Optimal Solutions for Hard Network Problems in Bioinformatics

Falk Hüffner

joint work with

Nadja Betzler Hannes Moser Christian Komusiewicz
Rolf Niedermeier Sebastian Wernicke Thomas Zichner

Friedrich-Schiller-Universität Jena
Institut für Informatik

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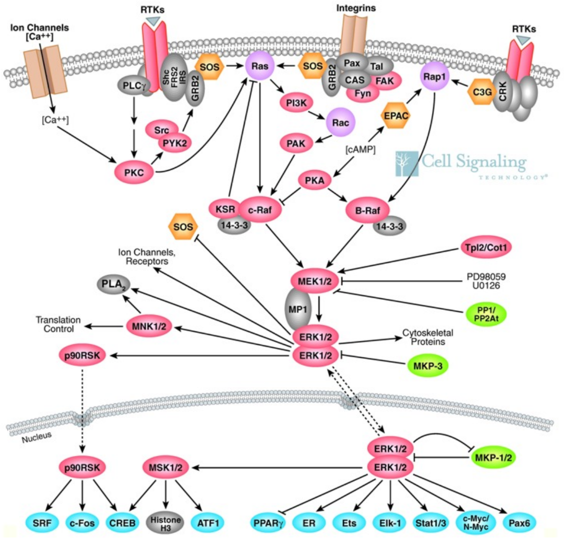
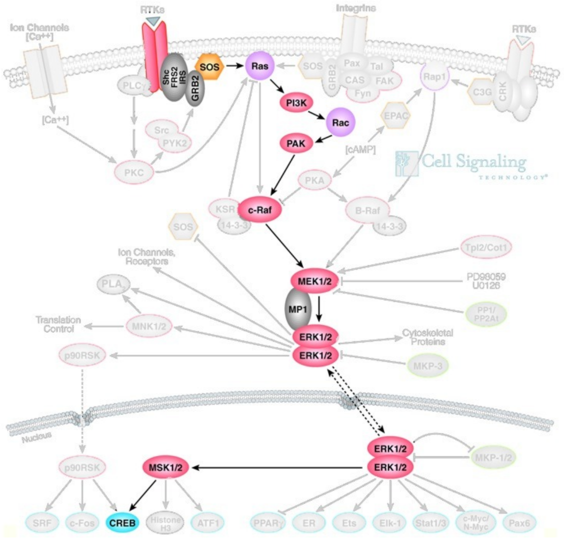
Outline

Signaling pathways



[www.cellsignal.com]

Signaling pathways



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Signaling pathways

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A signaling pathway is a cascade of successive protein interactions that the cell uses to react to stimuli.

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Goal

Automated discovery of linear signaling pathways

[Steffen et al., BMC Bioinf. 2002]

Graph model

Protein interaction network:

- Proteins are nodes
- Interactions are undirected edges
- Edges are annotated with interaction probability (obtained e. g. by two-hybrid screening)

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MOST PROBABLE PATH [SCOTT et al., J. Comp. Biol. 2006]

Input: Graph $G = (V, E)$, interaction probabilities $p : E \to [0, 1]$, integer $k > 0$.
Task: Find a non-overlapping path $v_1, \ldots, v_k$ of length k in G that maximizes $p(v_1, v_2) \cdot \ldots \cdot p(v_{k-1}, v_k)$.

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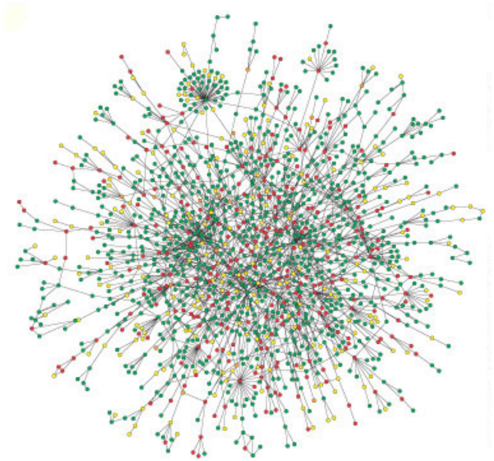
Setting $w(e) := -\log(p(e))$:

Minimum-Weight Path

Input: Graph $G = (V, E)$, weights $w : E \to \mathbb{R}_+$, integer $k > 0$.
Task: Find a non-overlapping path $v_1, \ldots, v_k$ of length k in G that minimizes $w(v_1, v_2) + \cdots + w(v_{k-1}, v_k)$.

