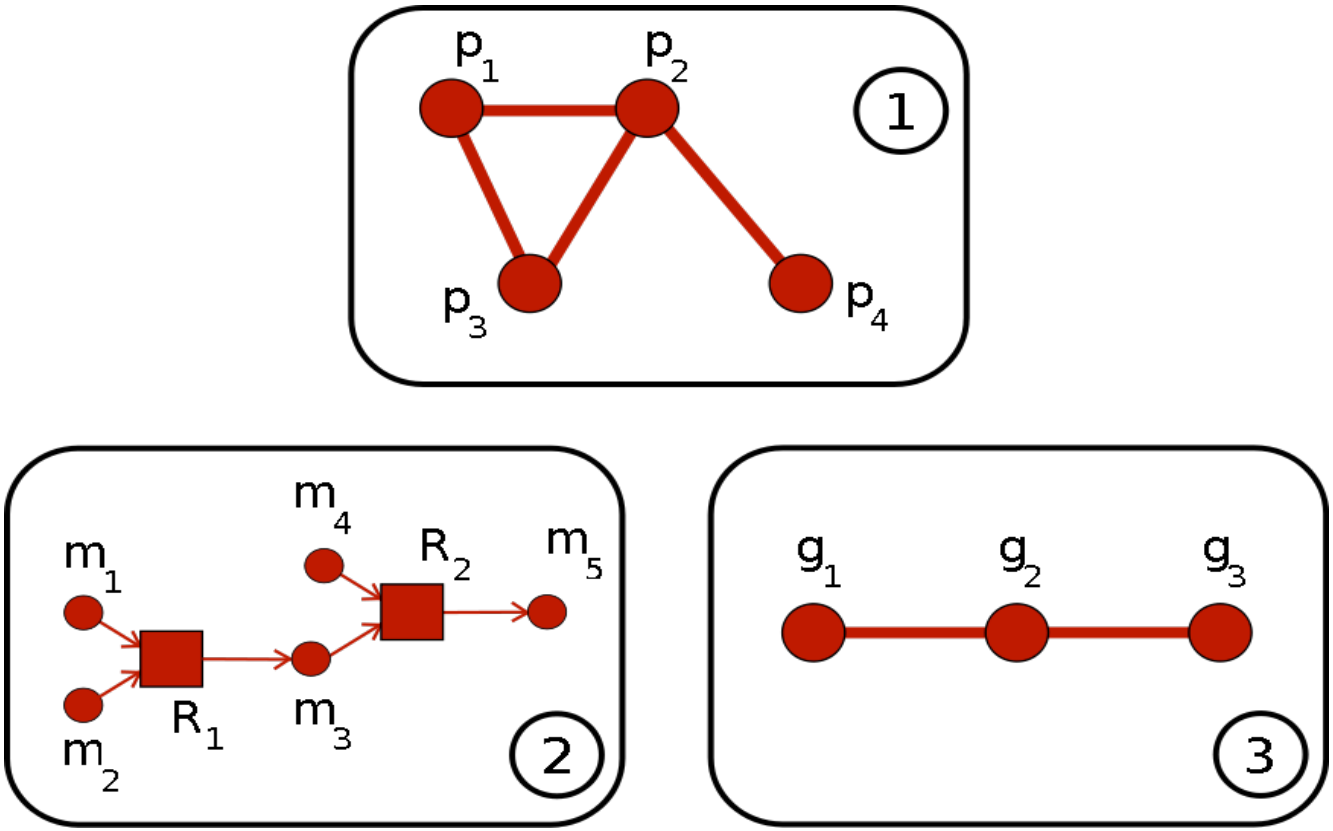
CPM' 09
20th Annual Symposium on Combinatorial Pattern Matching
June 22-24 2009, Lille, France
Special Anniversary Edition

Multiple alignment of biological networks: a flexible approach

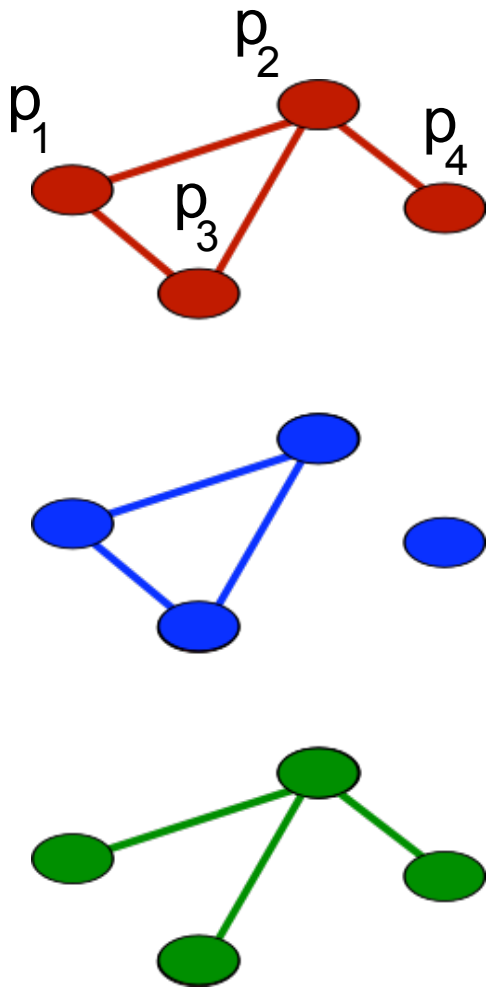
Yves-Pol Denielou, Fréderic Boyer,
Marie-France Sagot, Alain Viari
Bamboo team, Inria Rhône-Alpes

Motivation



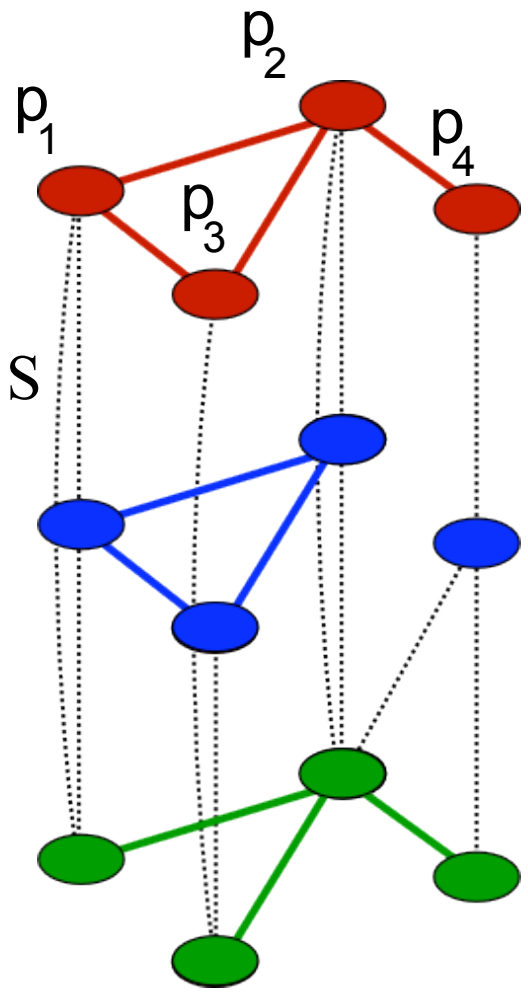
Aligning Networks

- **Local or Global**
- **Pairwise or Multiple**



Aligning Networks

- **Local or Global**
- **Pairwise or Multiple**
- **Definition of a correspondence relation S between vertices of the different networks**



Aligning Networks

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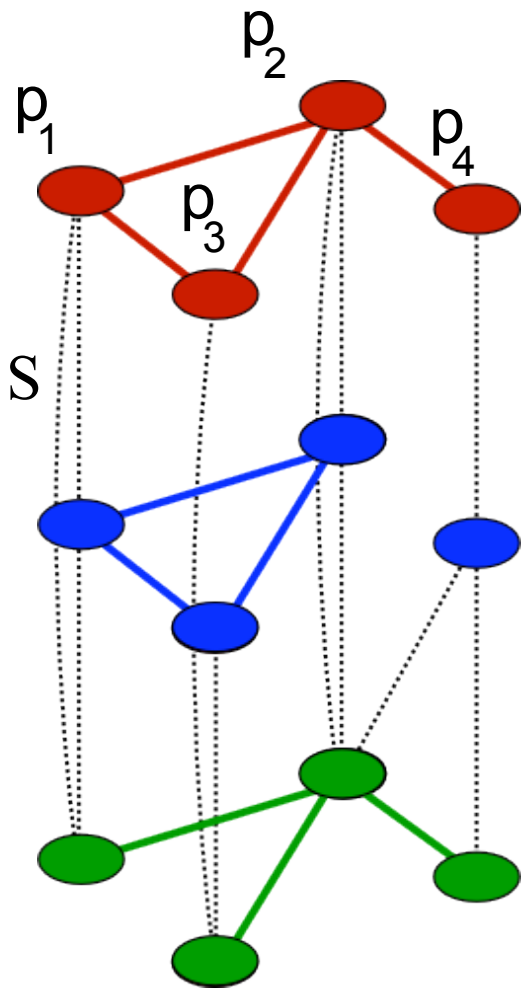
➢ **Extract conserved subnetworks**



