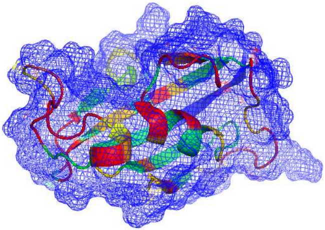
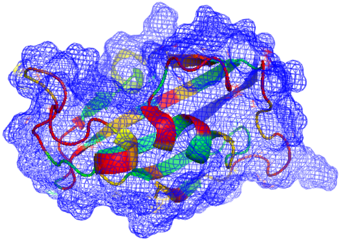
Improving the Resolution of Hydrogen/Deuterium Exchange Data

Stefan Canzar

Centrum Wiskunde & Informatica



Motivation



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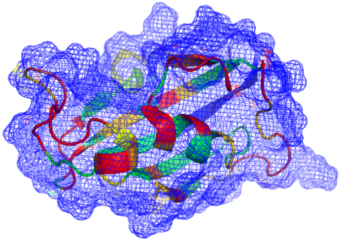

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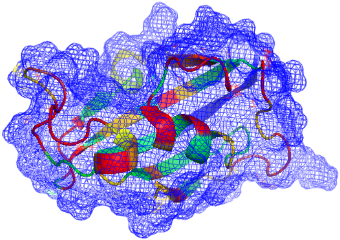

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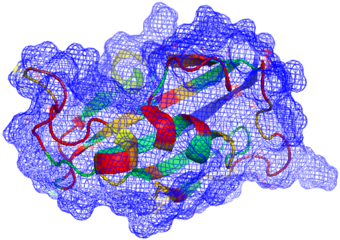

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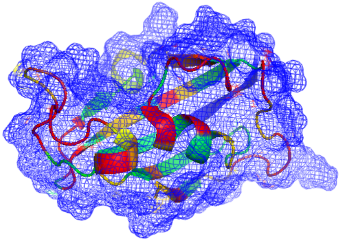

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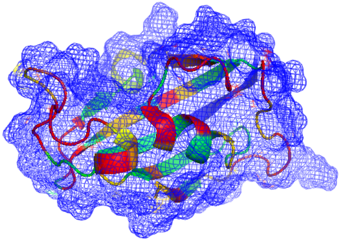

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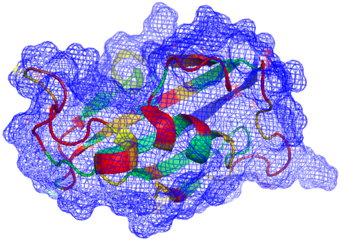

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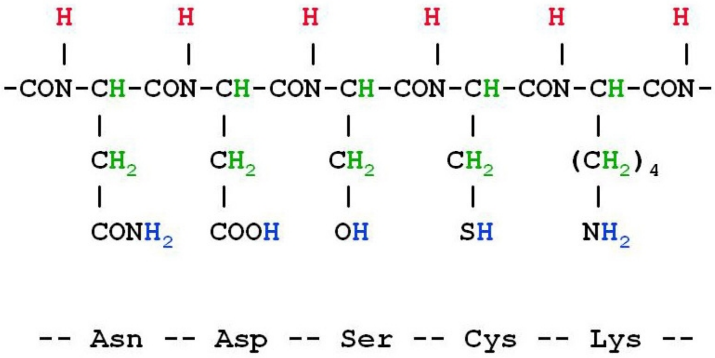
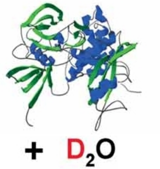
⇒ Increase resolution from fragments to single residues!

Hydrogens in Proteins



H/D Exchange + MS



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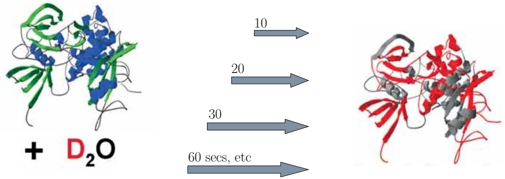