Example: yeast network



4 400 proteins, 14 300 interactions, looking for paths of length 5–15

Minimum-Weight Path

Theorem

MINIMUM-WEIGHT PATH *is NP-hard* [GAREY & JOHNSON 1979].

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Idea

Exploit the fact that the paths sought for are rather short ($\approx$ 5–15): restrict the exponential part of the runtime to k (parameterized complexity).

Fixed-parameter tractability

Parameterized complexity is an approach to finding exact solutions to NP-hard problems by confining the combinatorial explosion to a parameter.

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Definition

A problem is called fixed-parameter tractable with respect to a parameter k if an instance of size n can be solved in $f(k) \cdot n^{O(1)}$ time for an arbitrary function f.

Color-coding

Color-coding is a method for solving MINIMUM-WEIGHT PATH that is fast for short path lengths.

Color-coding [ALON, YUSTER & ZWICK, J. ACM 1995]

- randomly color each vertex of the graph with one of k colors
- hope that all vertices in the subgraph searched for obtain different colors (colorful)
- solve the MINIMUM-WEIGHT PATH under this assumption (which is much quicker)
- repeat these trial until it is reasonably certain that the path was colorful at least once

Result: exponential part of the runtime depends only on k

Dynamic programming for Minimum-Weight Colorful Path

Idea

Table entry $W[v, C]$ stores the minimum-weight path that ends in v and uses exactly the colors in C.

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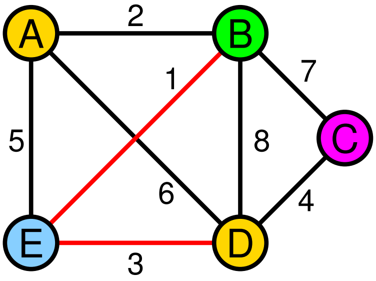

$W[B, \{$🔵, 🟢, 🟡$\}] = 4$

Dynamic programming for Minimum-Weight Colorful Path

Coloring $c : V \to \{1, \ldots, k\}$

Recurrence

$$W[v, C] = \min_{u \in N(v)} (W[u, C \setminus \{c(v)\}] + w(u, v))$$

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- Each table entry can be calculated in $O(n)$ time
- $n \cdot 2^k$ table entries

$\rightsquigarrow$ Running time per trial: $O(2^k \cdot n^2)$

Color-coding running time

- $O(2^k \cdot n^2)$ time per trial
- To obtain error probability ε, one needs $O(-\ln \varepsilon \cdot e^k)$ trials

Theorem ([Alon et al., JACM 1995])

Minimum-Weight Path *can be solved in* $O(-\ln \varepsilon \cdot 5.44^k |G|)$ *time.*

Implementations of color-coding

- Find minimum-weight paths of length 10 in the yeast protein interaction networks within 3 hours ($n = 4\,400$, $k = 10$)

  [Scott et al., J. Comp. Biol. 2006]
- Pathway queries

  [Shlomi et al., BMC Bioinformatics 2006]
- Tree queries

  [Dost et al., RECOMB 2007]
- Protein docking

  [Mayrose et al., Nucleic Acids Research 2007]
- Balanced paths

  [Cappanera & Scutellà, INOC 2007]
- Automated text headline generation

  [Deshpande et al., NAACL HLT 2007]

Increasing the number of colors

Idea

Use $k + x$ colors instead of k colors.

Trial runtime:

$$O(2^k|G|) \to O(2^{k+x}|G|)$$

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Probability P_c for colorful path ($k = 8$, $\varepsilon = 0.001$):

x	0	1	2	3	4	5
P_c	0.0024	0.0084	0.0181	0.0310	0.0464	0.0636
trials	2871	816	378	220	146	106

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Theorem

MINIMUM-WEIGHT PATH *can be solved in* $O(-\ln \varepsilon \cdot 4.32^k|G|)$ *time by choosing* $x = 0.3k$.