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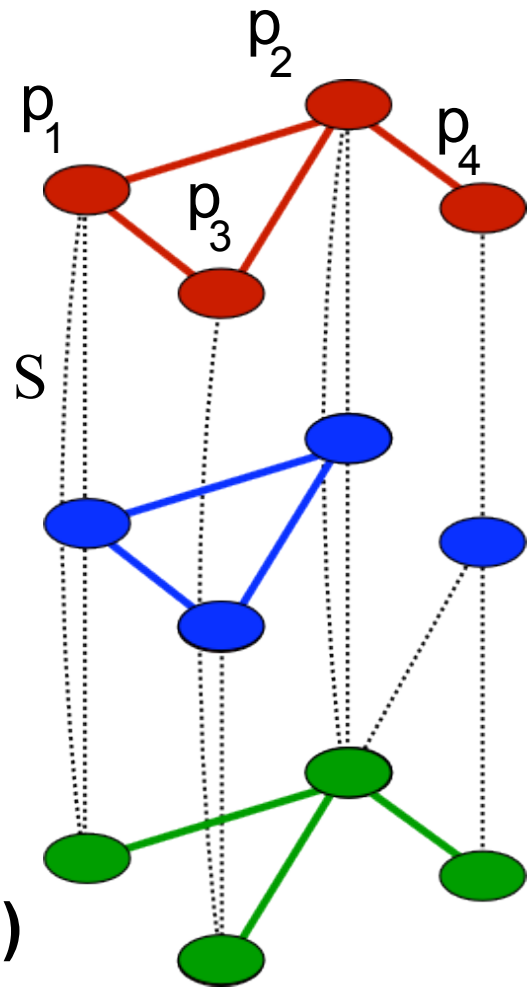


➢ **Extract conserved subnetworks**

➢ **A merged representation :**

the Network Alignment Graph (NAG)

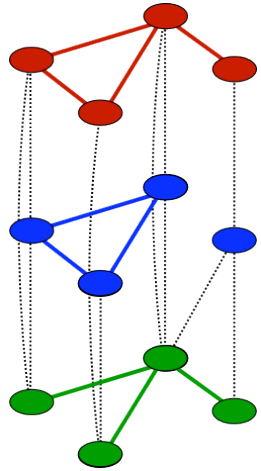
Sharan et al 2006

Network Alignment Graph

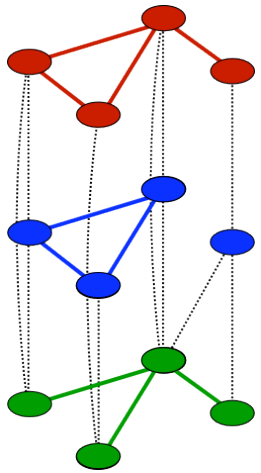
Given :

- n networks Gi = (Vi, Ei) i = 1..n

- a relation S between the vertices of V = $\cup_i$ Vi



Network Alignment Graph



Given :

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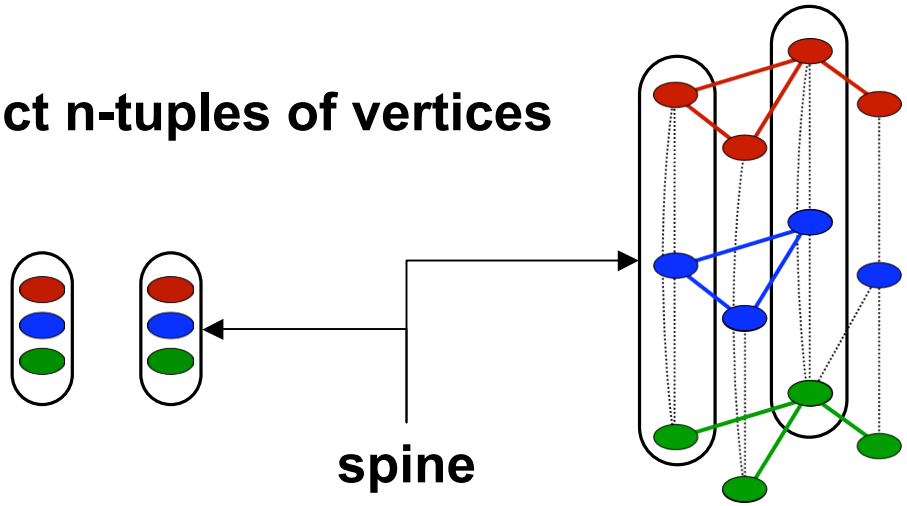
- a relation S between the vertices of V = $\cup_i V_i$

- **Select n-tuples of vertices**



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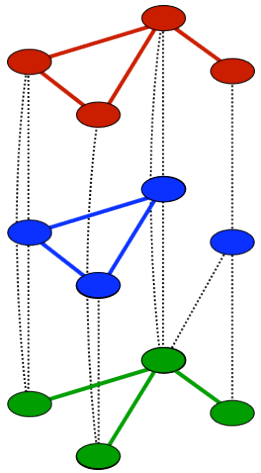

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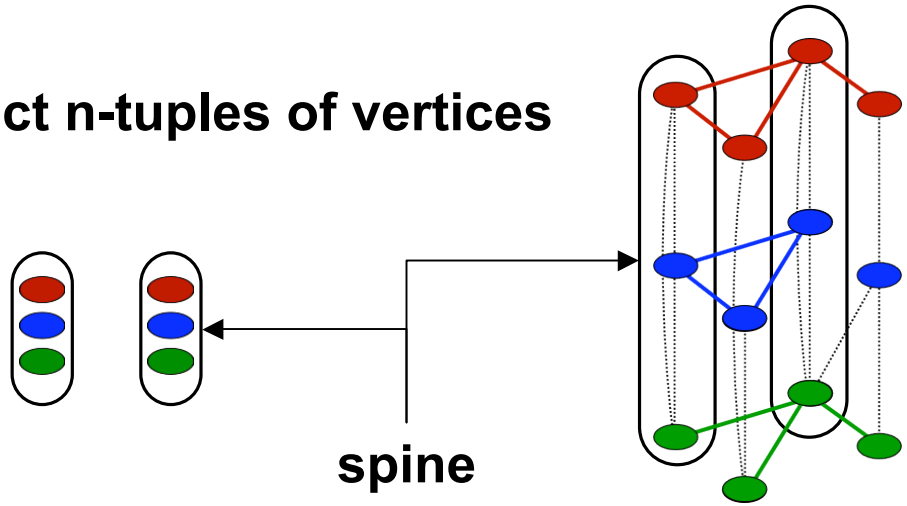
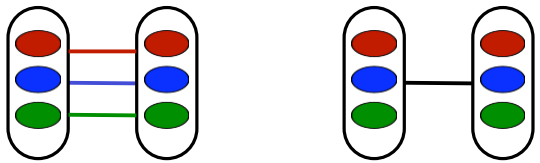
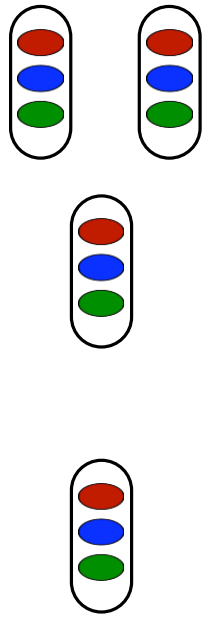


- Select n-tuples of vertices
- Connect these spines with edges from the sets Ei



3 main choices

1- How to select n-tuples using S ?



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1- How to select n-tuples using S ?

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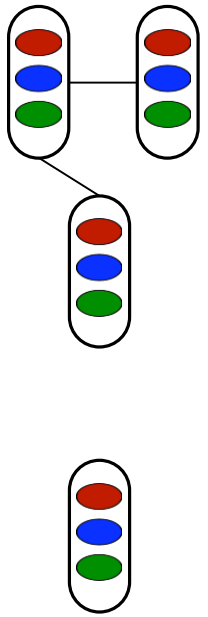
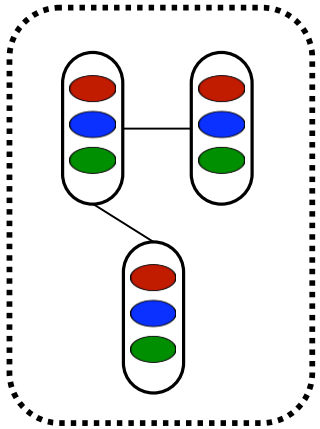


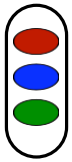
3 main choices

1- How to select n-tuples using S ?

