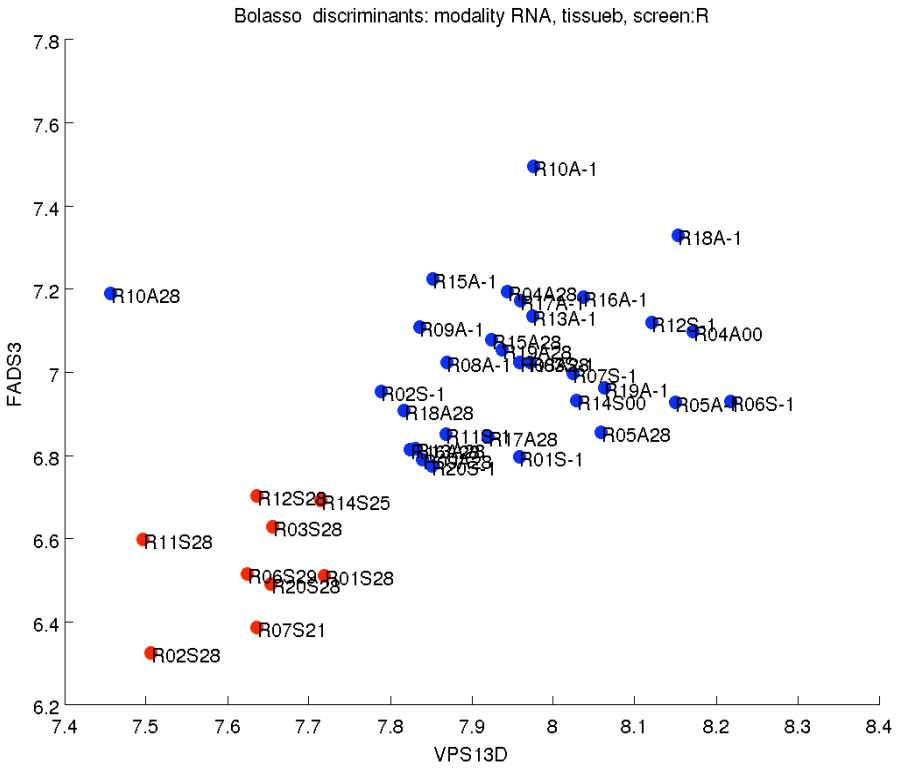
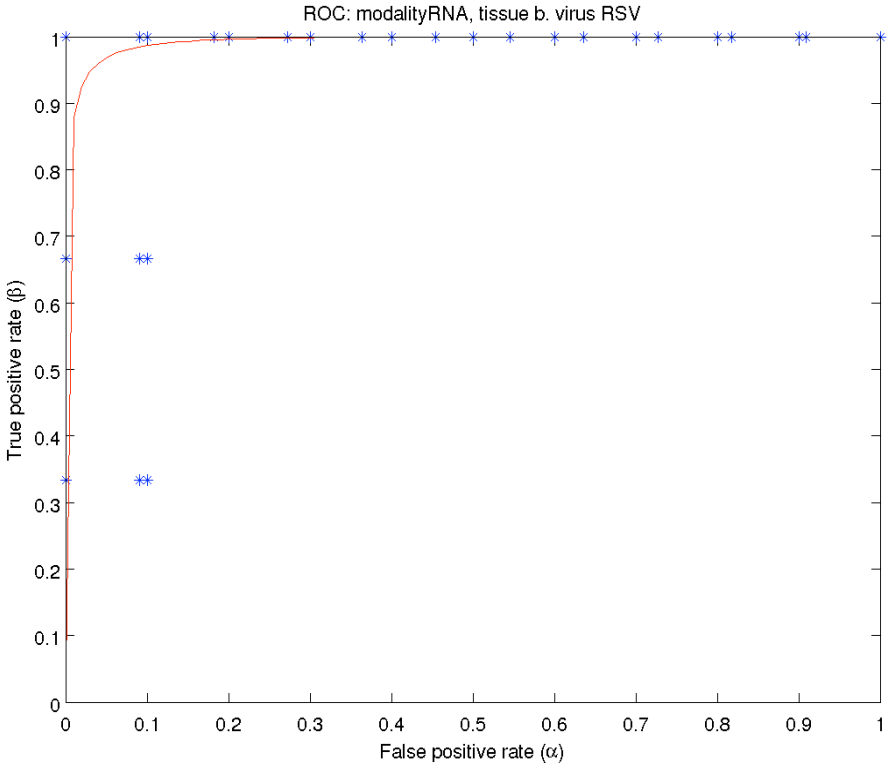
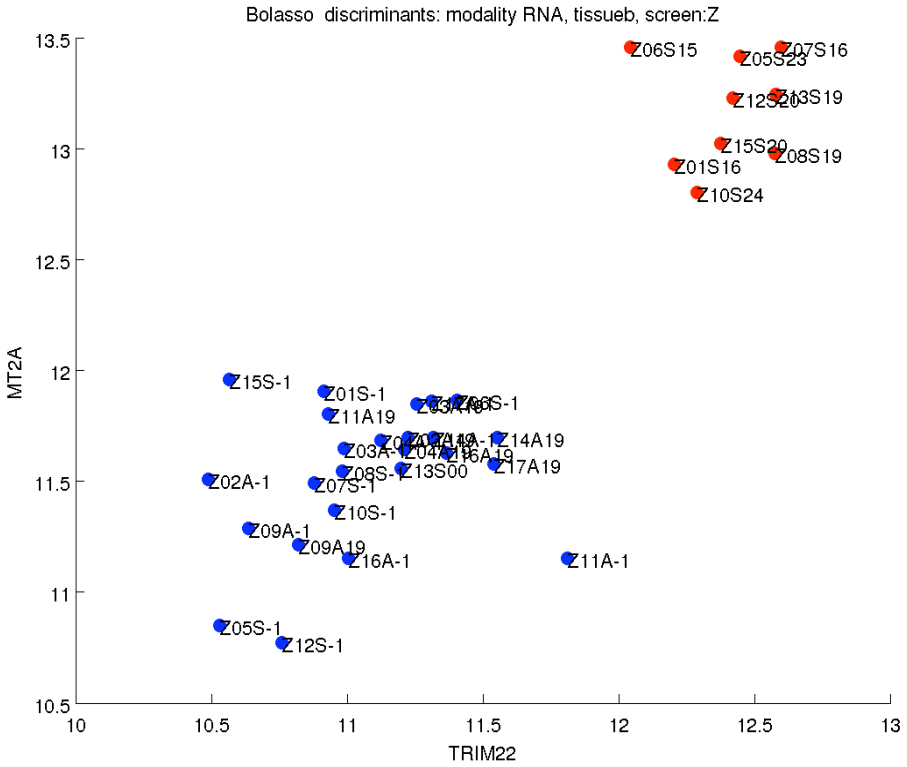
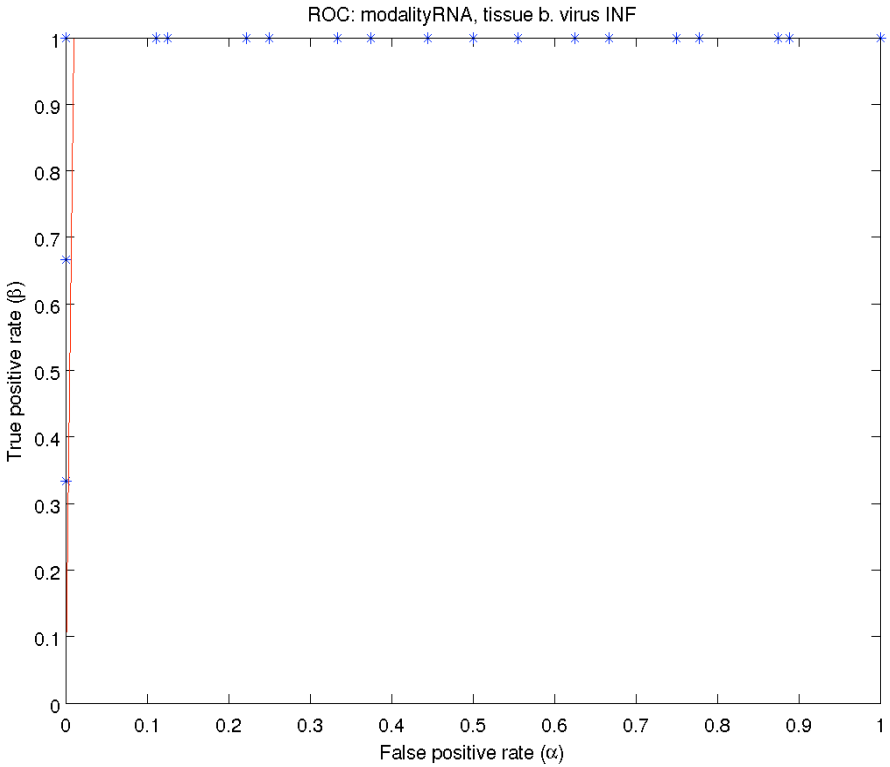
ROC analysis: Linear classifier – RNA blood RSV