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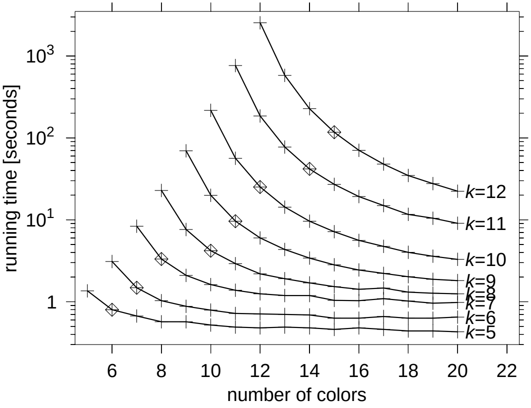
But: Higher memory usage

Increasing the number of colors



Running times for the yeast protein interaction network (highlighted point of each curve marks worst-case optimum)

State space search

Idea

Consider the dynamic programming as a state space search problem (shortest path problem in an implicitly defined graph).

From a state (u, C), we can go to $(v, C \cup \{c(v)\})$ for $v \in N(u)$ with $c(v) \neq c(u)$, at cost $w(u, v)$.

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- can be used to prune states
- can guide the search (A*)

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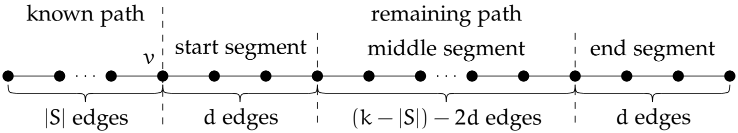
Simple lower bound:

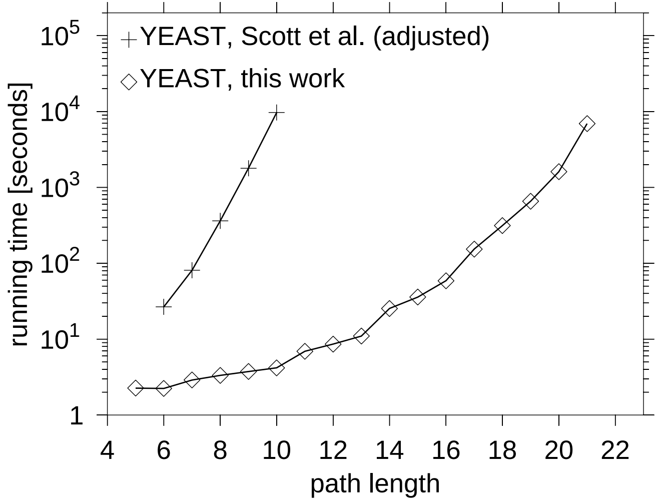
$$\text{weight} + (\text{minimum edge weight} \cdot \text{edges left})$$

Precalculated lower bounds

For each vertex u and a range of lengths $1 \leq i \leq d$, determine the minimum weight of a path of i edges that starts at u.



Yeast network



Network Comparison

	$\lvert V\rvert$	$\lvert E\rvert$	clust. coeff.	avg. degree	max. degree
	4 389	14 319	0.067	6.5	237
	7 009	20 440	0.030	5.8	175

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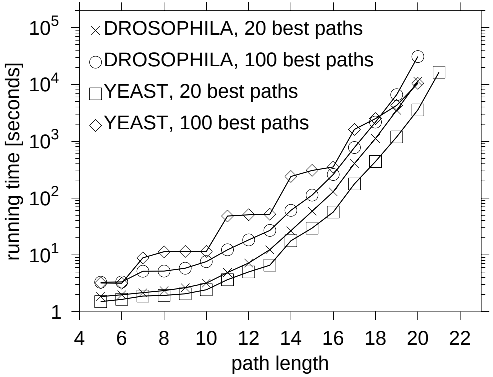
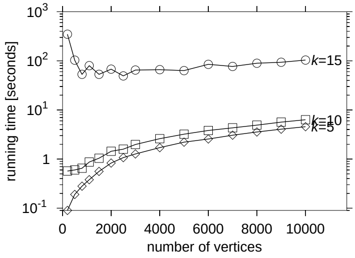
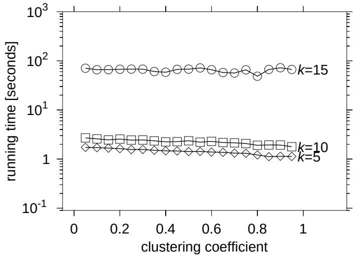
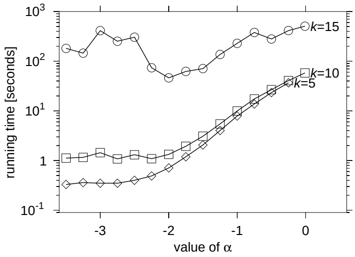
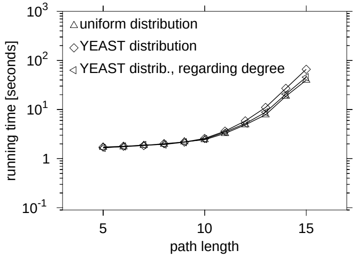