2- Which primary edges to keep ?

3- Which topological condition on the subnetworks ?

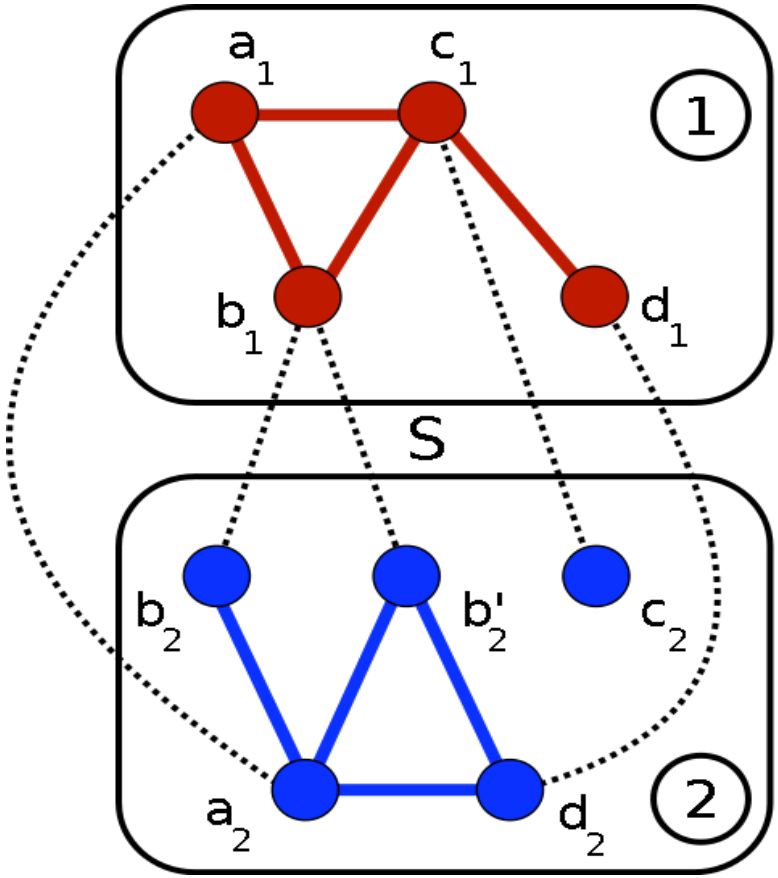




State of the art

Method	n-tuples construction	edges construction	topology
PathBLAST	pairs (n=2)	conserved	paths
NetworkBLAST	CC ($n \leq 3$)	conserved	clusters / paths
NetworkBLAST-M	paths	all edges	dense clusters on each network
GRAEMLIN 1.0	non-overlap--ping CC	conserved	user-defined
CAPPI	non-overlap--ping CC	all edges > threshold	CC
HopeMap	pairs	conserved	CC
MaWISH	pairs	conserved	max-weight subgraph
PHUNKEE	pairs	all edges	max shared-edges ratio
C3PART	cliques or stars	all edges	common CC

NAG: Pairwise case



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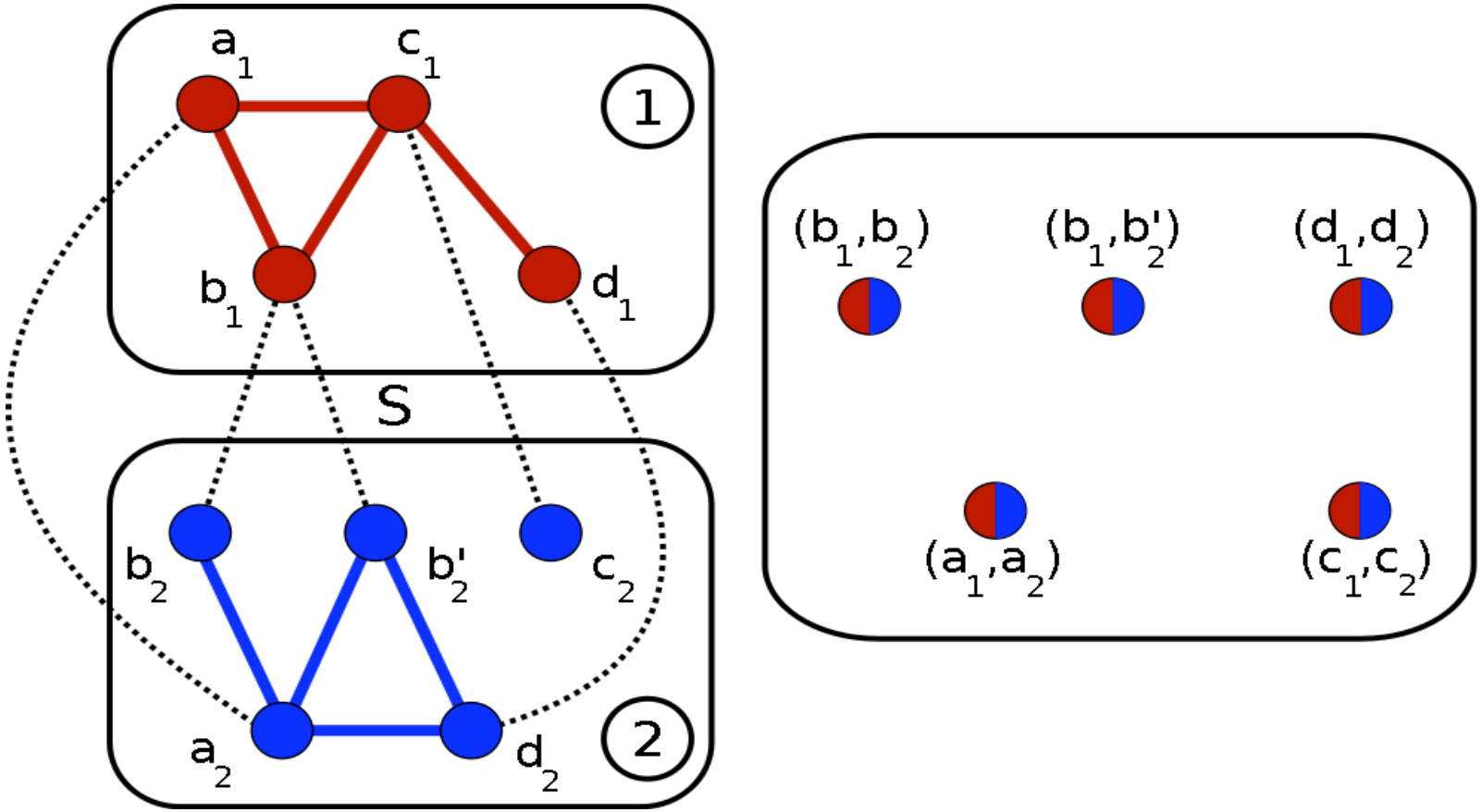
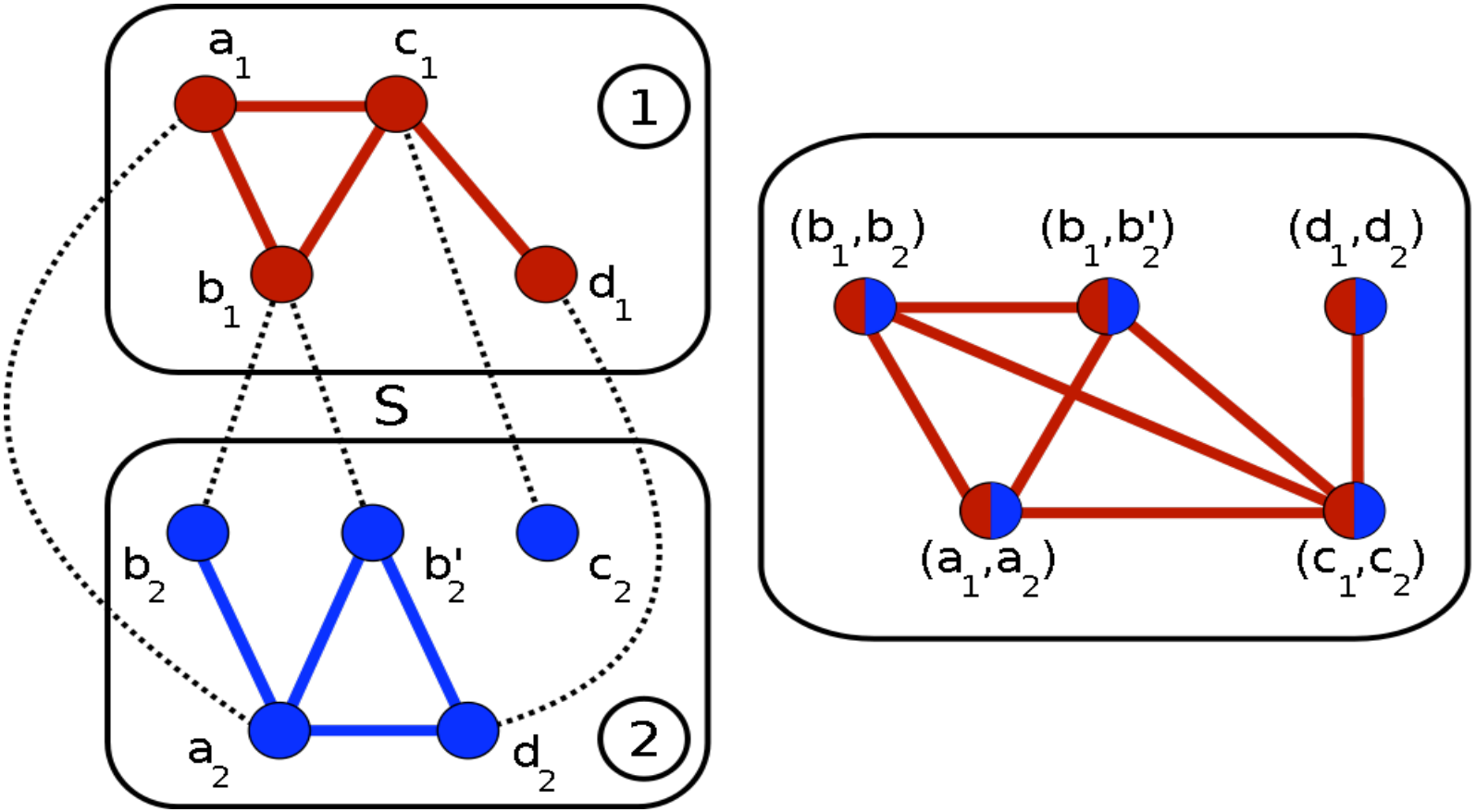


