Evidence for dynamically organized modularity in the yeast protein–protein interaction network

- 文章类型：**knowledge discovery**

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The process of knowledge discovery

1. **Hubs Vs. non-hubs, in node removals?**
2. **Hub category: to date or party?**
3. **Behaviors of each kind of hub**
4. **Conclude: organized modularity**

Abstracts

- **scale-free protein–protein interaction networks IE. interactome networks**
- **random node removal(failure) Vs. targeted removal of hubs**
- **A link between the potential scale-free topology of interactome networks and genetic robustness seems to exist(gene knockouts)**
  - “party” hubs, which interact with most of their partners simultaneously,
  - and “date” hubs, which bind their different partners at different times or locations
- **organized modularity in which date hubs organize the proteome, connecting biological processes—or modules—to each other, whereas party hubs function inside modules**

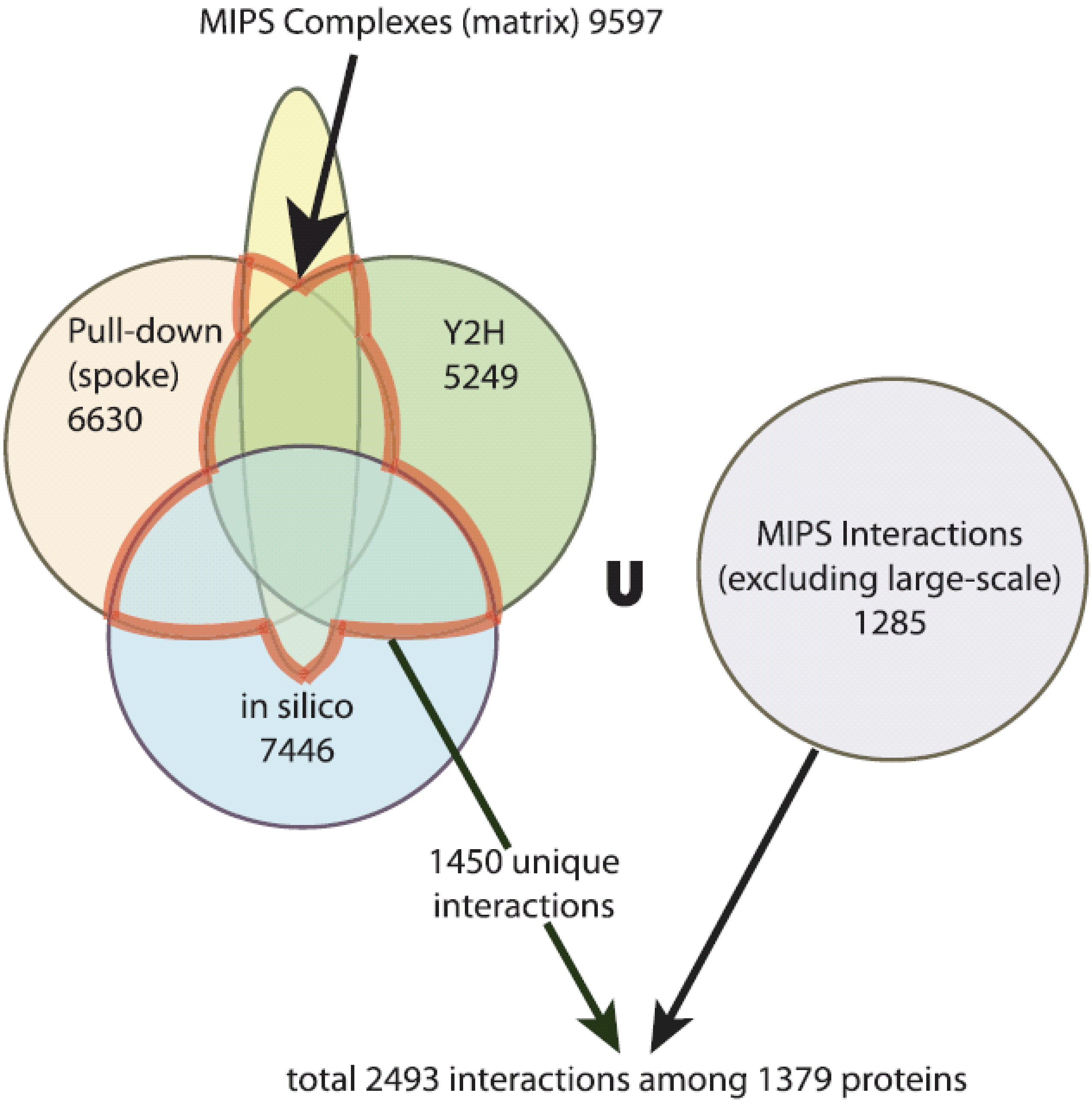
Data availability

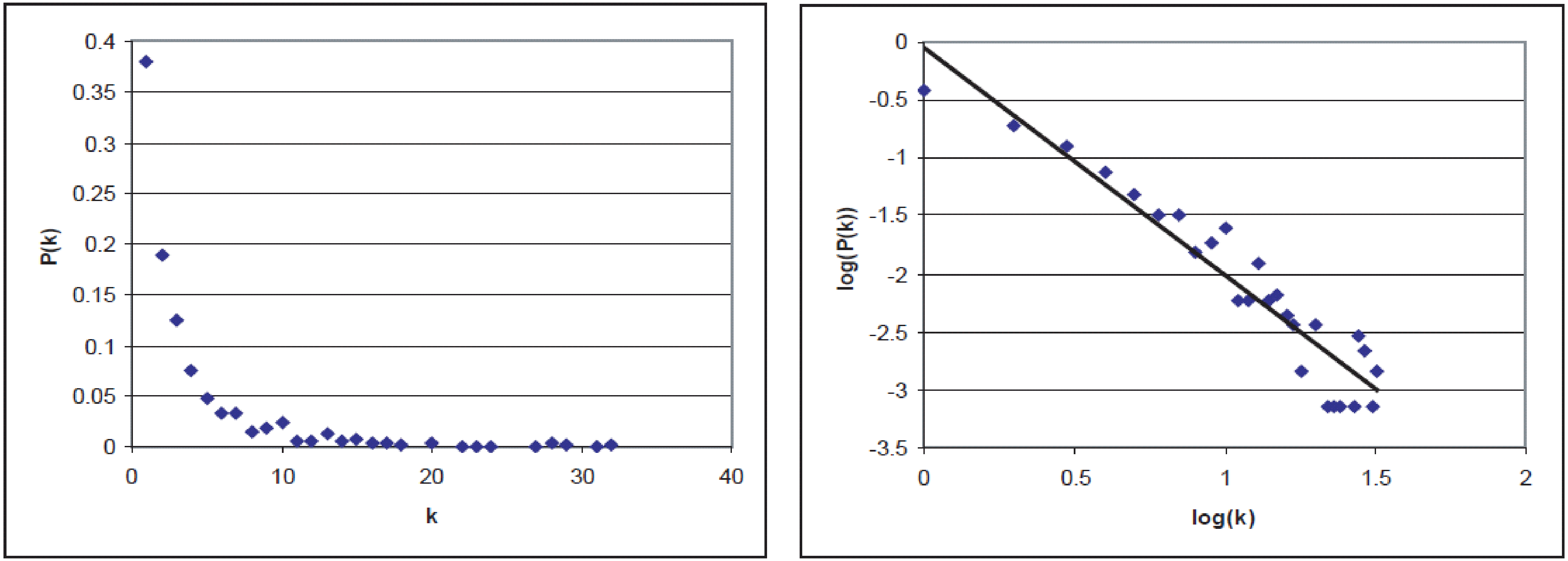
- **Using compilations of yeast messenger RNA expression profiling data**

- **Problem: Hubs connected by false-positive interactions**
  - *(uncorrelated in mRNA expression with their interaction partners, resemble date hubs)*

Data integrating and/or combination

- **“filtered yeast interactome”(FYI) data set**
- **Construction: intersecting data generated by several different interaction detection methods**
- **contains 2,493 high-confidence interactions, <u>each observed by at least two different methods</u>**


MIPS Complexes (matrix) 9597
Pull-down
(spoke)
6630
Y2H
5249
in silico
7446
U
MIPS Interactions
(excluding large-scale)
1285
1450 unique
interactions
total 2493 interactions among 1379 proteins