Simulations: Robustness of Algorithm







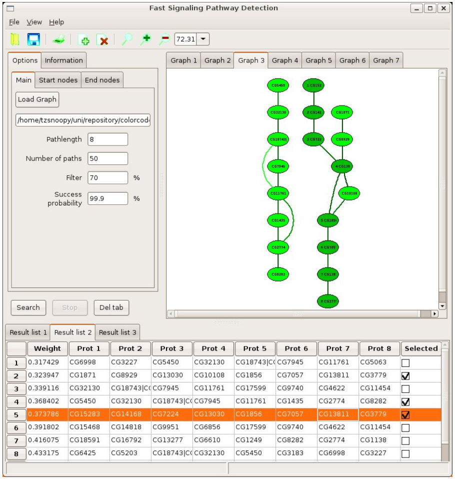


Pathway Query

Queries of *S. cerevisiae* pathways in the *D. melanogaster* network

Path length	Avg. Time [s]	Max. Time [s]	Successful Queries
4	2.24	2.57	98%
5	2.33	3.61	93%
6	3.00	23.02	81%
7	4.52	93.32	52%
8	7.49	225.61	31%
9	11.38	245.78	13%

Graphical user interface: FASPAD


Fast Signaling Pathway Detection
File View Help
72.31
Options Information
Main Start nodes End nodes
Load Graph
Graph 1 Graph 2 Graph 3 Graph 4 Graph 5 Graph 6 Graph 7
Search Stop Del tab
Result list 1 Result list 2 Result list 3

/home/tzsnoopy/uni/repository/colorcod

Pathlength 8

Number of paths 50

Filter 70 %

Success probability 99.9 %

	Weight	Prot 1	Prot 2	Prot 3	Prot 4	Prot 5	Prot 6	Prot 7	Prot 8	Selected
1	0.317429	CG6998	CG3227	CG5450	CG32130	CG18743|C(	CG7945	CG11761	CG5063	☐
2	0.323947	CG1871	CG8929	CG13030	CG10108	CG1856	CG7057	CG13811	CG3779	✓
3	0.339116	CG32130	CG18743|C(	CG7945	CG11761	CG17599	CG9740	CG4622	CG11454	☐
4	0.368402	CG5450	CG32130	CG18743|C(	CG7945	CG11761	CG1435	CG2774	CG8282	✓
5	0.373786	CG15283	CG14168	CG7224	CG13030	CG1856	CG7057	CG13811	CG3779	✓
6	0.391802	CG15468	CG14818	CG9951	CG6856	CG17599	CG9740	CG4622	CG11454	☐
7	0.416075	CG18591	CG16792	CG13277	CG6610	CG1249	CG8282	CG2774	CG1138	☐
8	0.433175	CG6425	CG5203	CG18743|C(	CG32130	CG5450	CG3183	CG6998	CG3227	☐

Free software, available at
http://theinf1.informatik.uni-jena.de/faspad/

Conclusion & Outlook

Color-coding, with some algorithm engineering, is a practical method for finding signaling pathways in protein interaction networks.