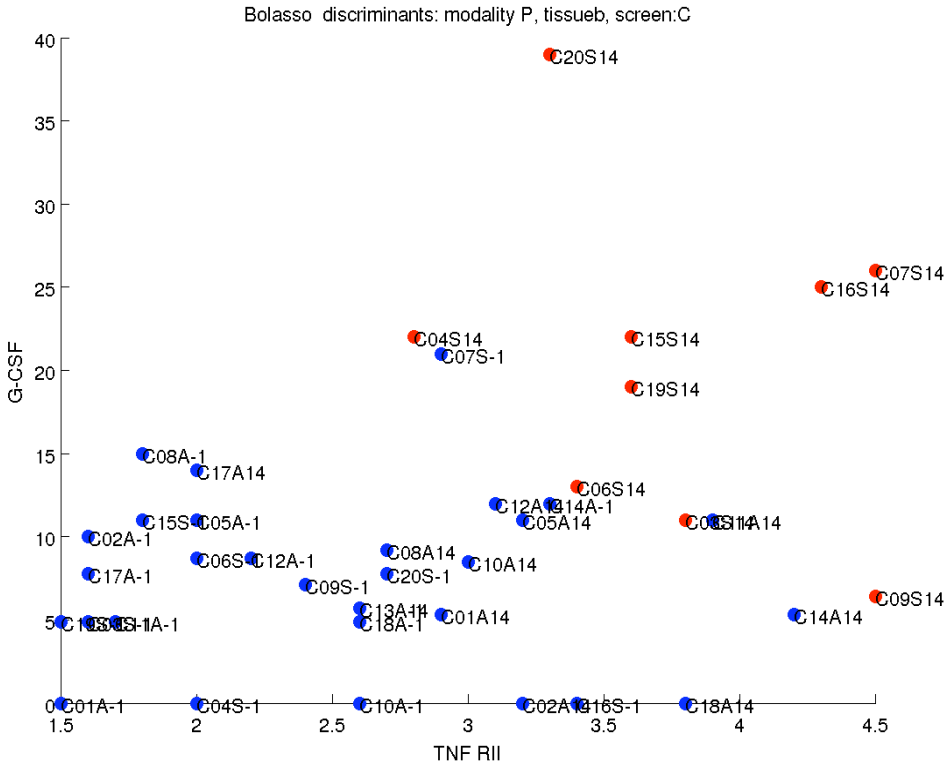


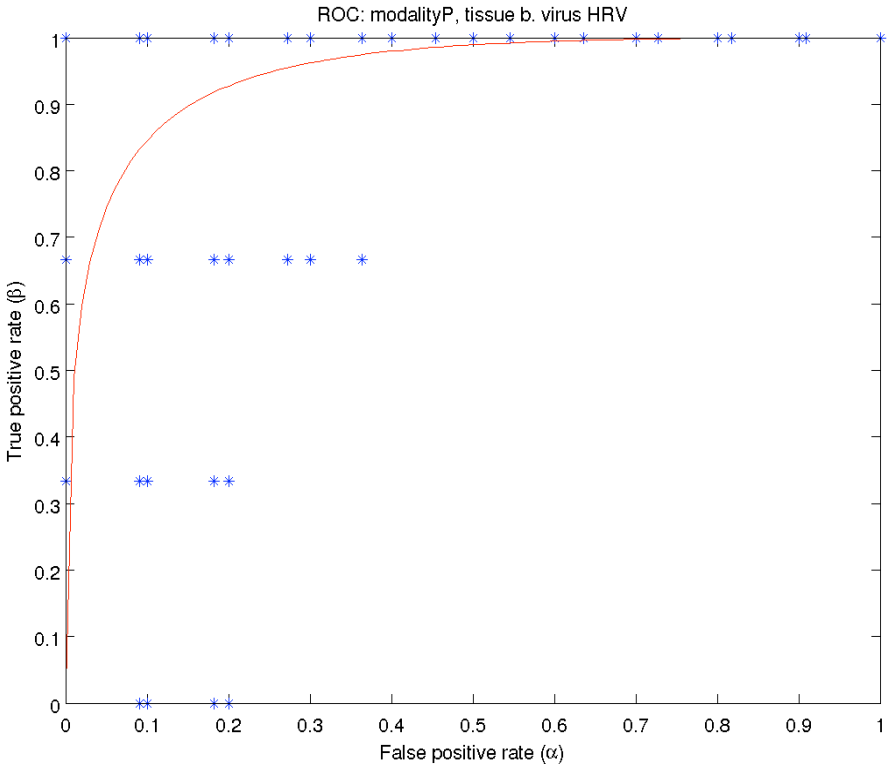
ROC analysis: Linear classifier – RNA blood INF



