Coexpression Analysis of Human Genes Across Many Microarray Data Sets

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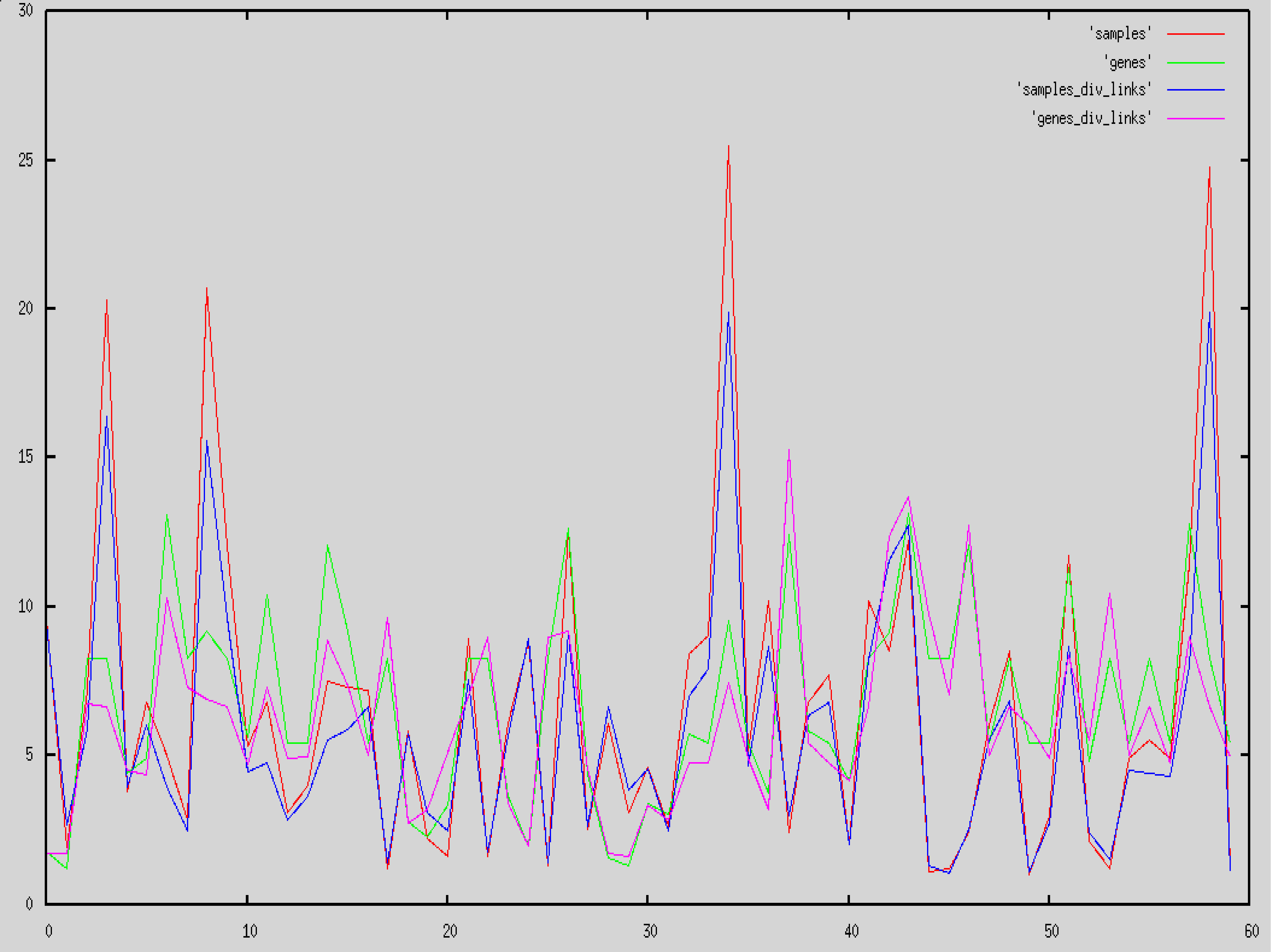
Coexpression Analysis of Human Genes Across Many Microarray Data Sets

Homin K. Lee, Amy K. Hsu, Jon Sajdak, Jie Qin and Paul Pavlidis

Genome Res. 2004 Jun;14(6):1085-94.

Experiment buildup

- **finding repeating co-expression links from different expression data sets.**
- 60 data sets
- find co-expression links in every data set independently
  - does dataset size and number of links correlate ?? (next slide)
  - using only statistically significant links
- count repeating links in different data sets
- use only links found in more than tree data sets (statistical issue!)