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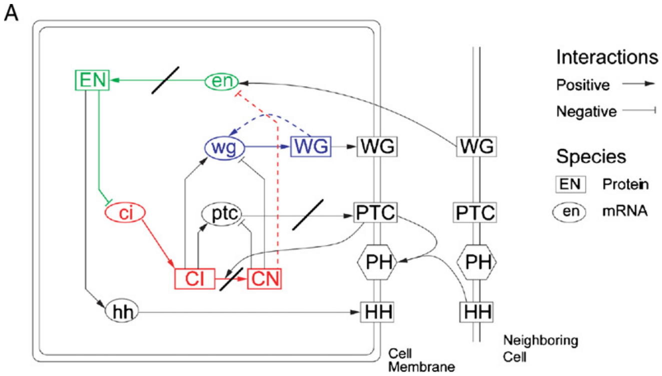
Future work:

- Richer motifs (cycles, trees, . . .)
- "Divide-and-color" [KNEIS et al., WG 2007; Chen et al., SODA 2007]: Improvement from 4.32^k to 4^k. But: "$\Theta(4^k)$"

Balanced subsystems

Drosophila regulatory network



[DasGupta et al., Biosystems 2007]

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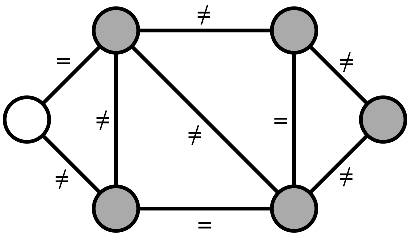
Theorem (Kőnig 1936)

A signed graph is balanced iff the vertices can be colored with two colors such that the relation on each edge holds.



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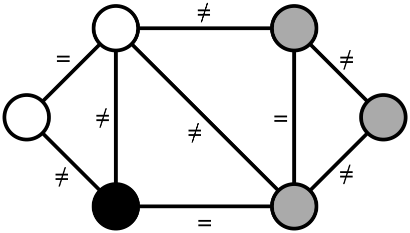

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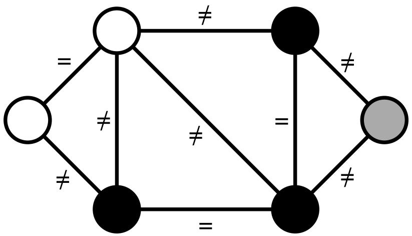

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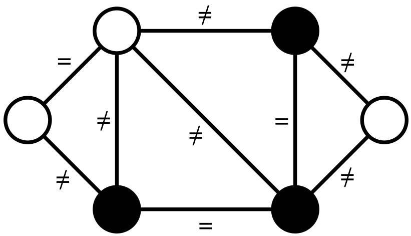
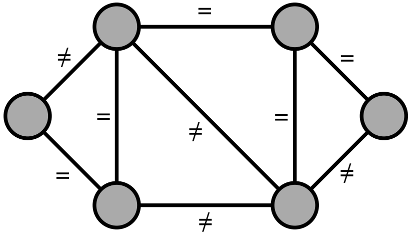


Balanced Subgraph



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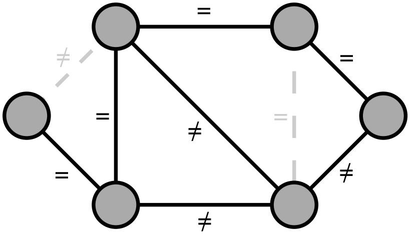

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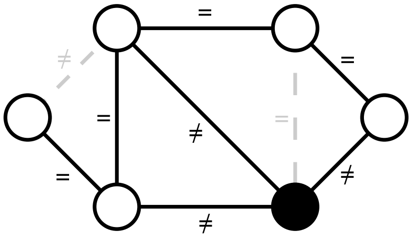

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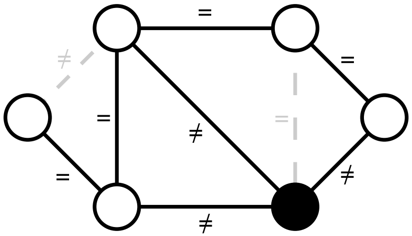


Definition (Balanced Subgraph)

Input: A graph with edges labeled by $=$ or $\neq$.
Task: Find a minimum set of edges to delete such that the graph becomes balanced.