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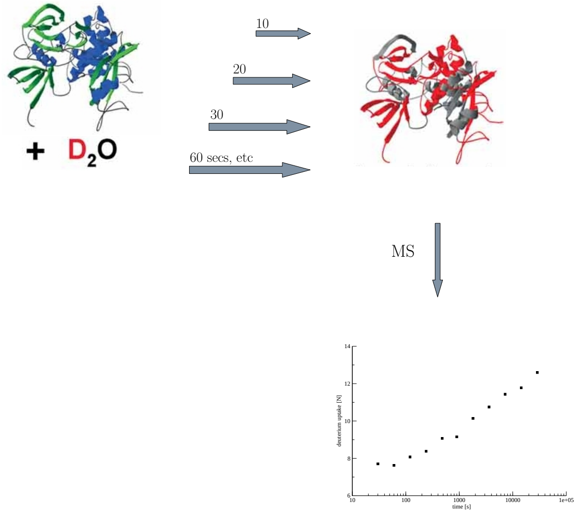

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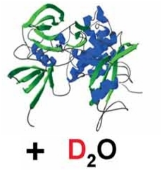


10

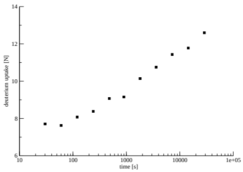
20

30

60 secs, etc

MS

Fit to 3-comp. model



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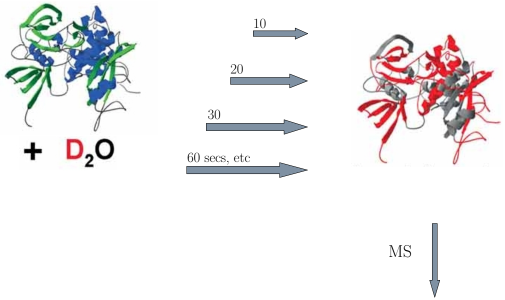

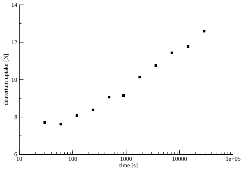

Fit to 3-comp. model

$\Rightarrow$ (F : 20, M : 14, S : 5)

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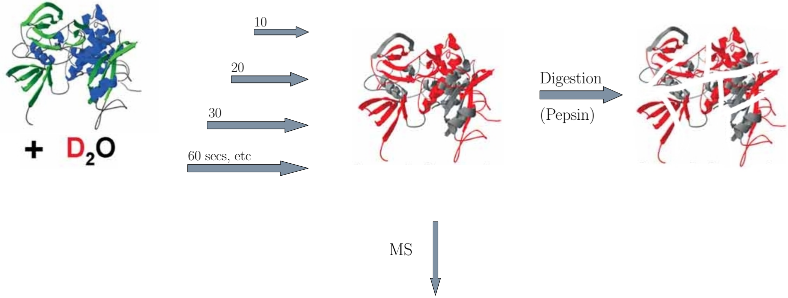

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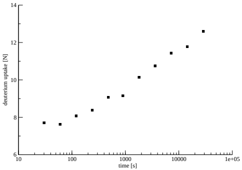

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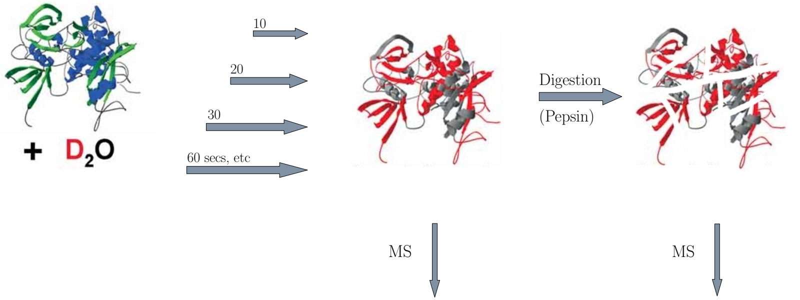
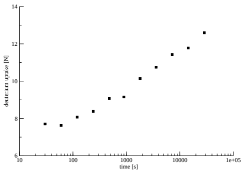


$(F_1 : 5, M_1 : 2, S_1 : 0)$
$(F_2 : 4, M_2 : 4, S_2 : 2)$
$\vdots$
$(F_k : 2, M_k : 5, S_k : 3)$



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G	R	Y	R	G	Y	R	R	Y
1	2	3	4	5	6	7	8	9

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Experiments

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↑ feasible assignment

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IntervalConstrainedColoring

Is there a *feasible* coloring, i.e. a function $\chi : V \mapsto [k]$ such that for every $I \in \mathcal{I}$ and all $c \in [k]$ we have $|\{j \in I \mid \chi(j) = c\}| = r(I, c)$?

An ILP Formulation

Variables:

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Each fragment I contains $r(I,j)$ residues exchanging at rate j:

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In Practice:

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Practically irrelevant, but related to

Maximum feasible subsystem problem with 0/1-coefficients!