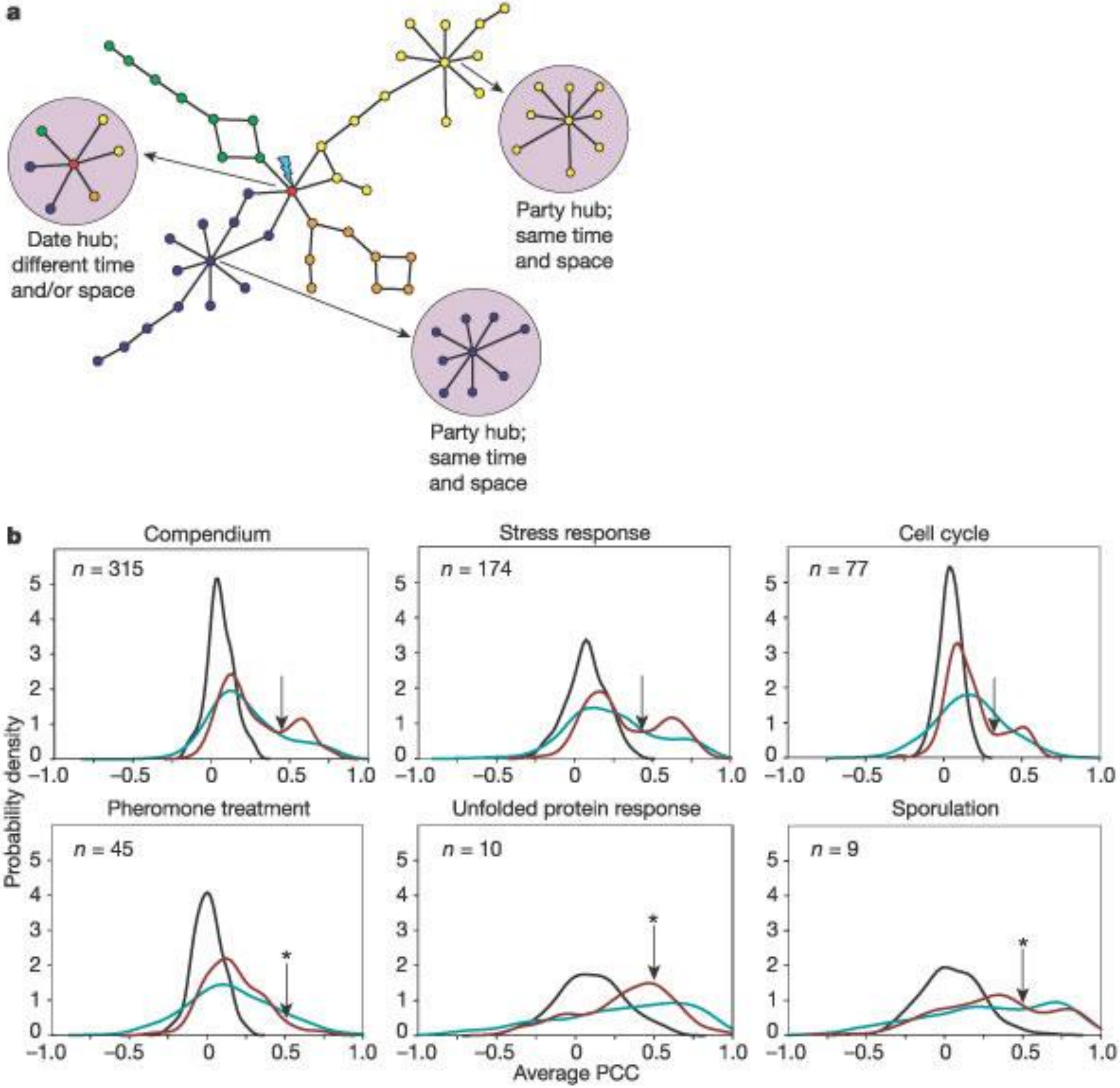


度分布符合scale-free networks的特点

PCCs of hubs follow bimodal dist.

- average PCCs of hubs, defined as nodes (proteins) with degree k greater than 5, follow a <u>bimodal distribution</u> in the whole compendium.

- In contrast, the average PCCs of non-hubs, defined as nodes with degree k of 5 or less, show a <u>normal distribution</u> centred on 0.1


a
Date hub;
different time
and/or space
Party hub;
same time
and space
Party hub;
same time
and space
b
Compendium
n = 315
Stress response
n = 174
Cell cycle
n = 77
Pheromone treatment
n = 45
Unfolded protein response
n = 10
Sporulation
n = 9
*
Probability density
0
1
2
3
4
5
−1.0
−0.5
0
0.5
1.0
Average PCC

Is this bimodal model predictive for real protein hubs?