Applications of Balanced Subgraph

- “Monotone subsystems” in gene regulatory networks

  [DasGupta et al., WEA 2006]
- Balance in social networks

  [Harary, Mich. Math. J. 1953]

  e. g. Harary: *A structural analysis of the situation in the Middle East in 1956*, J. Conflict Resolution 1961
- Minimum energy state of magnetic materials (spin glasses)

  [Kasteleyn, J. Math. Phys. 1963]
- Stability of fullerenes

  [Došlić & Vukičević, Discr. Appl. Math. 2007]
- Integrated circuit design

  [Chiang et al., IEEE Trans. CAD of IC & Sys. 2007]

Balanced Subgraph: known results

- BALANCED SUBGRAPH is NP-hard, since it is a generalization of MAX-CUT (MAX-CUT is the special case where all edges are $\neq$)
- A solution that keeps at least 87.8 % of the edges can be found in polynomial time

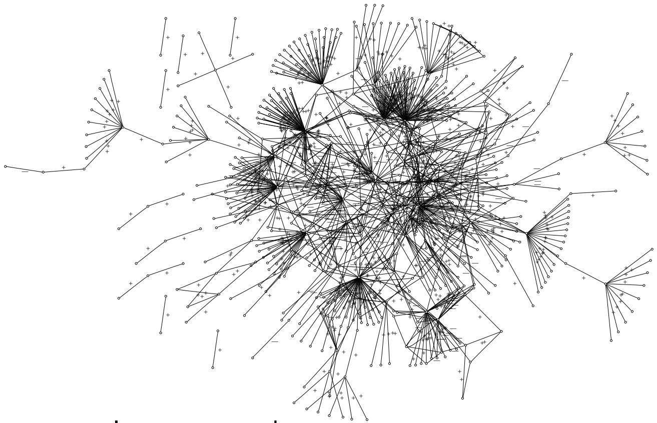
  [THAGARD & VERBEURGT, Cogn. Sci. 1998]
- A solution that deletes at most c times the edges that need to be deleted can probably not be found in polynomial time

  [KHOT, STOC 2002]

Graph structure

Idea

Exploit the structure of the relevant networks



Yeast gene regulatory network

Data reduction

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Replace the instance in polynomial time by a simpler, equivalent one.

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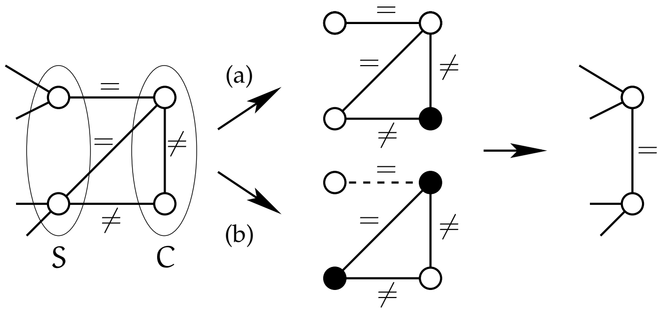
Example

Delete all degree-1 vertices.

Vertex cut-based data reduction



Data reduction scheme

Data reduction scheme

- Find cut S that cuts off small component C
- For each of the (up to symmetry) $2^{|S|-1}$ colorings of S, determine the size of an optimal solution for $G[S \cup C]$
- Replace in G the subgraph $G[S \cup C]$ by an equivalent smaller gadget

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Subsumes all 8 data reduction rules given by [Wernicke, 2003] for Edge Bipartization

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- Need to restrict both $|S|$ and $|C|$: we use $|S| \leq 4$ and $|C| \leq 32$

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- Need to restrict both $|S|$ and $|C|$: we use $|S| \leq 4$ and $|C| \leq 32$
- How to construct gadgets that behave equivalently to $S \cup C$?

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Idea

Use atomic gadgets and describe their effect by cost vectors.

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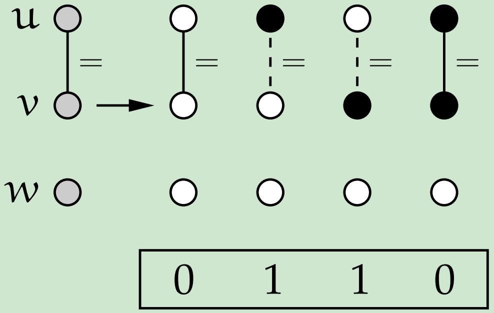

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- 4-cuts: 2948 atomic gadgets

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Given a set S of n vectors of length l with nonnegative integer components and a target vector t of length l, find a sub-(multi)-set of vectors from S that sums to t.