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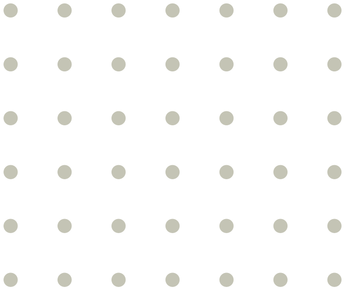

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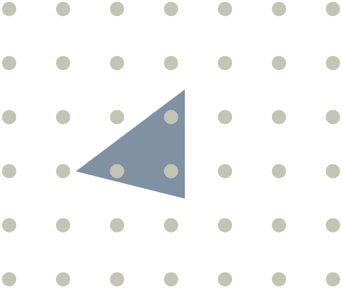

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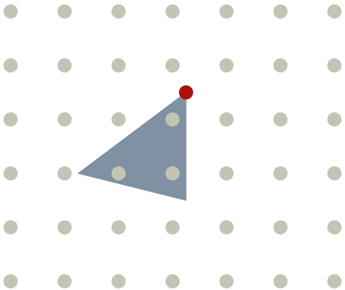

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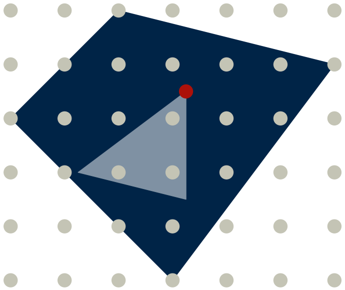

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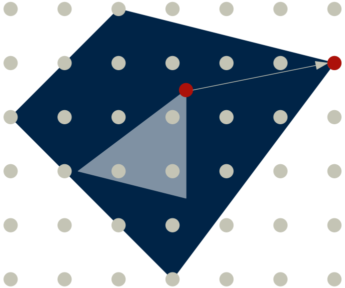

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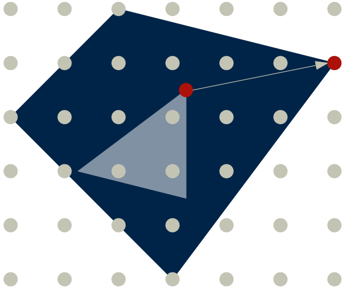

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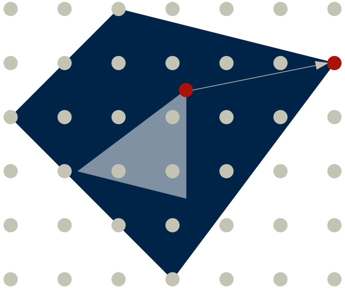

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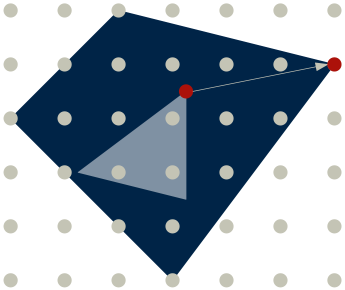

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- Guarantees polynomial delay in enumeration

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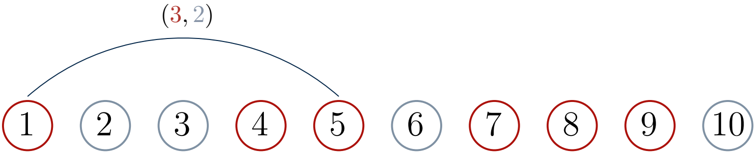

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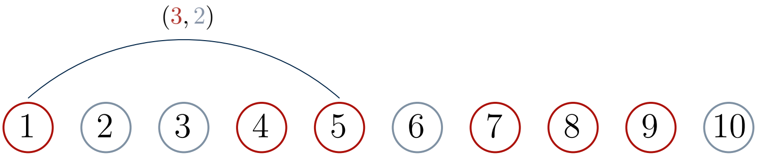

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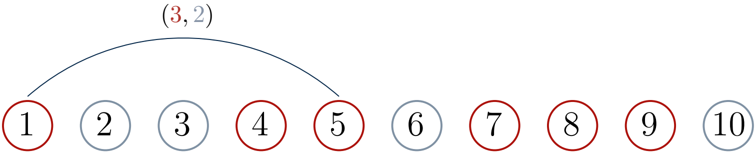

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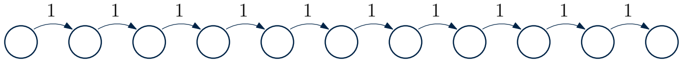
Idea: Add edges such that shortest path lengths from a new source vertex define a feasible d.