- Highlighting bio-significance by behabior study of date Vs. party hubs

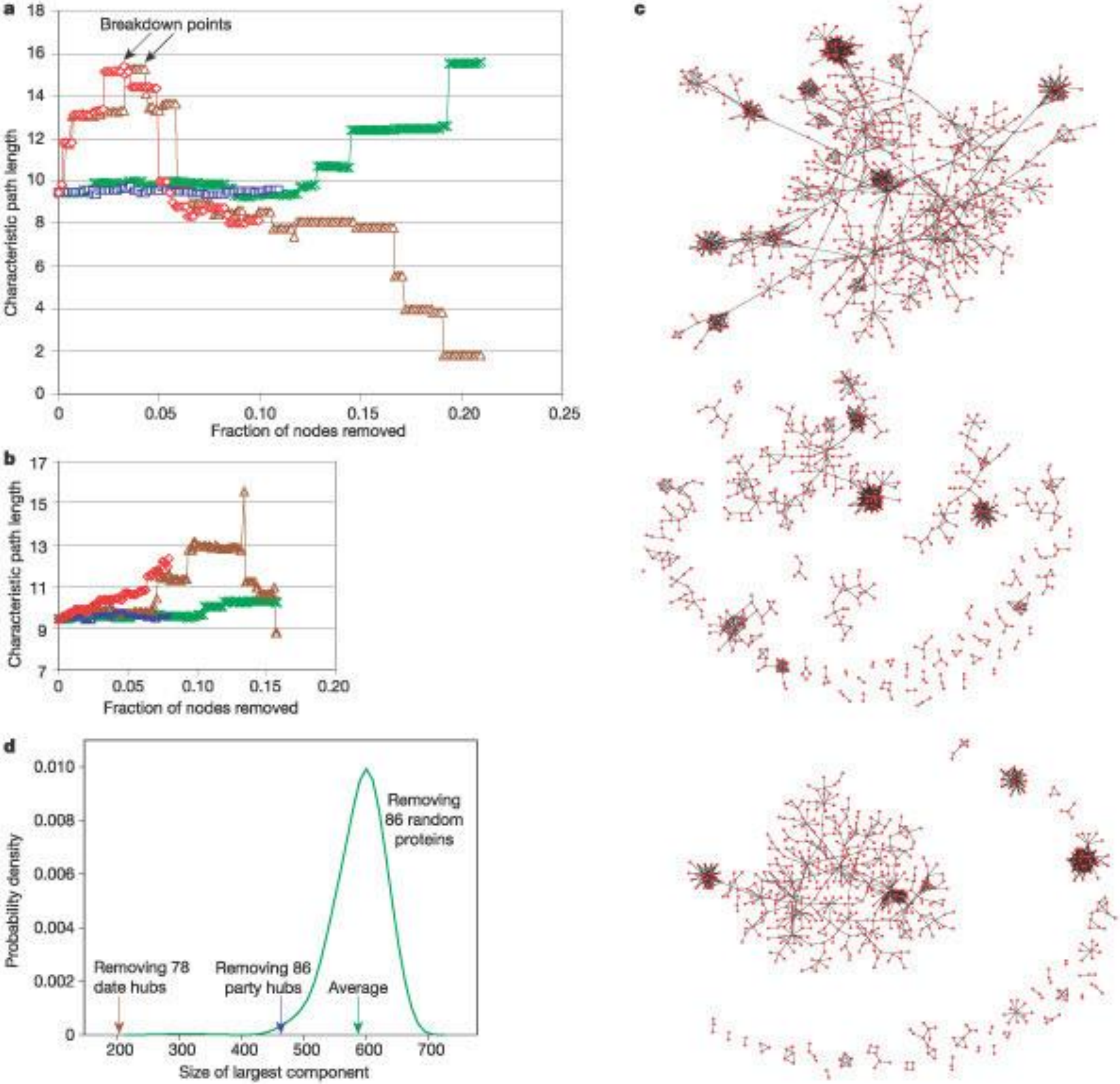
- Not only by expression timing but also spatial dist.-that is, subcellular localization

- Gene expression data Vs. protein localization data

Again, the old-fashioned Attacking strategy(*in silico*)

- *The characteristic path length, defined as the average distance (shortest path length) between node pairs, reflects the overall network connectivity*

- **Removal of party hubs does not affect connectivity and thus resembles failures,**
- **whereas attacks directed against date hubs account for a vast majority of the effect observed when attacking all hubs**