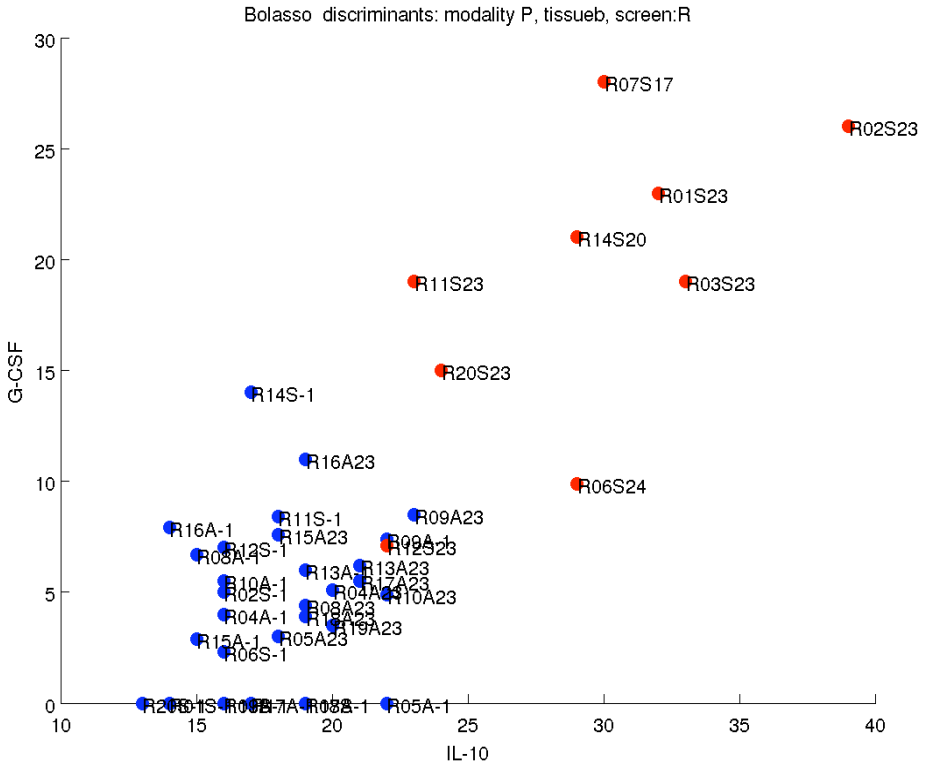


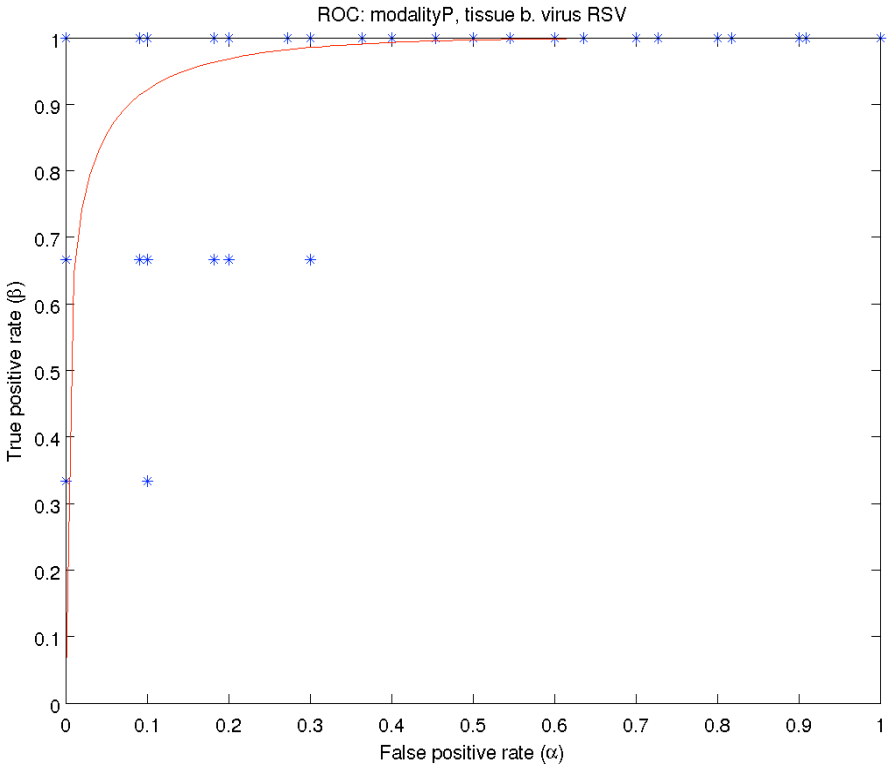
ROC Analysis: Linear classifier – Proteomics blood HRV