Constraint Graph Construction



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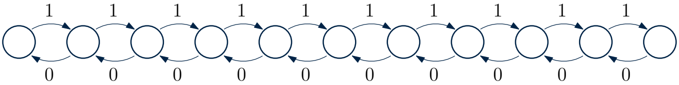

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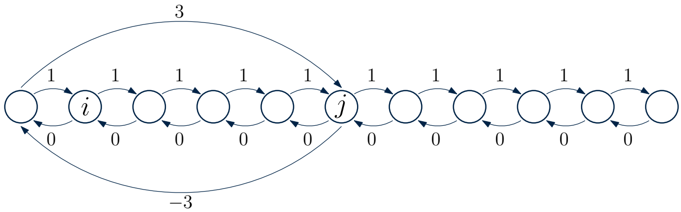

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3. Fragment $I = [i, j]$ contains $r(I, 1)$ red vertices:

$$d(j) - d(i-1) = r(I, 1)$$

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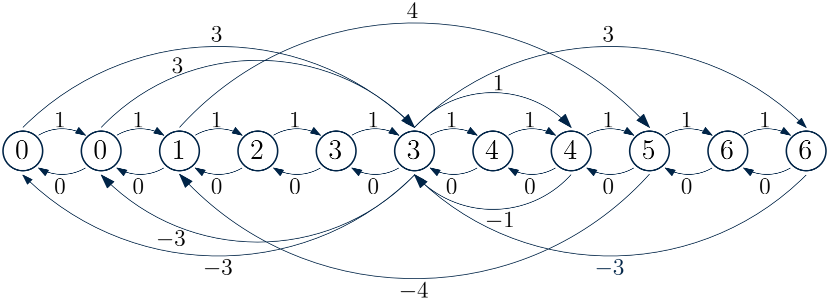

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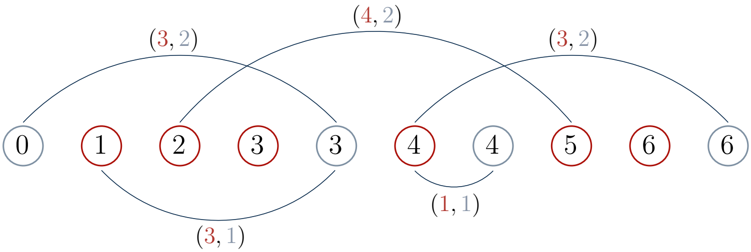

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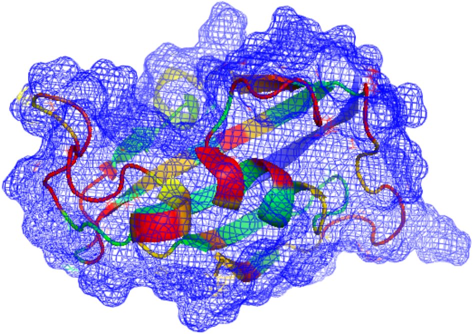
Structural View of FKBP



red = fast
yellow = medium
green = slow

Acknowledgments

Experiments & Data:

- M.R. Emmett - Department of Chemistry, FSU
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- J. Tipton - Department of Chemistry, FSU
- H. Zhang - Institute of Molecular Biophysics, FSU

Theory & Implementation

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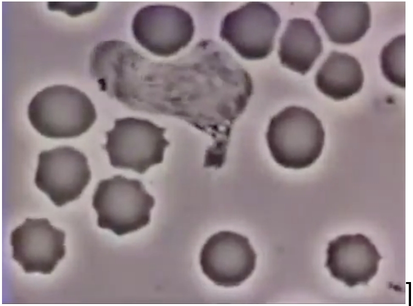
- C. Ehrler - Universität des Saarlandes
- K. Elbassioni - MPI Saarbrücken
- A. Karrenbauer - Institute of Mathematics, EPFL Lausanne
- J. Mestre - University of Sydney

Analysis of Live Cell Video

with K. Elbassioni, G. Klau, J. Mestre



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Given live cell video, we want to track individual cells

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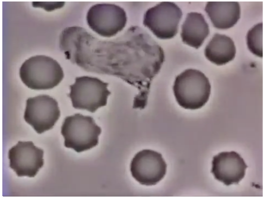

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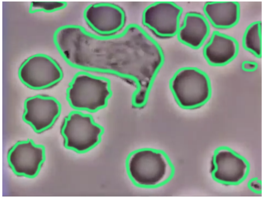