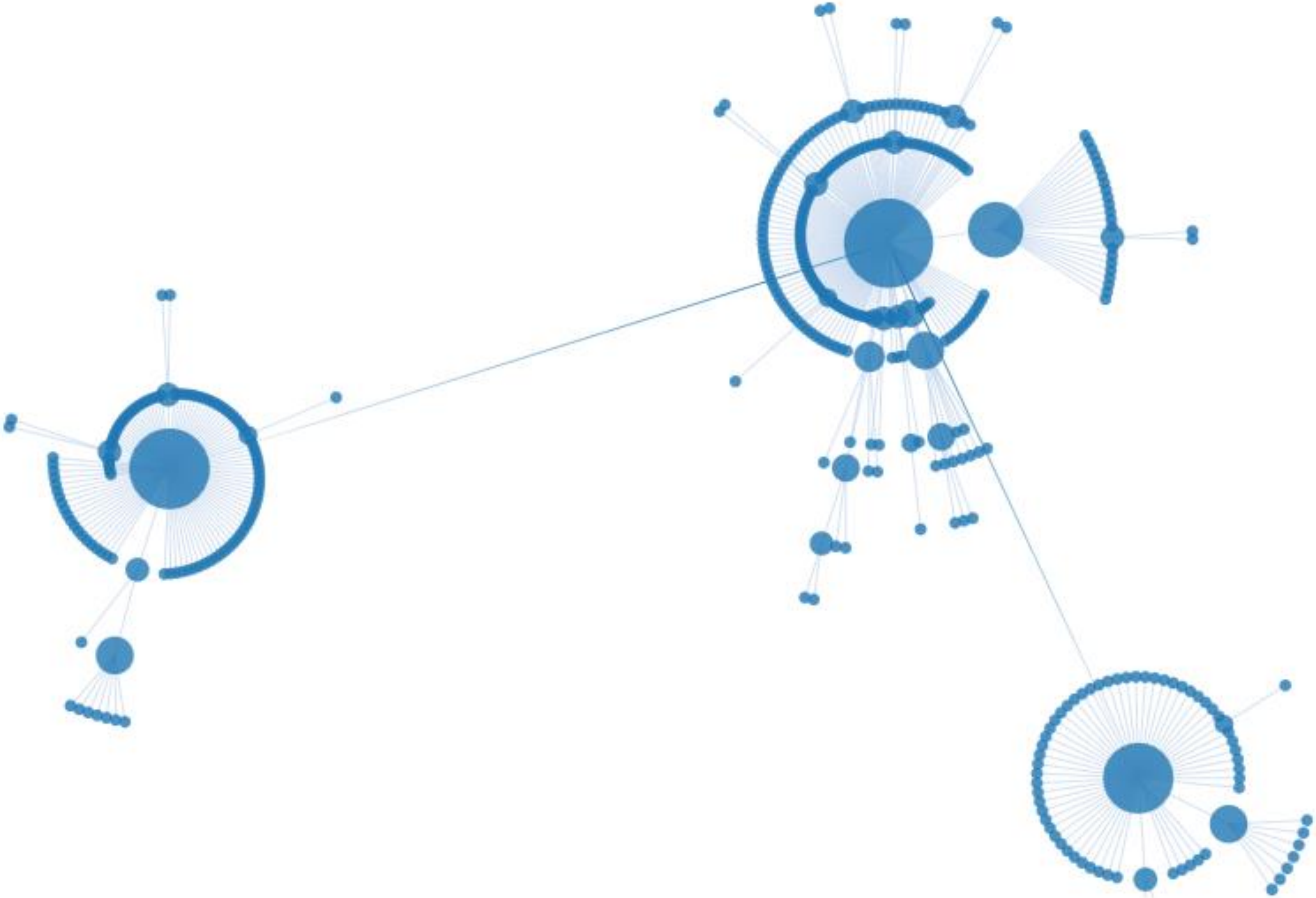

a
Breakdown points
Characteristic path length
0
2
4
6
8
10
12
14
16
18
0
0.05
0.10
0.15
0.20
0.25
Fraction of nodes removed
b
Characteristic path length
7
9
11
13
15
17
0
0.05
0.10
0.15
0.20
Fraction of nodes removed
c
d
Probability density
0
0.002
0.004
0.006
0.008
0.010
200
300
400
500
600
700
Size of largest component
Removing 86 random proteins
Removing 78 date hubs
Removing 86 party hubs
Average

