Bioquali : tool for analyzing regulatory networks

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What is Bioquali?

- Software dedicated to the analysis of regulatory networks following the rule: "All variation of a product should be explained by an influence from one of its predecessors"
- Examples:



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Which network analyse?

- Network:
 - Nodes:
 - Proteins, complexes, signals
 - Edges Influences:
 - A is an activator [+] of C
 - D is an inhibitor [-] of C
 - A regulates B in a complex way [?]

As a file:
 A -> B ?
 A -> C +
 D -> C -



Which experimental data provide?

from Microarrays:



- Comparison of 2 conditions
- Decide a threshold (T): 2fold, 3-fold, etc.
- Classify data in:
 - geneA = + (geneA was Tfold up-regulated)
 - geneB = (geneB was Tfold down-regulated)

- from Literature:
 - Comparison of 2 conditions
 - Classify data in:
 - geneA = + (geneA was upregulated)
 - geneB = (geneB was down-regulated)

- Not all products of a network will be observed!
- As a file:

geneA = + geneB = -

What can we do ?

Consistency Rule: "An up/down regulation of a product in a network should be at least explained by one of its predecessors"

- Check consistency
- Diagnostic if inconsistent
- Prediction of products' variation if consistent

Examples of Inconsistency diagnostic





Solving the inconsistency (diagnostic)

Inconsistency between network and Experimental data

B

A = +

 $\mathbf{B} = +$

Diagnosis: Correction of model or data, or both

Predicting when consistent





- Mathematics
 - Coding the network and experiment as qualitative equations:
 1 equation per node
 - Solving the whole system using algebra among +,-,? values.
- Informatics
 - Whole system is coded as a decision diagram using Python

Example: Escherichia Coli

- Obtained from RegulonDB 2007
- Network
 - Interactions:
- Transcription factor gene
- Formation of complexes
 - Sigma factor gene
- 1763 nodes 4491 edges
- Experimental data
 - Growth phase: Stationary phase vs Log phase
 - 50 products up/down regulated extracted from literature

Example: Escherichia Coli

Checking the consistency of E.Coli regulatory network



Bioquali			×
Data example			
Step 1 :			
Interactions data file Use the previous graph		Browse	
Step 2 :	un Baus Baus Baus ann Baus		1
Submit Query		Browse	
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Graph uploaded is coherent.			
No experimental data uploaded.			
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Example: Escherichia Coli

Checking the consistency of E.Coli regulatory network with experimental data

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Vous êtes ici : Accueil > Outils > Réseaux d'interactions > Bioquali



Bioquali	X
Step 2 :	^
Experimental data set Browse	
Submit Query	
Bioquali results ④ Graph nodes number :1763 ④ Graph edges number :4491 ③ Prediction number :0	
Graph uploaded is coherent.	ini s
Datas are not coherent.	
nconsistent sub-graph and associated data description.	
Factor Target Influence hns appY -	

Example: Solving the problem

Is experimental data correct?



References:

- Dersch et al. 1993 "Synthesis of the Escherichia coli K-12 nucleoid-associated DNA-binding protein H-NS is subjected to growth-phase control and autoregulation"
- Atlung et al. 1996 "The histone-like protein H-NS acts as a transcriptional repressor for expression of the anaerobic and growth phase activator AppY of Escherichia coli"



... Example: Escherichia Coli

 Testing Consistency of E.Coli regulatory network corrected with experimental data





Validation of the Prediction

- Microarray data set:
 - from Faith *et al.* 2007 and Allen *et al.* 2003
 - Condition: Stationary Phase after 720min vs log phase
 - Threshold = 2-fold
 - 720 products
- 526 variations predicted
- Comparison between predictions and microarray
 - 177 common observed products
 - 77% of them agreed
- Similar results with other experimental conditions





Conclusion

- Bioquali allows to perform analysis, diagnostic and prediction in regulatory networks following the consistency rule
- Large scale network analysis
- Future work:
 - Help in the diagnostic
 - Experimental plan



Thank you!