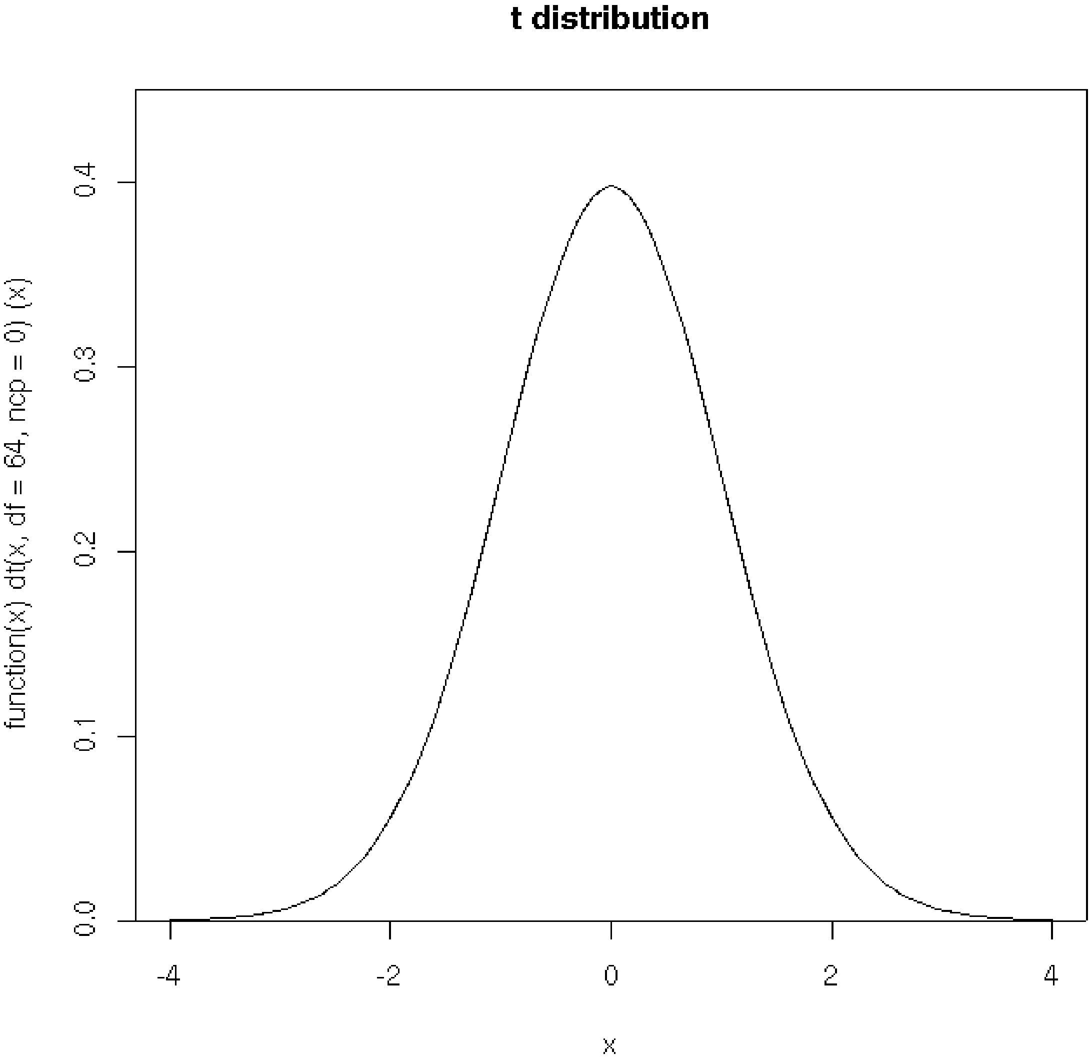


'samples'
'genes'
'samples_div_links'
'genes_div_links'
30
25
20
15
10
5
0
0
10
20
30
40
50
60