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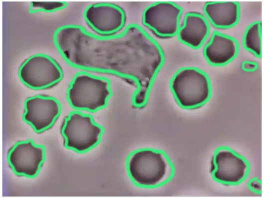

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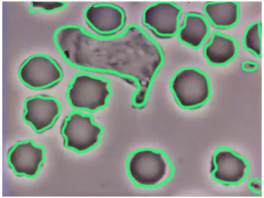

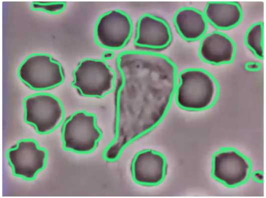

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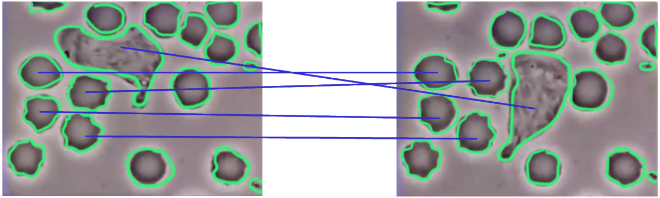
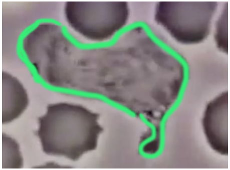


Over/under segmentation



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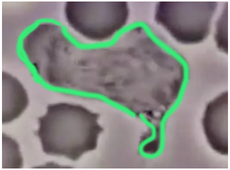

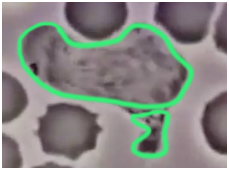

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Challenge: Biological cell division vs. over-segmentation

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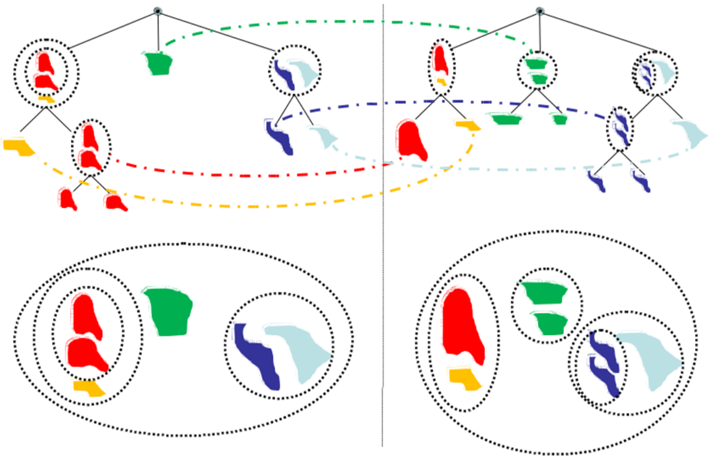
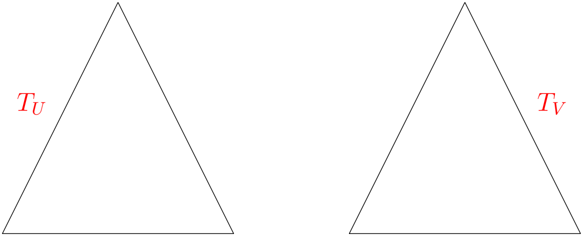
⇒ [Mosig *et al.*, 2009]: Integrate identification and tracking steps!

Cosegmentation



Tree-Constrained Matching



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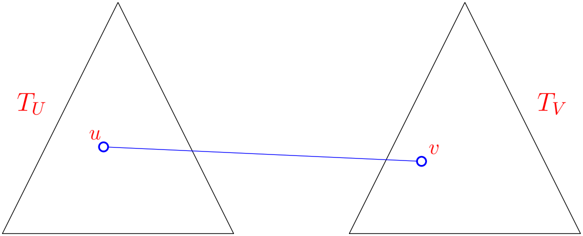

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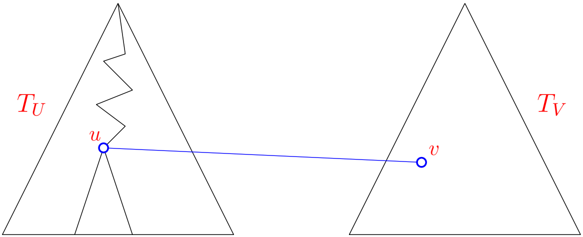