ROC analysis: Linear classifier – Proteomics blood RSV





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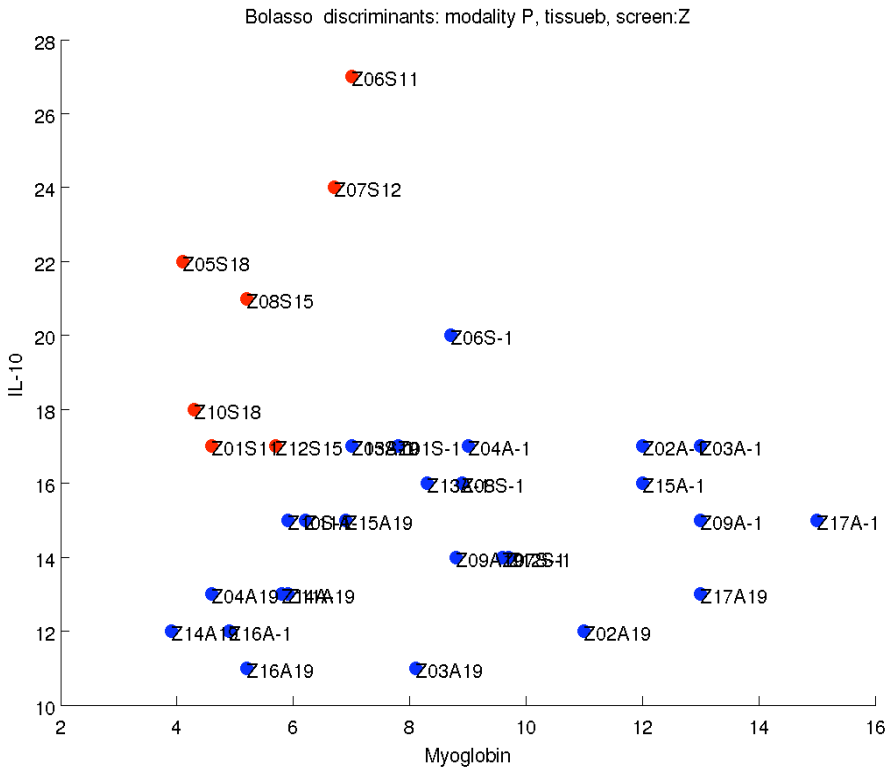
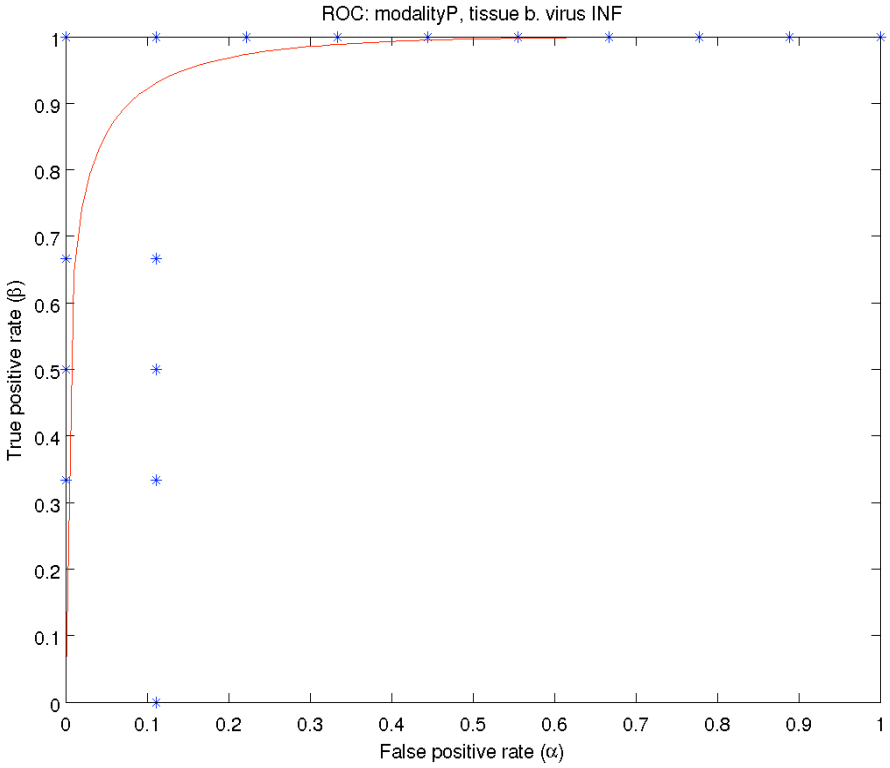
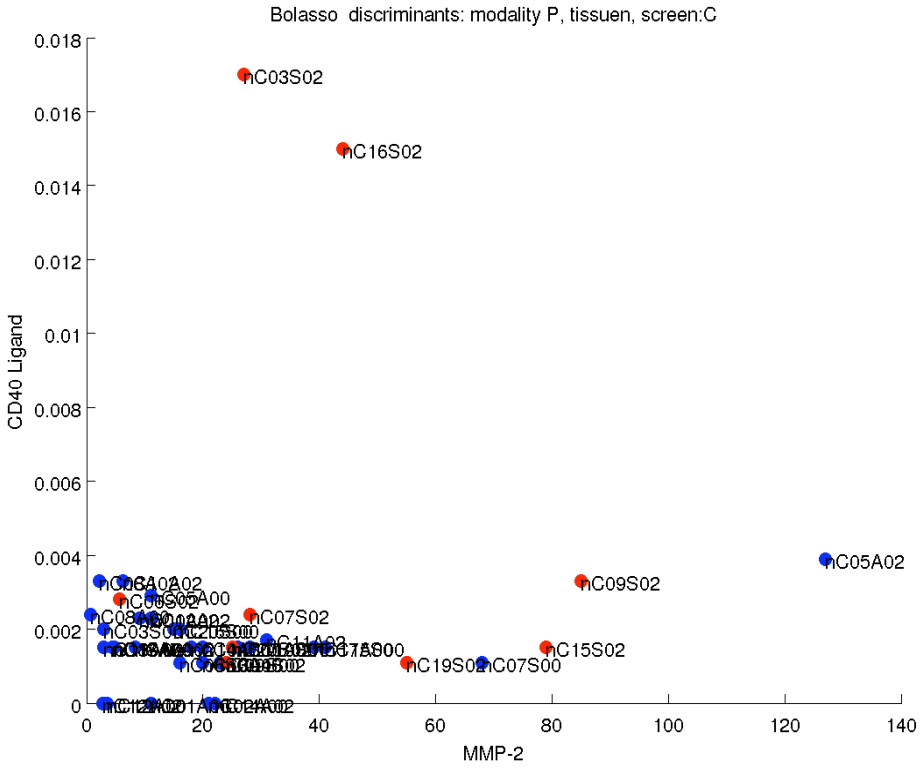
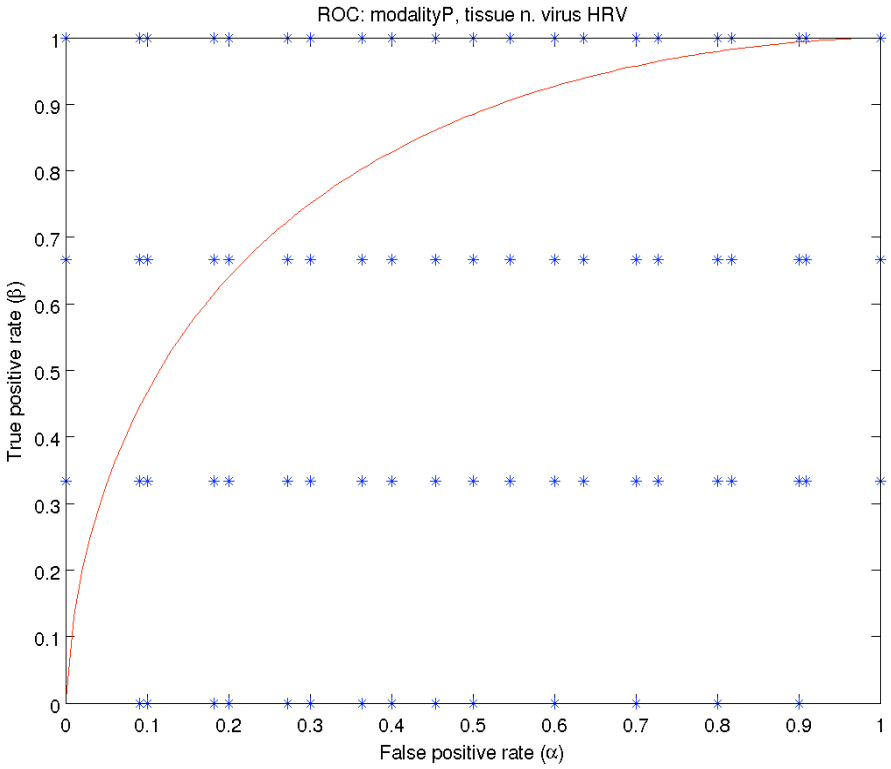