1: all S-related pairs

NAG: Pairwise case



1: all S-related pairs
2: keep all primary edges (multigraph)

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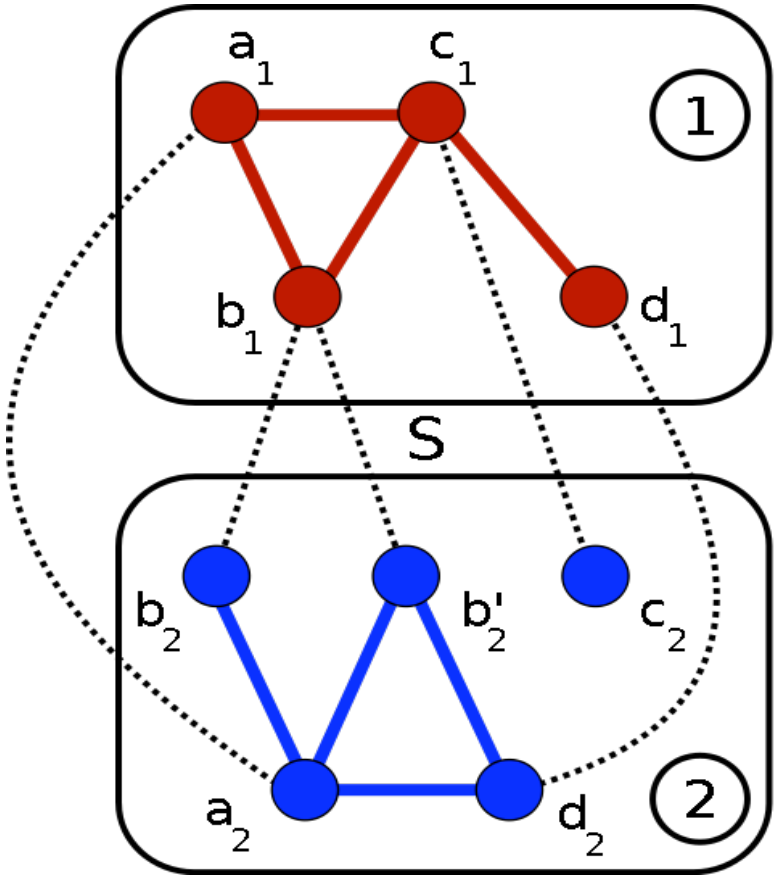

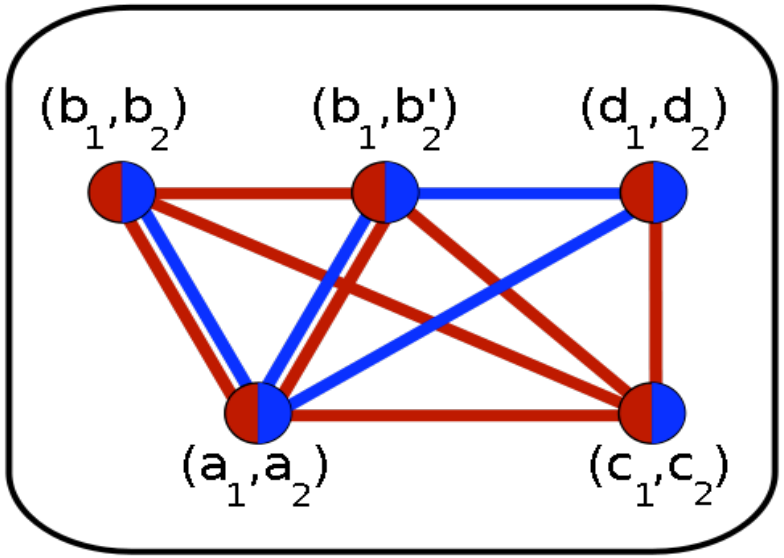

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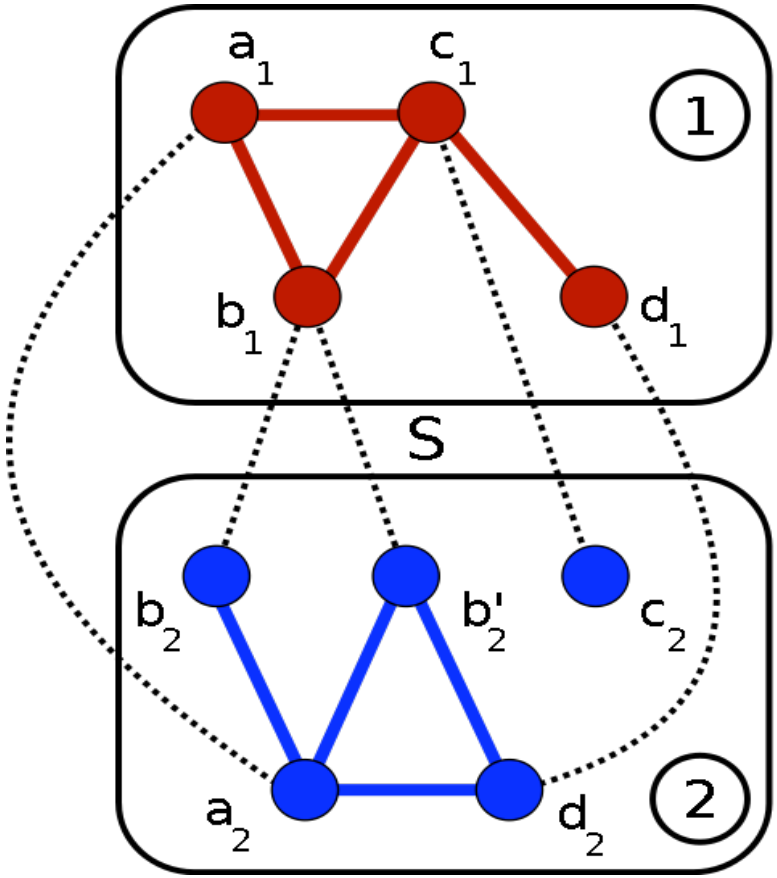
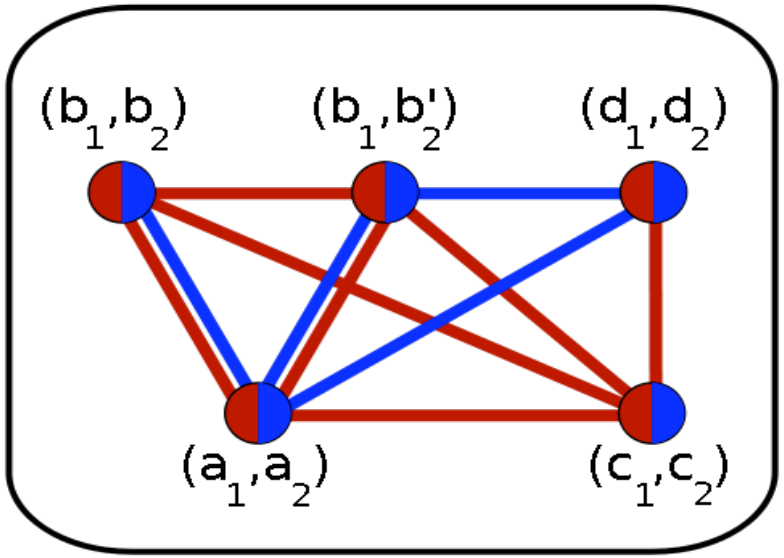
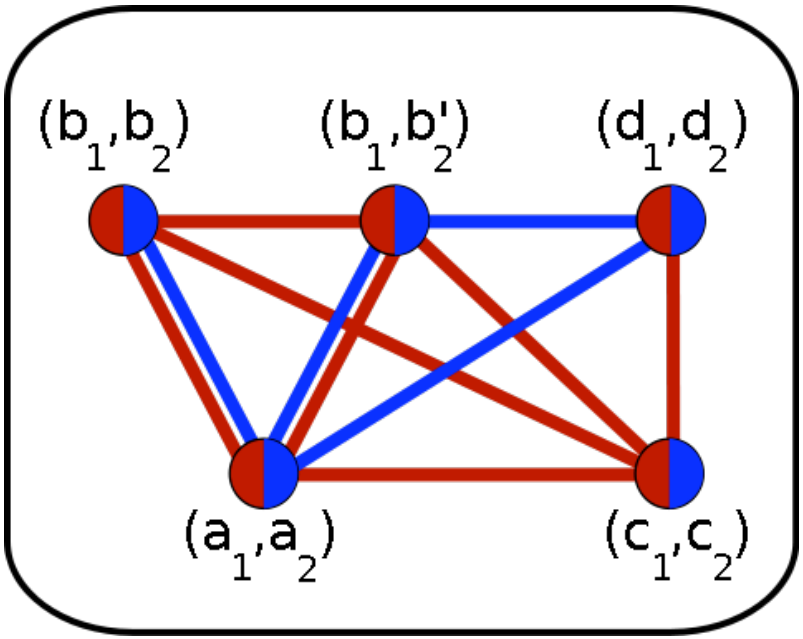