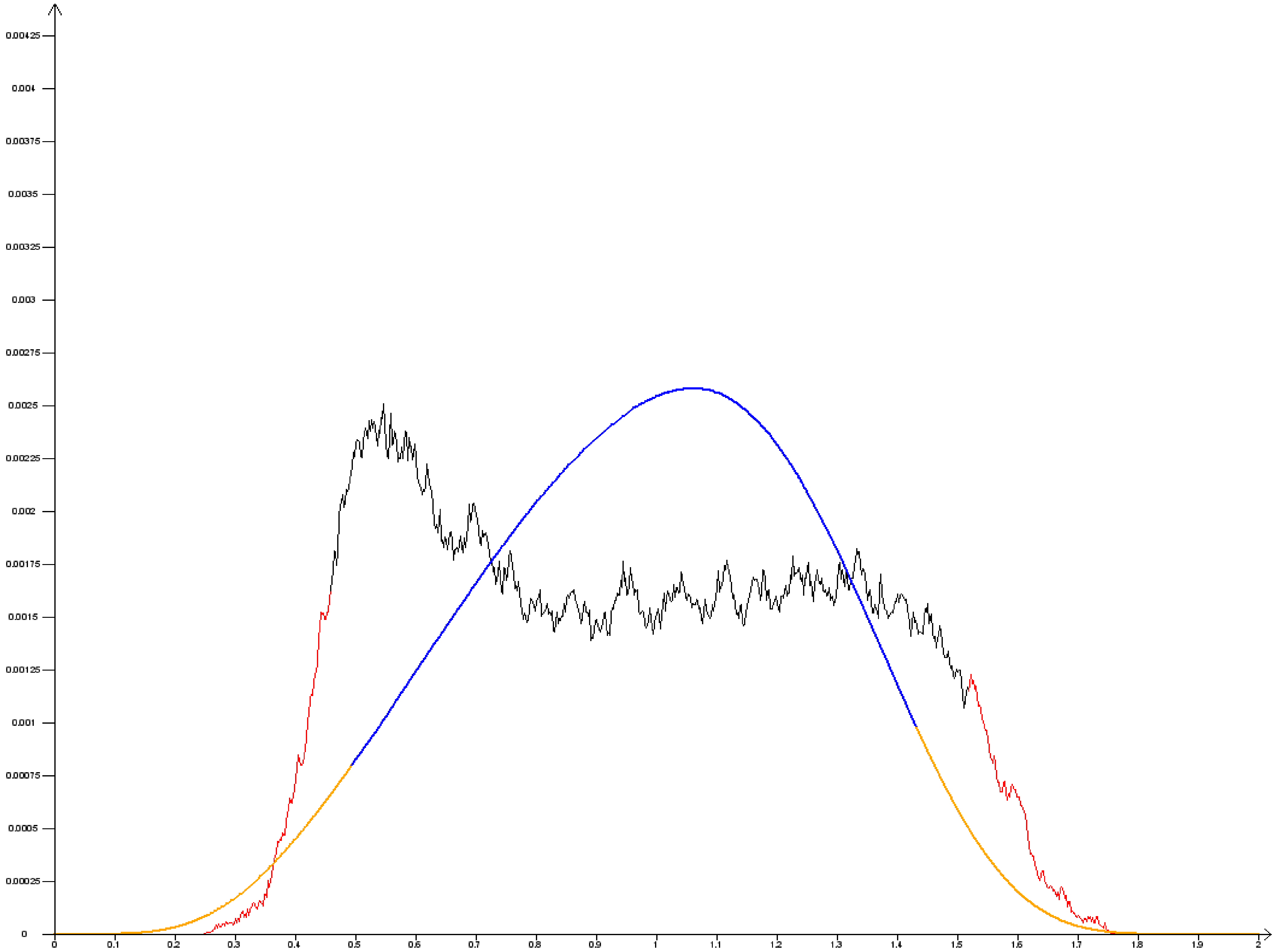
Co-expression link identification

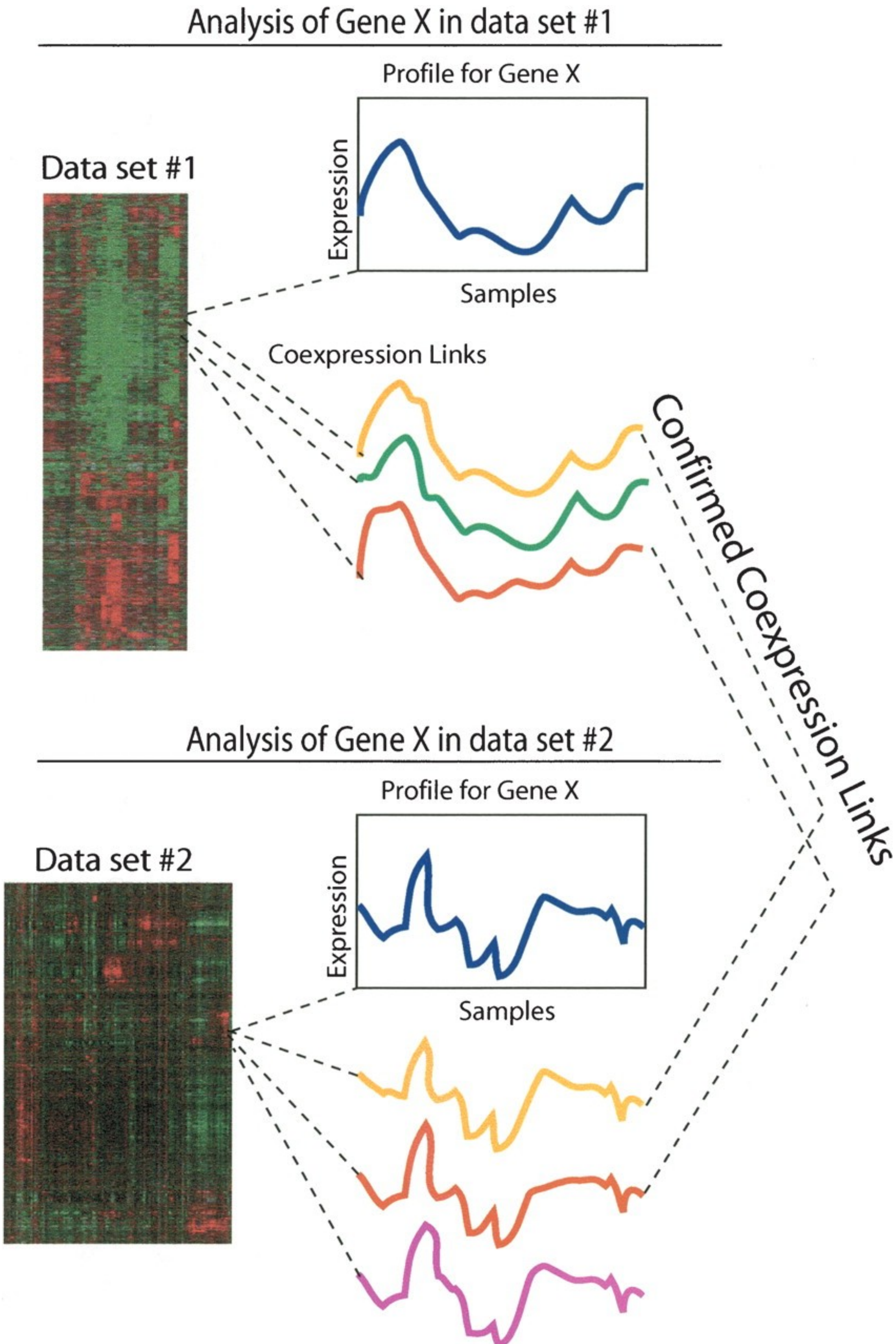
- Using *t* distribution with *n* - 2 degrees of freedom, where *n* is number of samples in data set.
- ***Null* hypothesis** - two genes have nothing in common if the correlation between them corresponds to above distribution.
- *P*-values were corrected using Bonferroni correction with α=0.01
- In addition only links among 0.5 % top or bottom were concidered for further study.
- alltogether 9.7 M “raw links”

t distribution



- *t* distribution, with *n* - 2 degrees of freedom
- *n* = 66 (average from data sets in article)


0.00425
0.004
0.00375
0.0035
0.00325
0.003
0.00275
0.0025
0.00225
0.002
0.00175
0.0015
0.00125
0.001
0.00075
0.0005
0.00025
0
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
1.1
1.2
1.3
1.4
1.5
1.6
1.7
1.8
1.9
2


Analysis of Gene X in data set #1
Profile for Gene X
Data set #1
Expression
Samples
Coexpression Links
Confirmed Coexpression Links
Analysis of Gene X in data set #2
Profile for Gene X
Data set #2
Expression
Samples