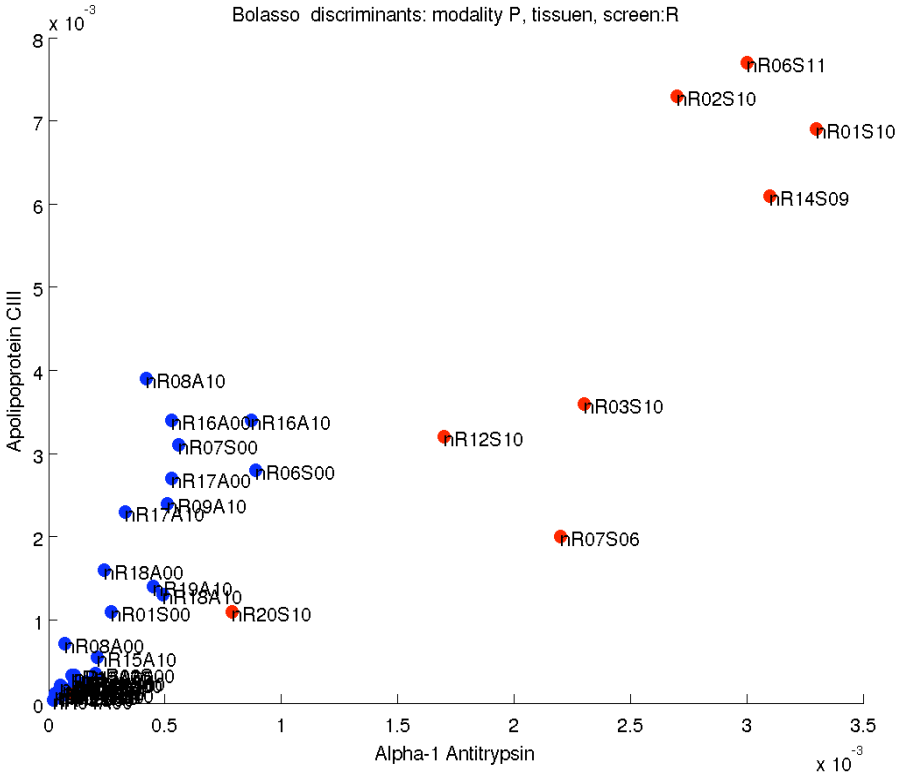


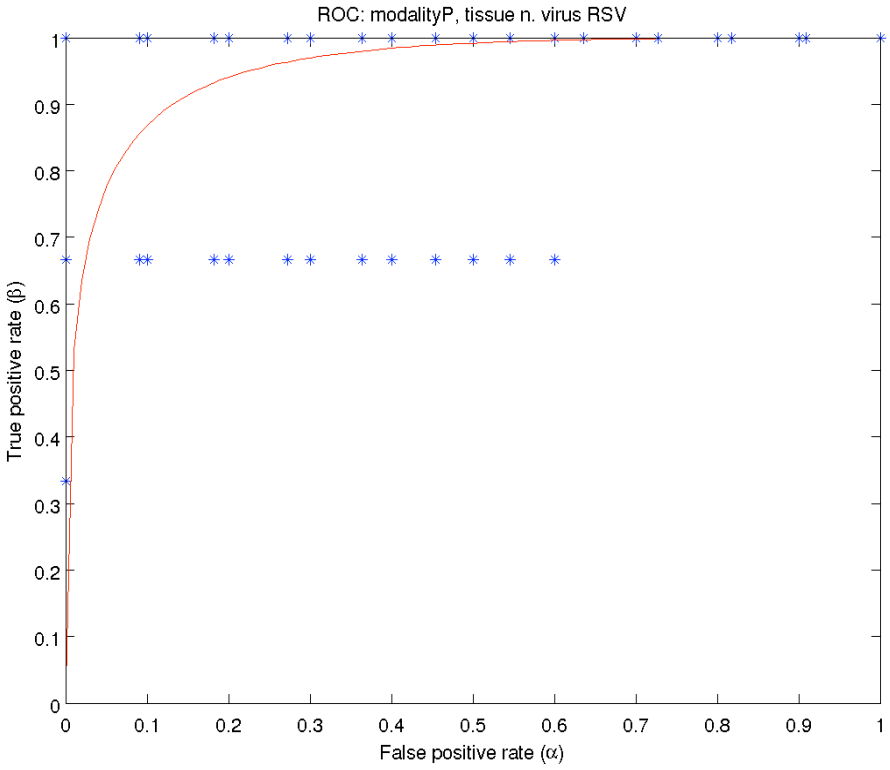
ROC analysis: Linear classifier – Protemoics nasal HRV