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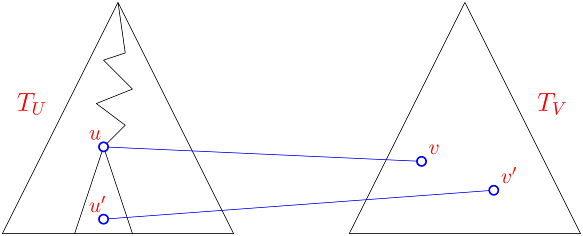

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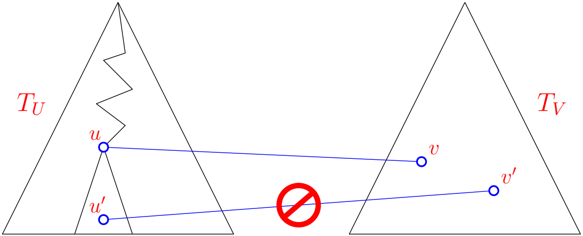

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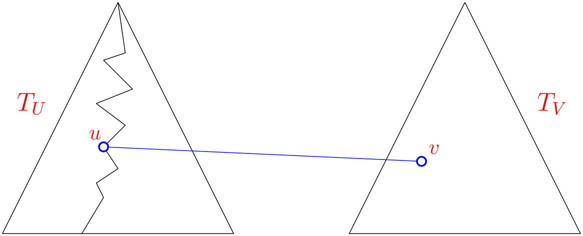

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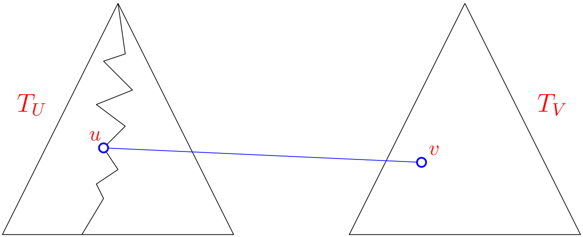

Given a weighted bipartite graph (U, V, E) and trees T_U and T_V over U and V, we want maximum weight matching $\mathcal{M}$ such that matched vertices in T_U and T_V are not comparable

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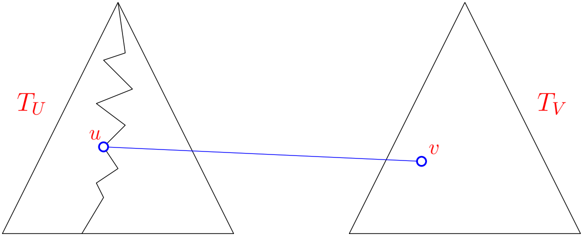

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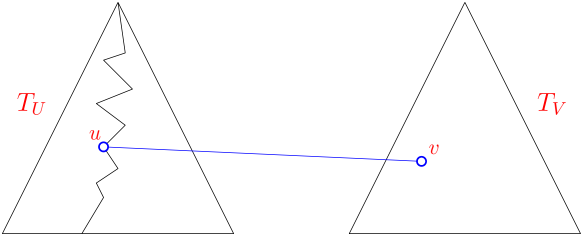

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But...

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with M. El-Kebir

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  - Now, we can plan more systematically

Powdery Mildew in Pepper

- Fungal disease incited by *Leveillula taurica*

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$\Rightarrow$ Host plant resistance is desired

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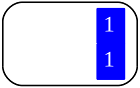

- Pungency is monogenic
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0	0	0	1
0	0	0	1

  - Wildtype is resistant but pungent

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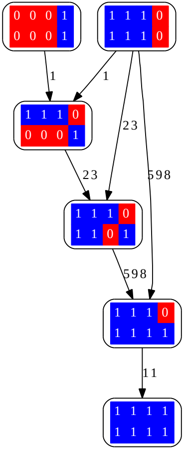
Optimal Schedule



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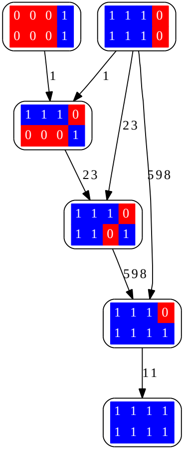

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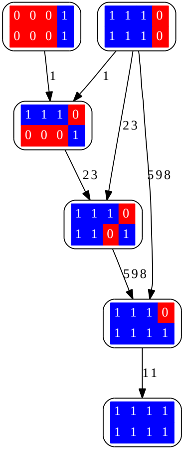

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- ingredients:
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  - implicit enumeration