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- “Equality-constrained multidimensional knapsack”

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Vector Sum Problem

Given a set S of n vectors of length l with nonnegative integer components and a target vector t of length l, find a sub-(multi)-set of vectors from S that sums to t.

- "Equality-constrained multidimensional knapsack"
- In our implementation: simple branch & bound

Gadget construction

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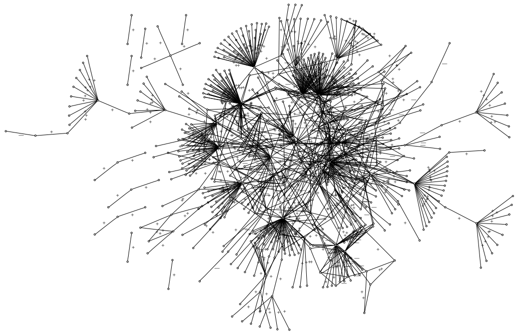
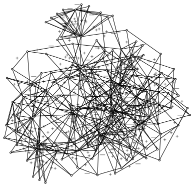
- "Equality-constrained multidimensional knapsack"
- In our implementation: simple branch & bound
- Sometimes this is a bottleneck!

Reduction. . . and then?

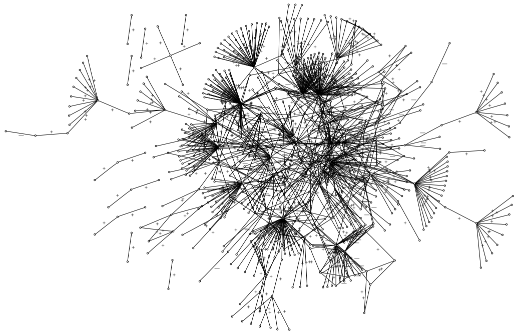


$n = 690,\ m = 1082$



$n = 144,\ m = 405$

Reduction... and then?



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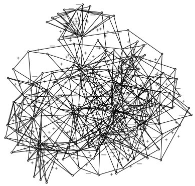

$n = 144,\ m = 405$

After data reduction, a hard "core" remains.

Idea

Exploit the fact that only few edges need to be deleted.

Fixed-parameter tractability

Theorem

BALANCED SUBGRAPH *can be solved in* $O(2^k \cdot m)$ *time by a reduction to* EDGE BIPARTIZATION *and using an algorithm based on iterative compression* [GUO et al. 2006].

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A heuristic speedup trick can give large speedups over this worst-case running time.

Experimental results

			Approximation			Exact alg.	
Data set	n	m	$k \geq$	$k \leq$	t [min]	k	t [min]
EGFR	330	855	196	219	7	210	108
Yeast	690	1082	0	43	77	41	1
Macr.	678	1582	218	383	44	374	1

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- Yeast is not solvable without reducing 4-cuts
- A real-world network with 688 vertices and 2208 edges could not be solved

Outlook

- Directed case of BALANCED SUBGRAPH (delete minimum number of edges to remove all unbalanced cycles): FPT?
  - Problem: Characterization by two-coloring does not work
- The data reduction scheme is applicable to all graph problems where a coloring or a subset of the vertices is sought. For example:
  - VERTEX COVER
  - DOMINATING SET
  - 3-COLORING
  - FEEDBACK VERTEX SET

  but: need small cuts (e. g., small-world networks)

Protein complexes

Clique Enumeration

Application

- Analysis of biological, social, and other networks
- Finding complexes in protein interaction networks
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Maximal clique enumeration

- Simple model
- NP-hard
- up to $3^{n/3}$ cliques

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Isolated cliques

- More specific model
- More efficient enumeration algorithms (FPT)

c-Isolation

Definition (Ito, Iwama & Osumi, ESA 2005)

A vertex set S is called c-isolated if on average the vertices in S have less than c neighbors outside of S.