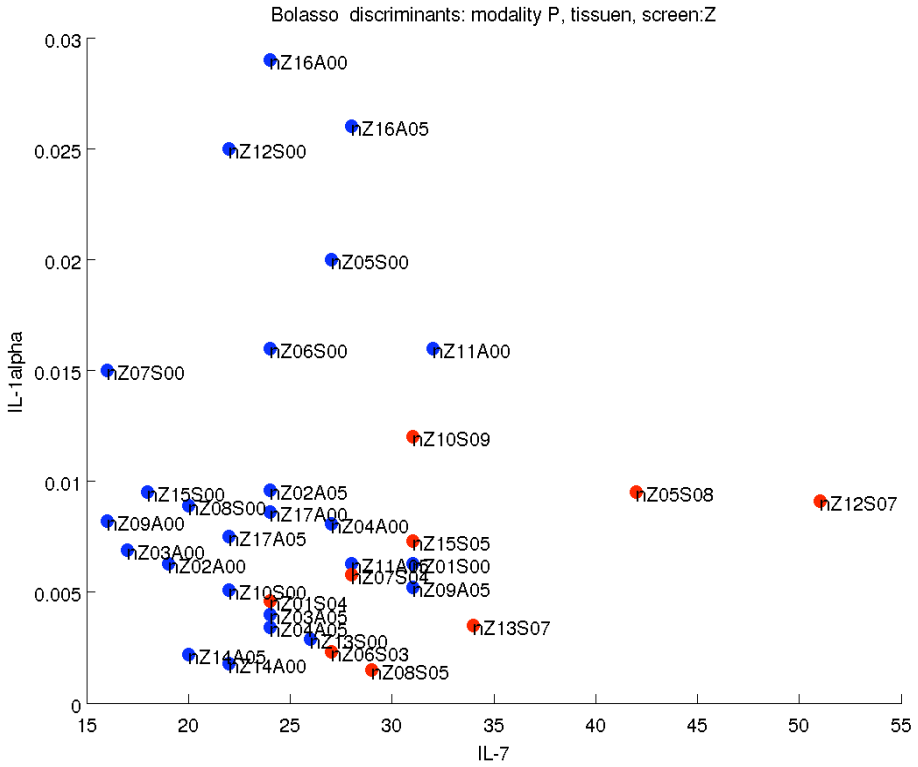


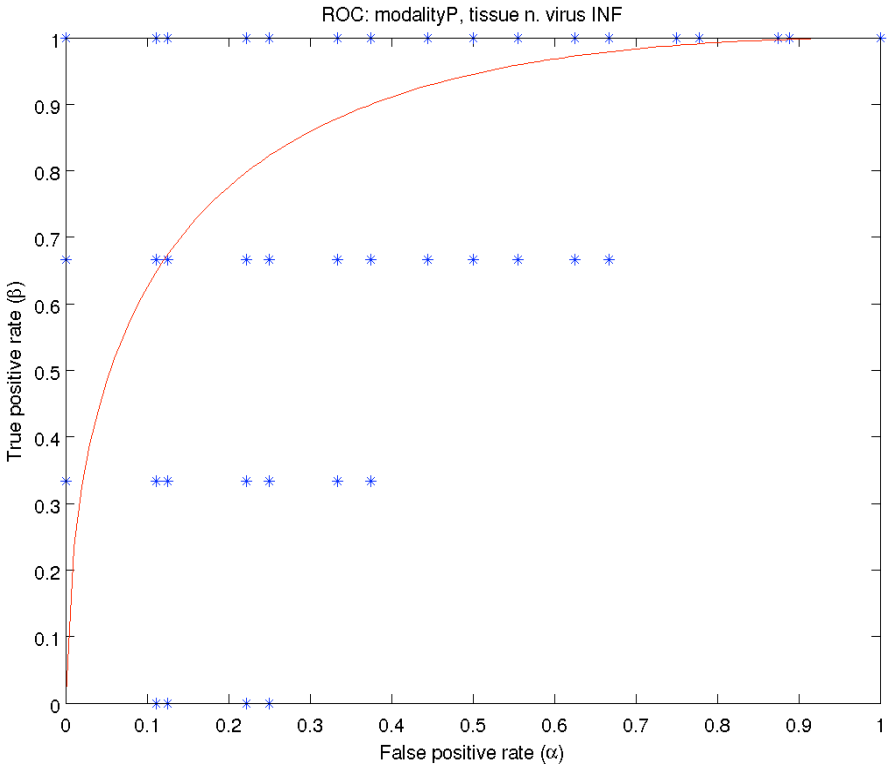
ROC analysis: Linear classifier – Proteomics nasal RSV