1: all S-related pairs
2: keep all primary edges (multigraph)
3: connected in each network

Defining Connectons

Connectons: maximal sets of vertices in the NAG connected on each network/color



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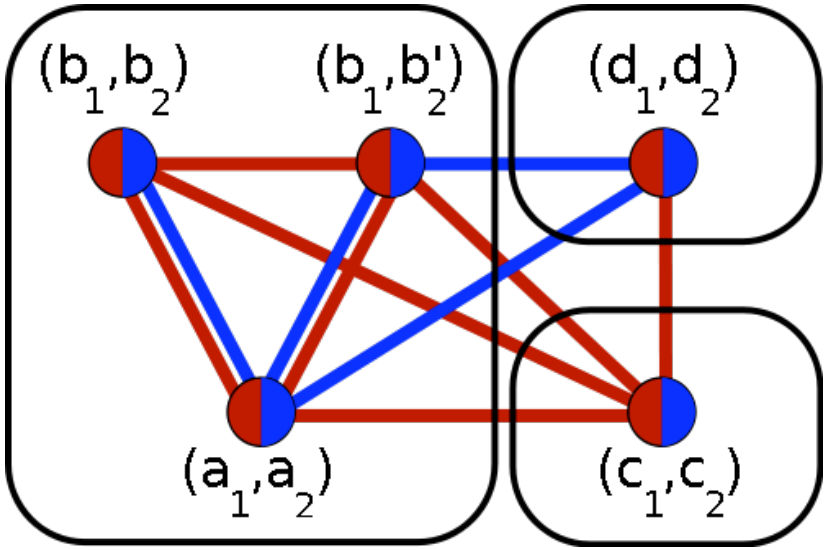

Defining Connectons

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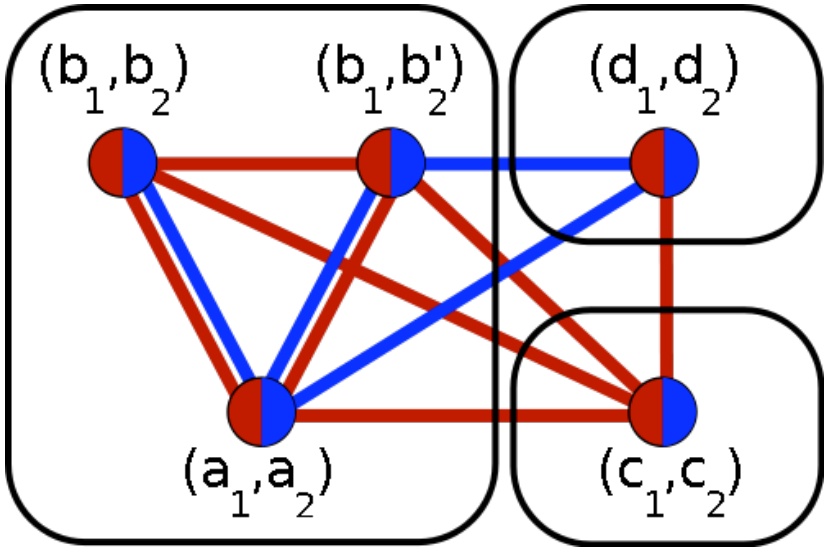
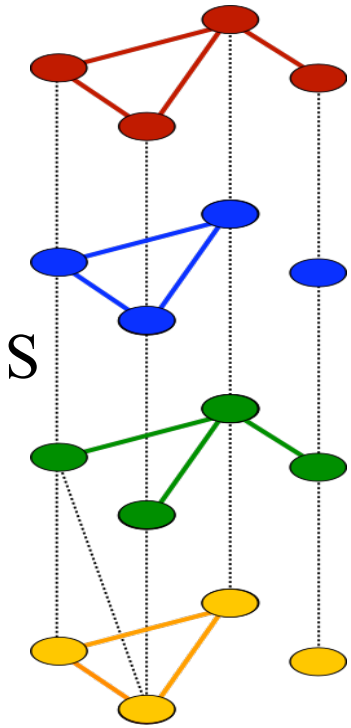
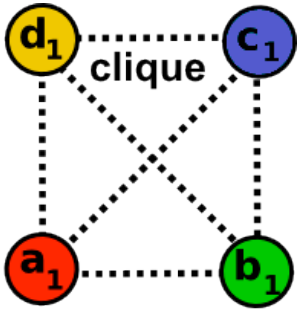
Connectons = Partition of the NAG vertices



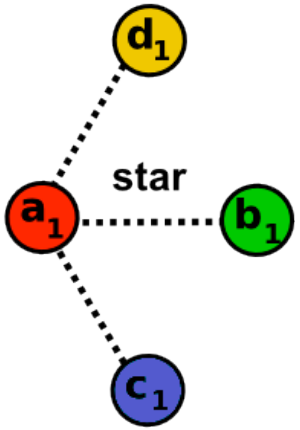
Extension to n networks

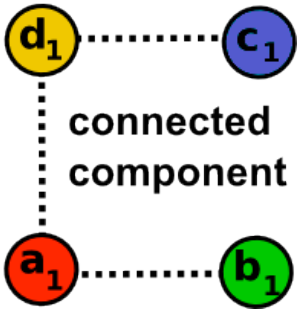


Selecting n-tuples :



(a_1, b_1, c_1, d_1)





in general :
S not one-to-one
S not transitive

Algorithm

Computing the connectons is doable, several partioning algorithms :

- **Boyer et al 2005 : O((N+M)*N) recursive intersection of CCs**
- **Gai et al 2003 : O((N+M*logN)*logN) Hopcroft-like partitioning approach**

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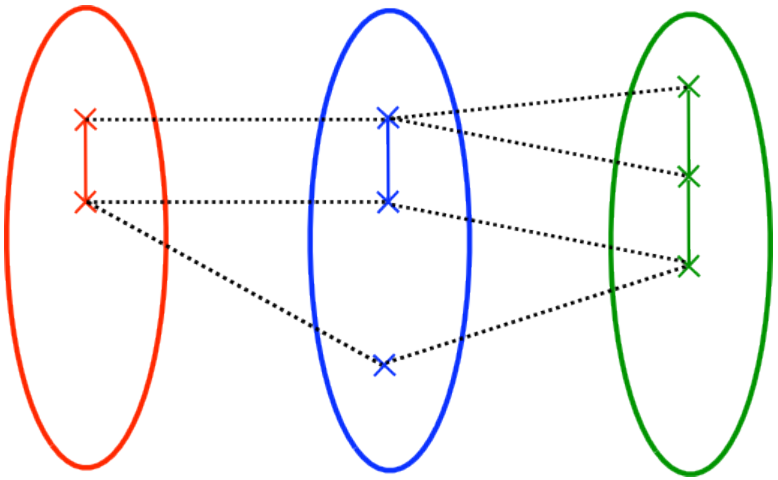
But : N ~ |network|^{n} in general (because of S)