Example: 2-isolation

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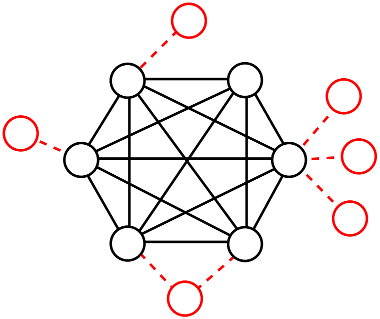
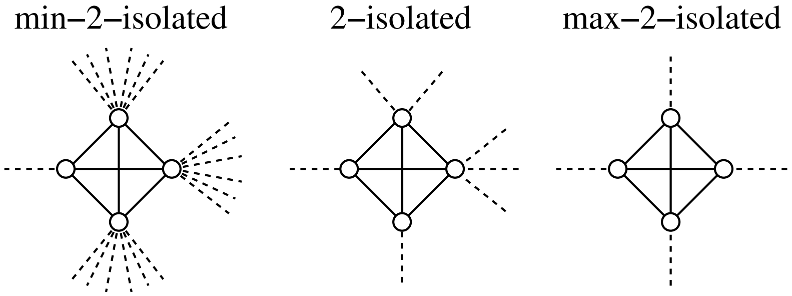


Enumerating maximal c-isolated cliques

Theorem

All maximal c-isolated cliques in a graph G can be enumerated in $O(2.89^c \cdot c^2 m)$ time.

Comparison of isolation concepts



Running times for enumeration of maximal cliques

min-c-isolation	$O(2^c \cdot cm + nm)$
c-isolation	$O(4^c \cdot c^4 m)$
max-c-isolation	$O(2.44^c \cdot cm)$

Finding complexes: Experimental setup

Question

Are isolated cliques a good model for complexes?

Experiment

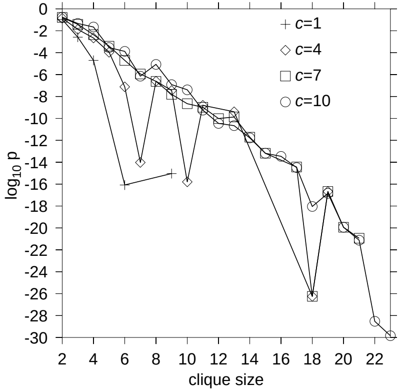
- We retrieved a protein interaction network from BioGRID: *S. cerevisiae*: 5 195 nodes, 70 911 edges.
- We retrieved annotation data for each protein from the Saccharomyces Genome Database (SGD).
- For each enumerated clique, we calculated the *p*-values for the enrichment of annotation terms with the GO Termfinder software, and chose the annotation term with the lowest *p*-value.

Finding complexes: Experimental results

General observations

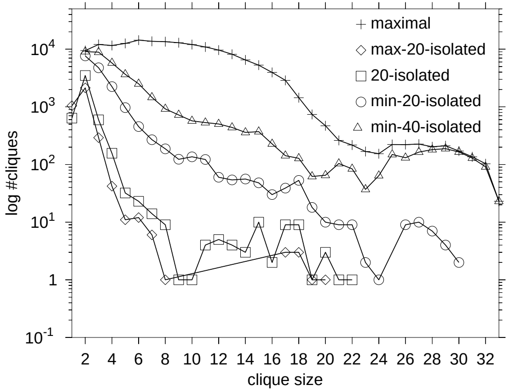
- running time: few seconds
- maximal isolated cliques show more significant enrichment of annotation terms than maximal cliques

Finding complexes: Experimental results



Comparison of mean p-values of the enumerated maximal min-c-isolated cliques and different values of c.

Finding complexes: Experimental results



Distribution of the number of enumerated cliques in the yeast network for different isolation concepts and strengths.

References

- Falk Hüffner, Sebastian Wernicke, and Thomas Zichner:
  Algorithm engineering for color-coding with applications to signaling pathway detection.
  Algorithmica.
  Accepted for publication, June 2007.
- Falk Hüffner, Nadja Betzler, and Rolf Niedermeier:
  Optimal edge deletions for signed graph balancing.
  Proc. 6th Workshop on Experimental Algorithms (WEA '07), 2007.
  LNCS 4525, pp. 297–310.
- Falk Hüffner:
  Algorithms and Experiments for Parameterized Approaches to Hard Graph Problems.
  PhD thesis, Universität Jena, to appear.