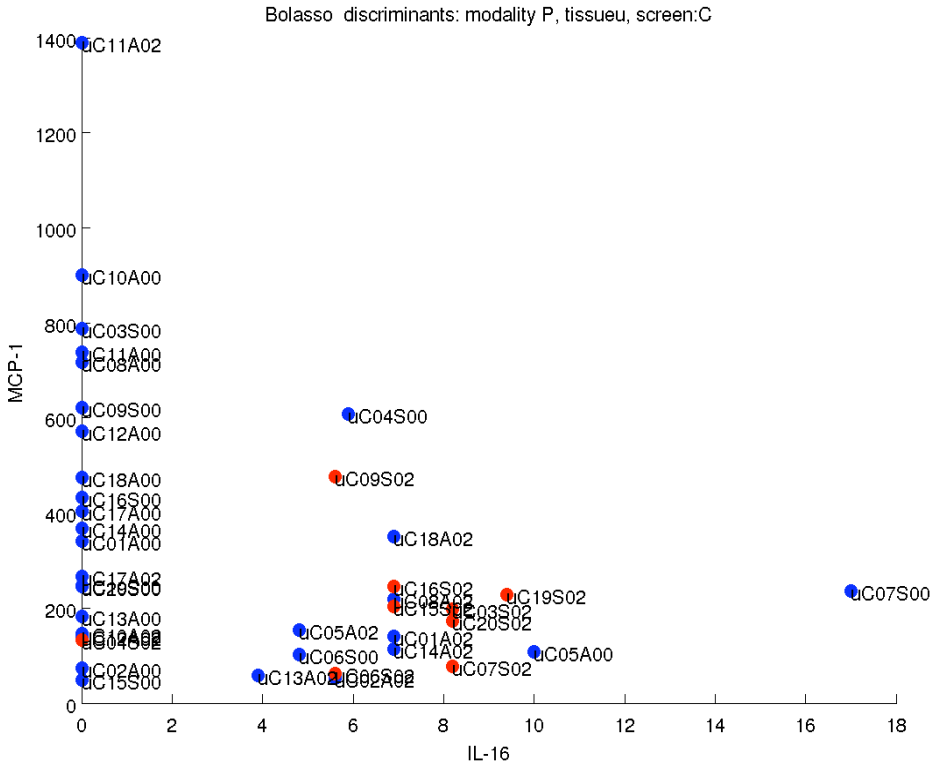


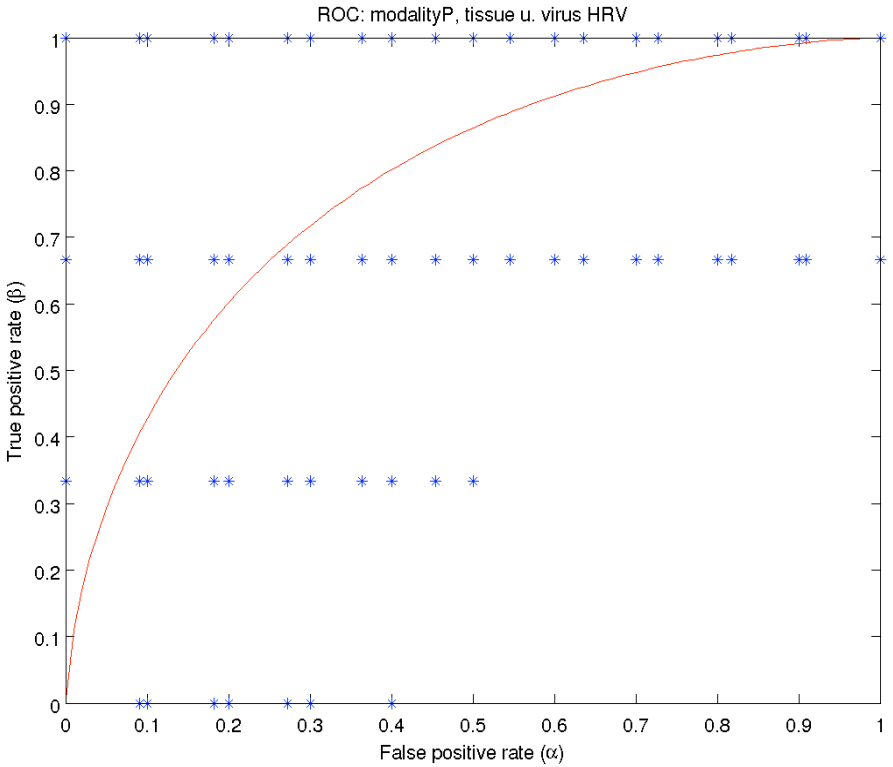
ROC analysis: Linear classifier – Proteomics urine INF