- **Avoid the explicit construction of the NAG**
- **On the fly partitionning**

On the fly expansion of NAG



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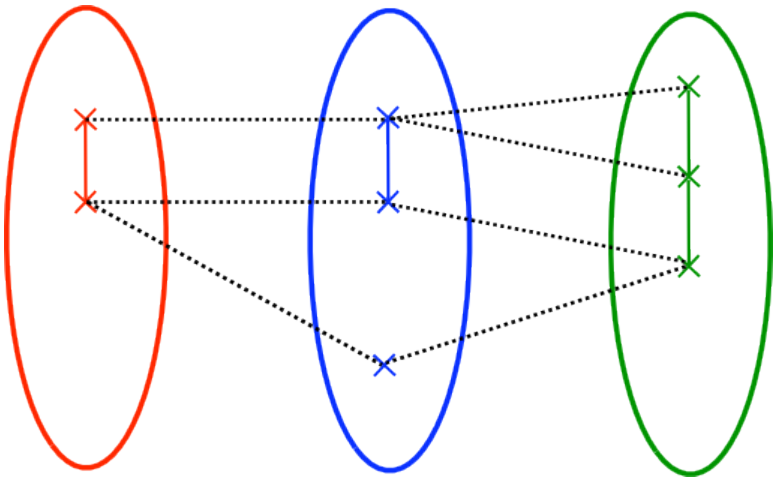

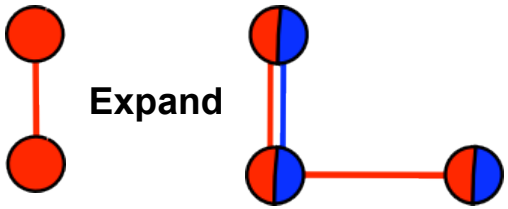

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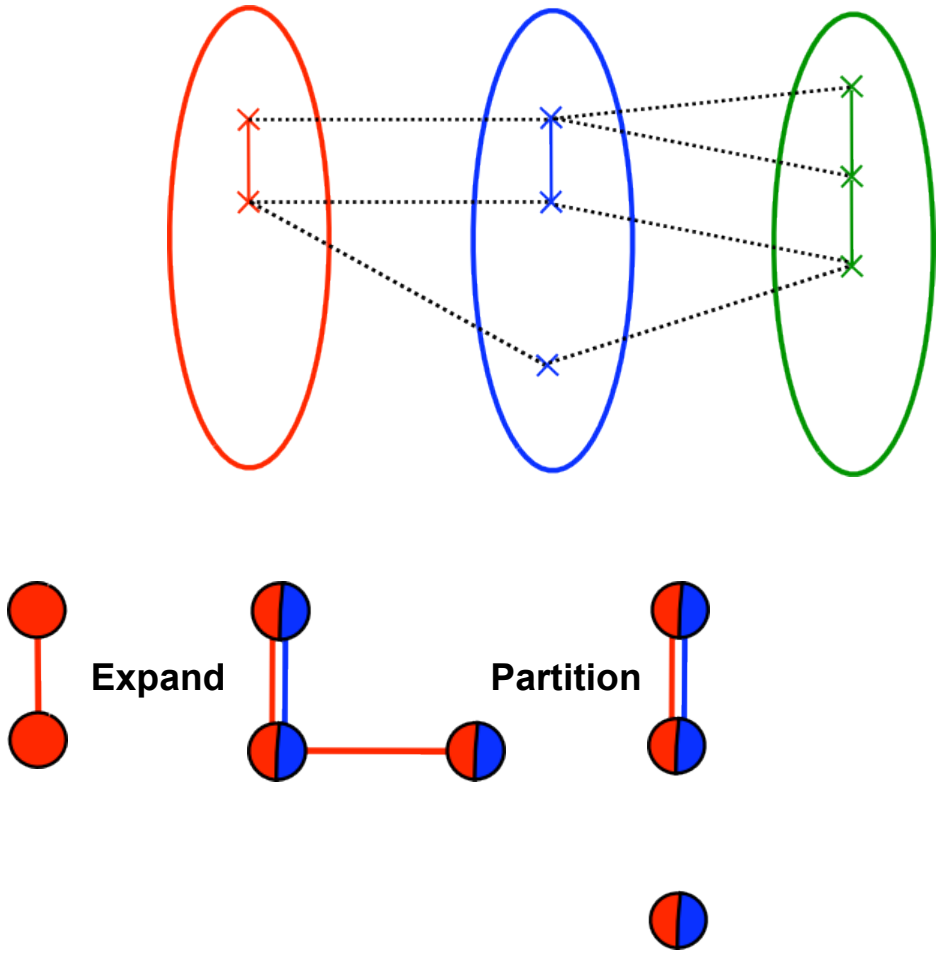

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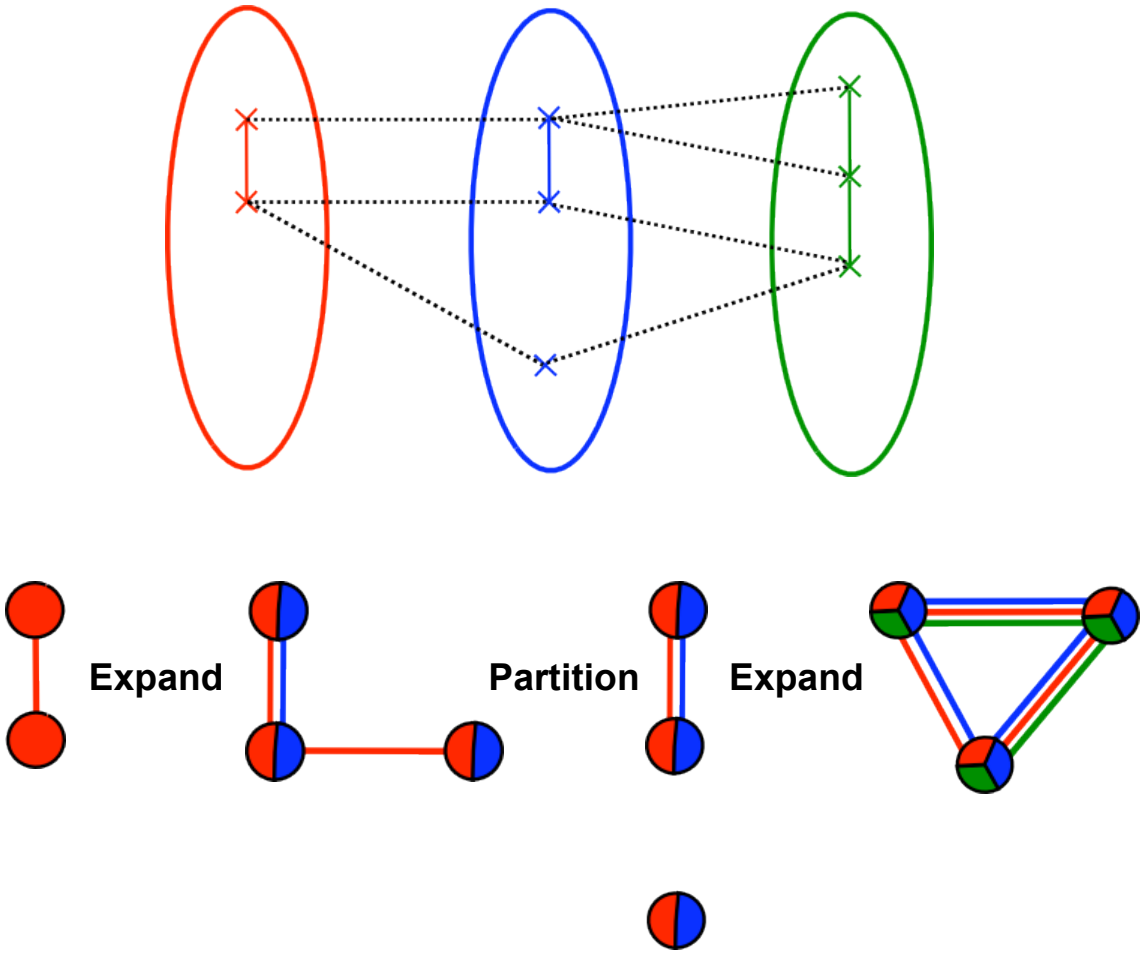