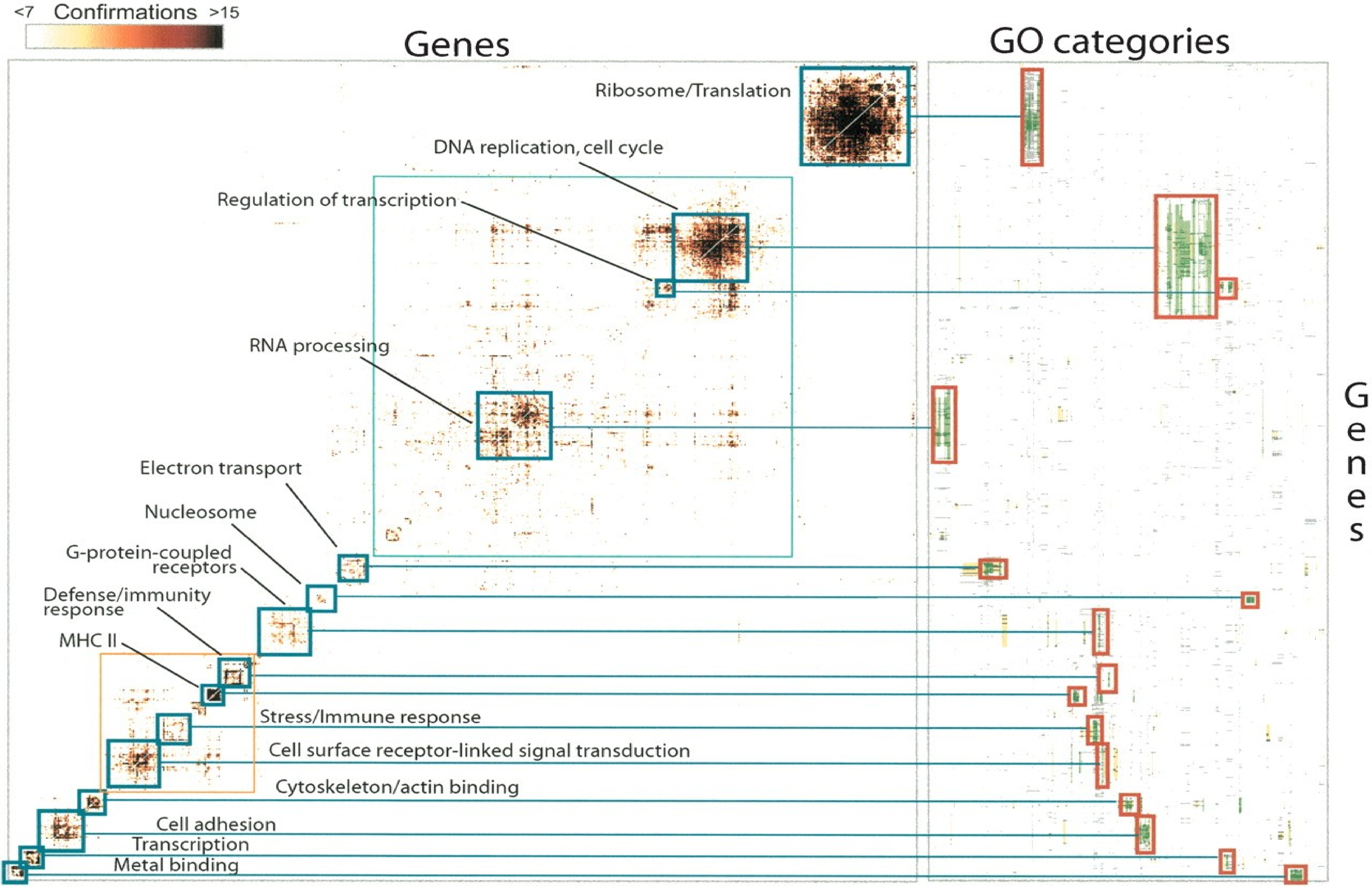
Link comfirmation

- “shuffled” data test
  - about the same number of links in each “shuffled” data set as origin
  - about the same number of positive and negative correlation
    - (positive correlations in real data more than negative)!
  - 100 such datasets
- the results:
  - **~ 5 % of “3+” links found in real data could also be found in randomized data**
  - ~ 24 % of “2+” links found in real data could also be found in randomized data