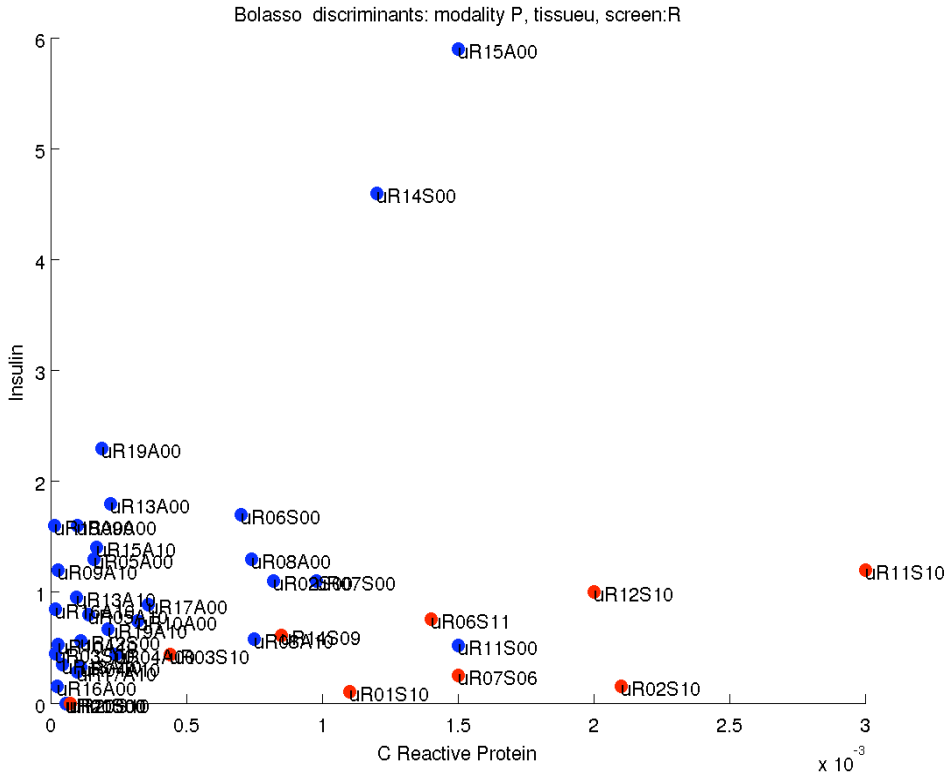


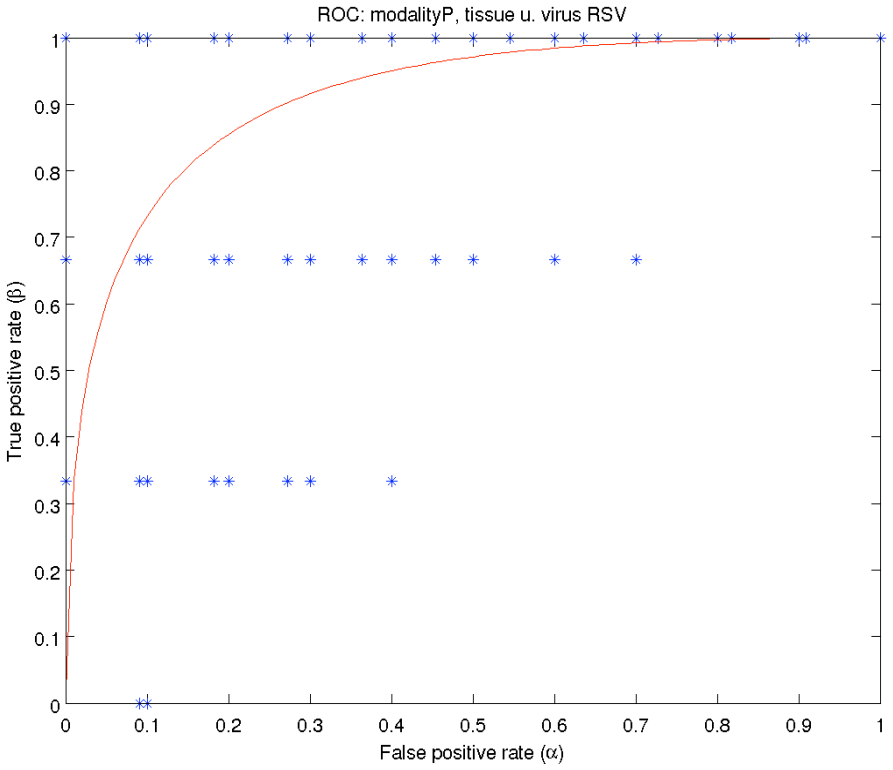
ROC analysis: Linear classifier – Proteomics urine HRV



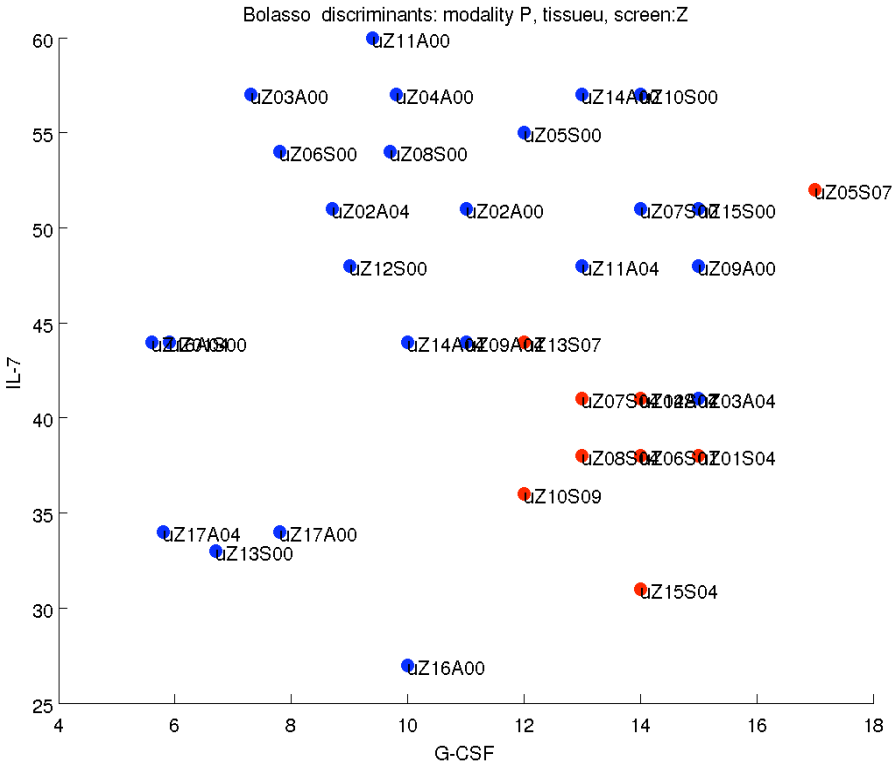


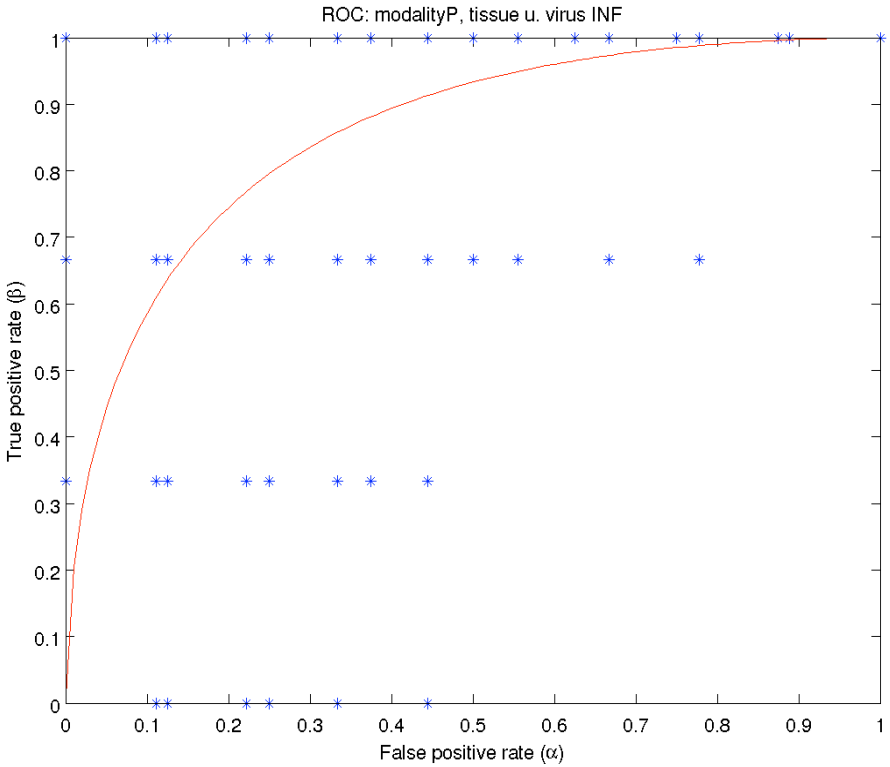
ROC analysis: Linear classifier – Protemoics urine RSV





ROC analysis: Linear classifier – Proteomics urine INF





Some concluding thoughts

1. Results do not inspire optimism on biased proteomics for nasal and urine samples

2. Assays do not seem to be as discriminating as mRNA on blood

3. Caveat: small sample size.
  - larger sample might reveal some non-responders as “outliers”

4. Caveat: only considered pre-inocculation and peak sx time

 - might there exist more discriminating early N or U proteomic signatures?