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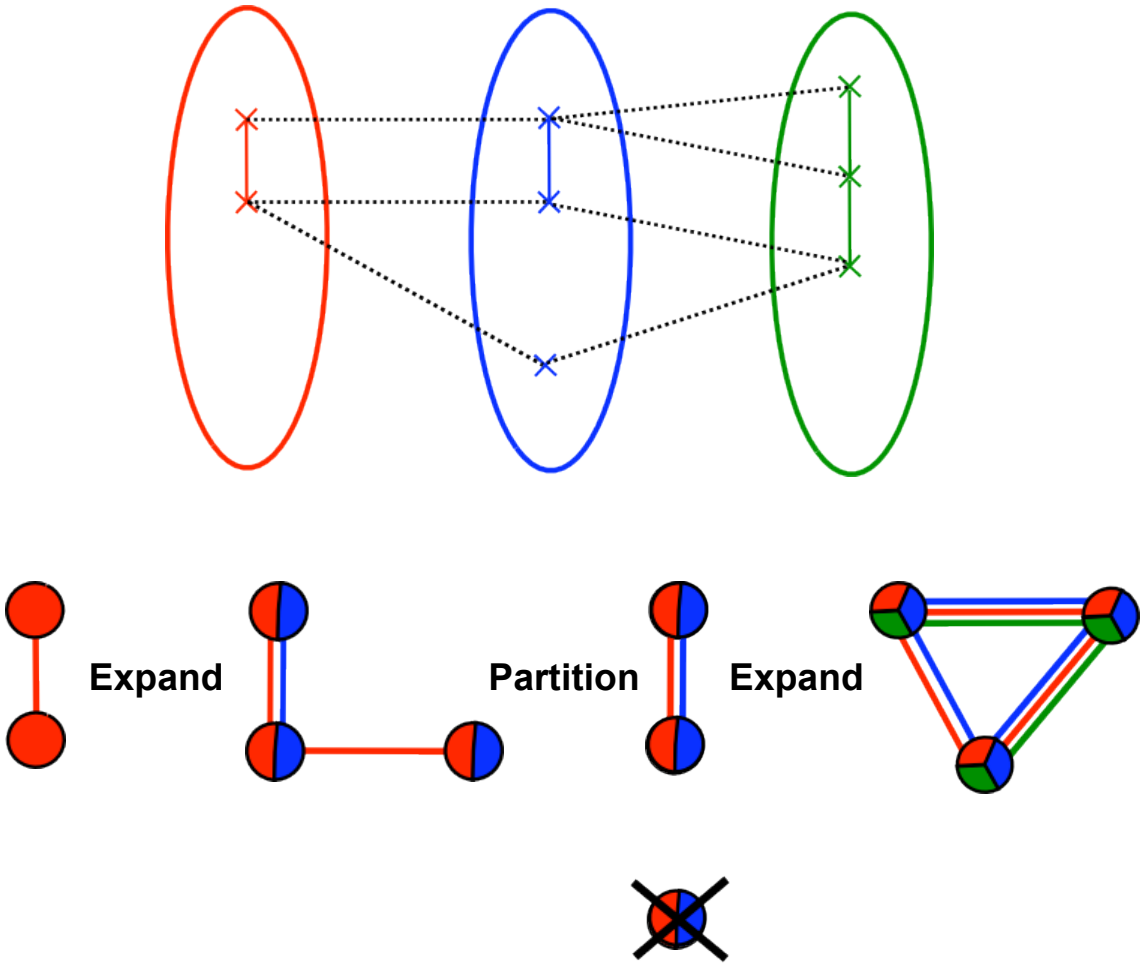


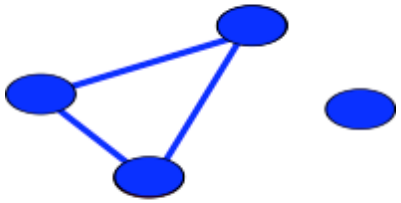
Results

Benchmark of 10 microbial PPI networks
from Srinivasan et al. 2006

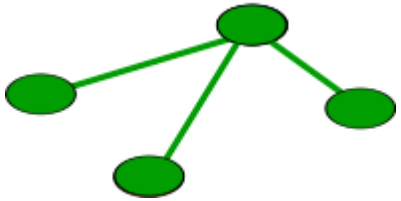
For a 0.5 threshold on the 10 networks :
N ~ 23000 proteins
E ~ 175000 interactions

Correspondence relation :
Sequence similarity with BlastP
Threshold : 10^{-10} Nb Hits /p : 5
~ 50000 edges

species A



species B



…

Selecting n-tuples : cliques / cc
Selecting edges : all edges
Topology : connectons

Comparison to Network Blast-M

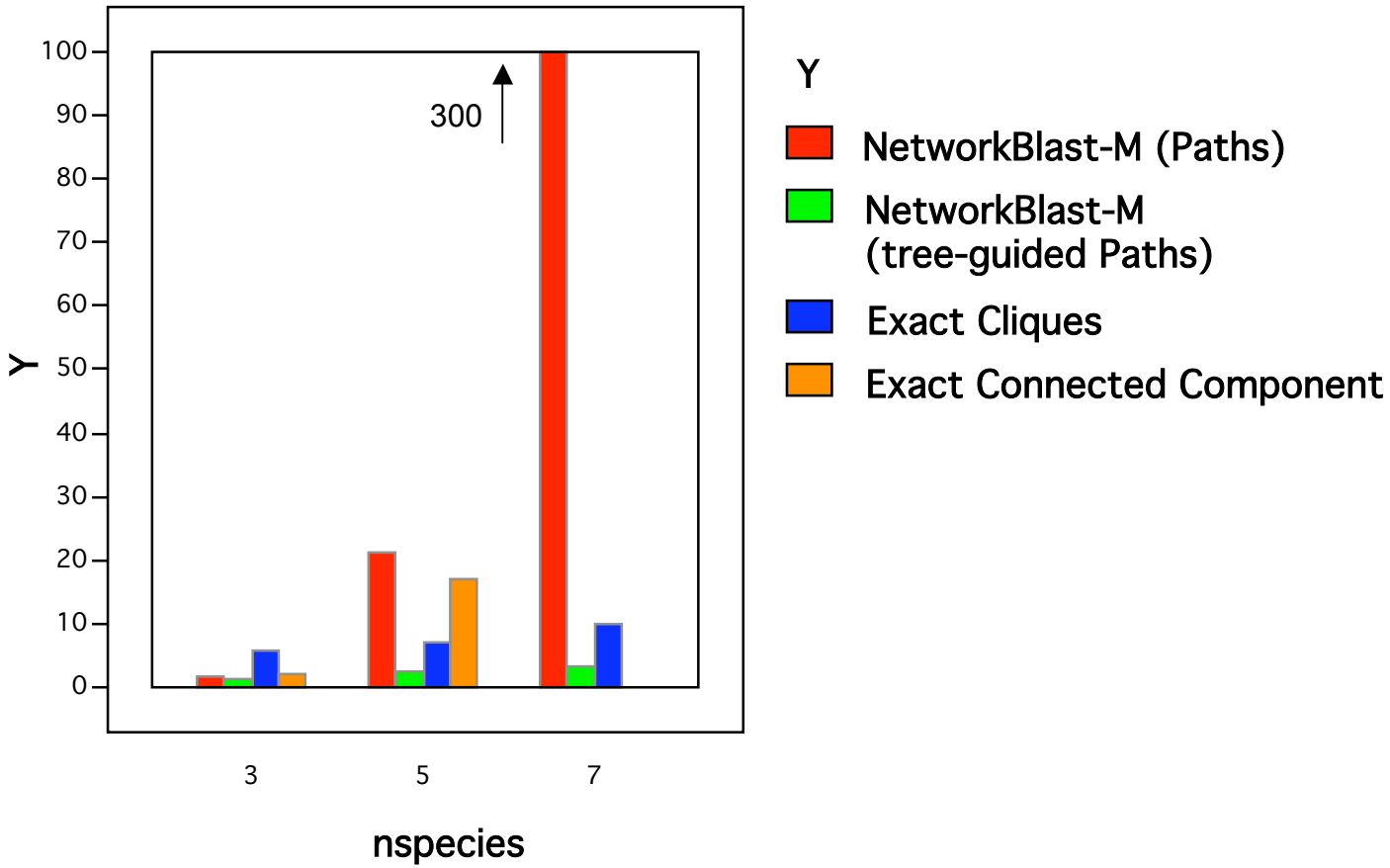
1 n-tuples : paths or tree-guided-paths
2 edges : all primary edges are kept
3 topology condition : dense in each network (*Sharan et al 2004*)