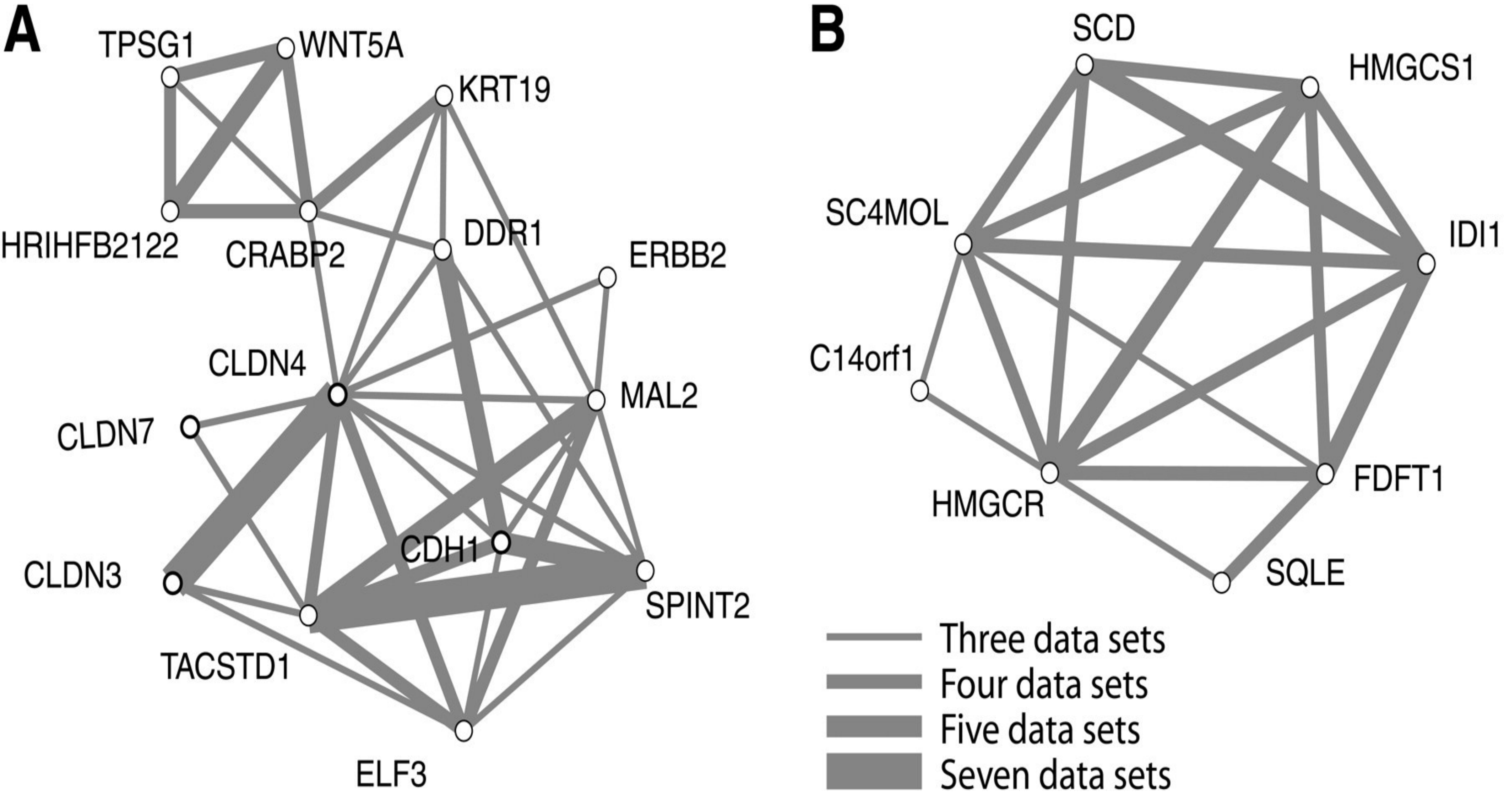
results

- from 9.7 M only 220 k of links were found in “3+” data sets
- 8805 genes of 14.172 compared genes have atleast one “3+” link (60 %)
- also a GO analysis, but not used for confimation, therefore not interestin in this article ...
- For cluster analysis only “7+” links were used
  - 720 genes
  - 10 089 links

results


<7
Confirmations
>15
Genes
GO categories
Ribosome/Translation
DNA replication, cell cycle
Regulation of transcription
RNA processing
Electron transport
Nucleosome
G-protein-coupled receptors
Defense/immunity response
MHC II
Stress/Immune response
Cell surface receptor-linked signal transduction
Cytoskeleton/actin binding
Cell adhesion
Transcription
Metal binding
Genes

To visualize smaller network bits



For discussion !

- Does this kind of statistical schema is good enough ?
- Could there be some better, improved, schema ?
  - Instead of *t* distribution use the distribution of **all distances** in given data set
  - or is it not statistical ?

tnx

- any other questions ?
- comments ?
- suggestions ?