Subsets to subnetworks, and ultimately modularity

- **MIPS database, for subnetworks analysis**
- **Biological modules:**
  - molecular machines or complexes (high PCC values)
  - Regulatory pathways, loosely(high PCC values) or densely(low PCC values) connected
- **Date hubs represents global connectors between modules, whereas party hubs function inside modules**

Summary and prospects

- **modules connected through date hubs**
  - Party hubs represent integral elements within distinct modules and, function at a lower level of the organization of the proteome
- **Emergent properties of the network**
  - genetic robustness and plasticity
- **Similar temporal or spatial dynamic analysis might also be applied to non-biological networks**
  - the WWW, epidemiological networks and social networks



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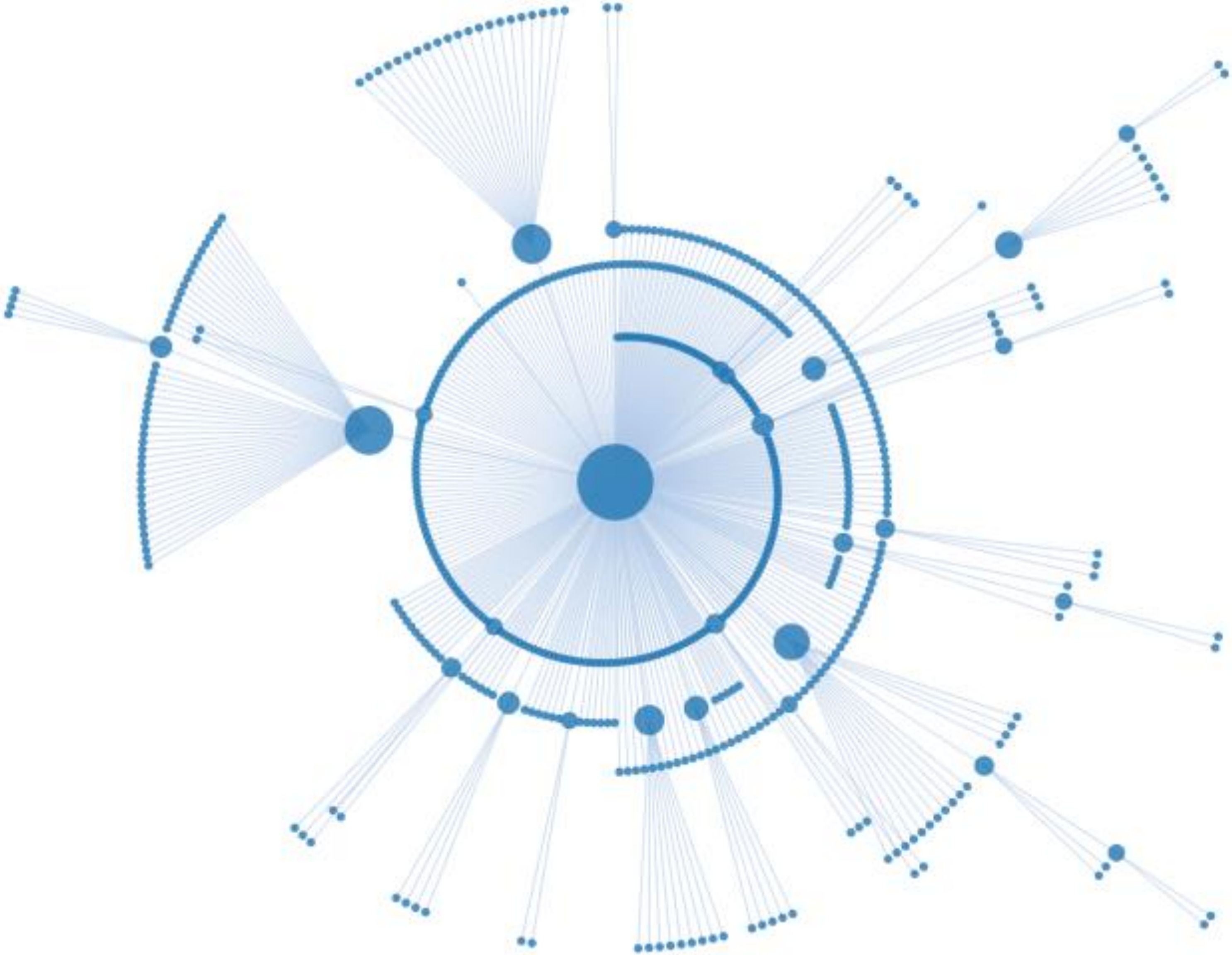

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Thank You !