Heuristic algorithm

General idea:
- build a set of n-tuple seeds
- extend them greedily in order to maximise a sum of density scores, one per PPI network

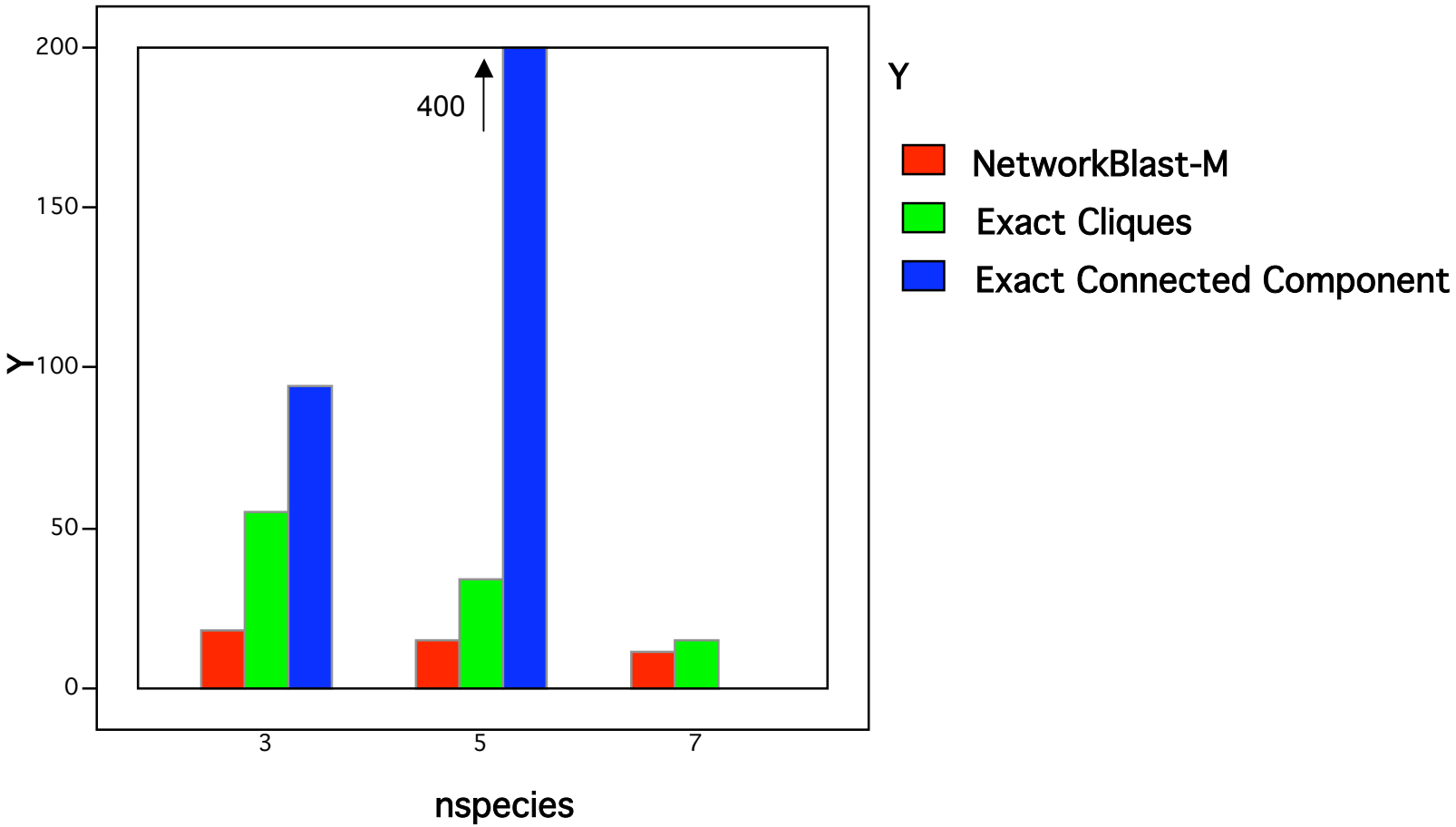
Comparison to NetworkBlast-M

-1- execution time



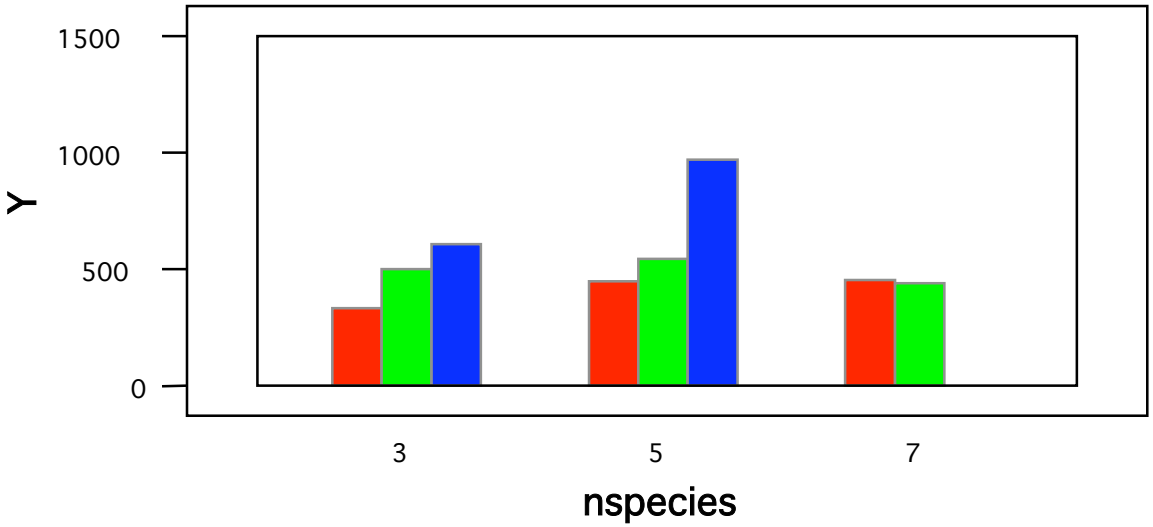
Comparison to NetworkBlast-M

-2- conserved subnetworks



Comparison to NetworkBlast-M

-3- proteins involved

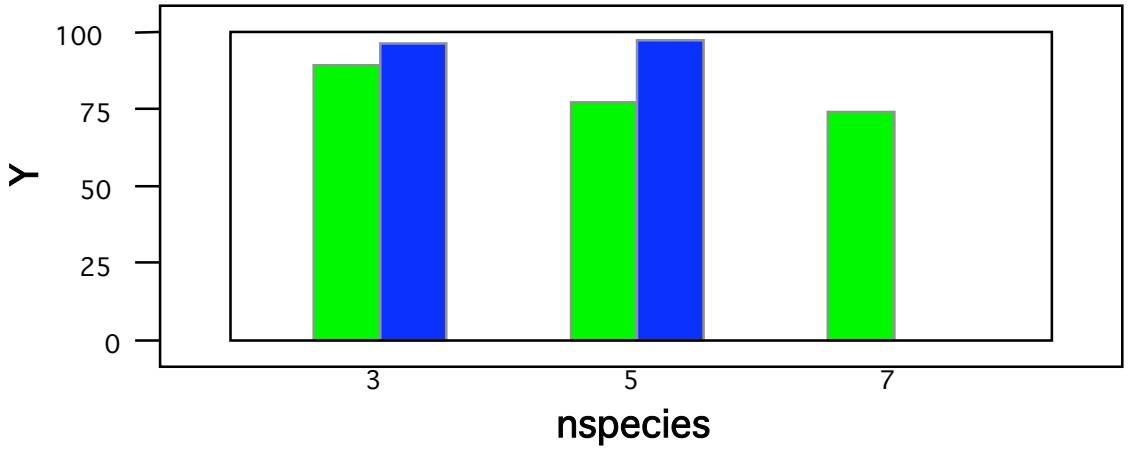


Y

NetworkBlast-M

Exact Cliques

Exact Connected Component



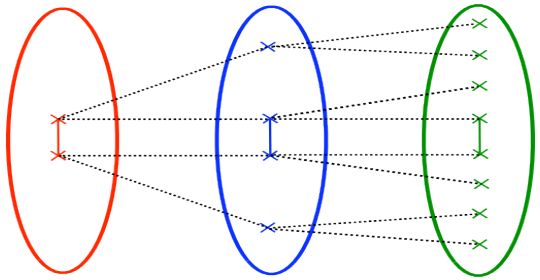
Y : %age of coverage of NetworkBlast-M results by

Exact Cliques

Exact Connected Component

Perspectives

- **Computing S correspondence on the fly**



- **Recovering connectons with missing vertices**

introducing k-tuples and quorum (q < k < n)