A practical FPT algorithm for Flow Decomposition and transcript assembly

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2017/07/19

North Carolina State University
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Motivation

The Problem

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TACCGAATACGAACTAGGATATCGATCGATCAGAGGCCCAATAGGGAATATCCG

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Shared segments between DNA/RNA strands create ambiguity in the assembly problem

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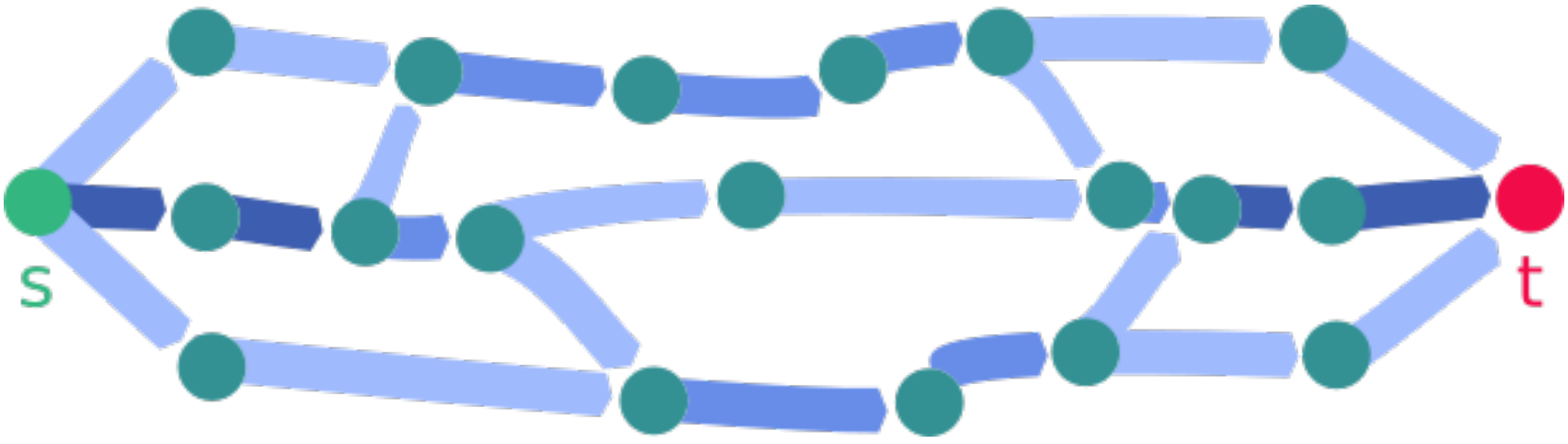
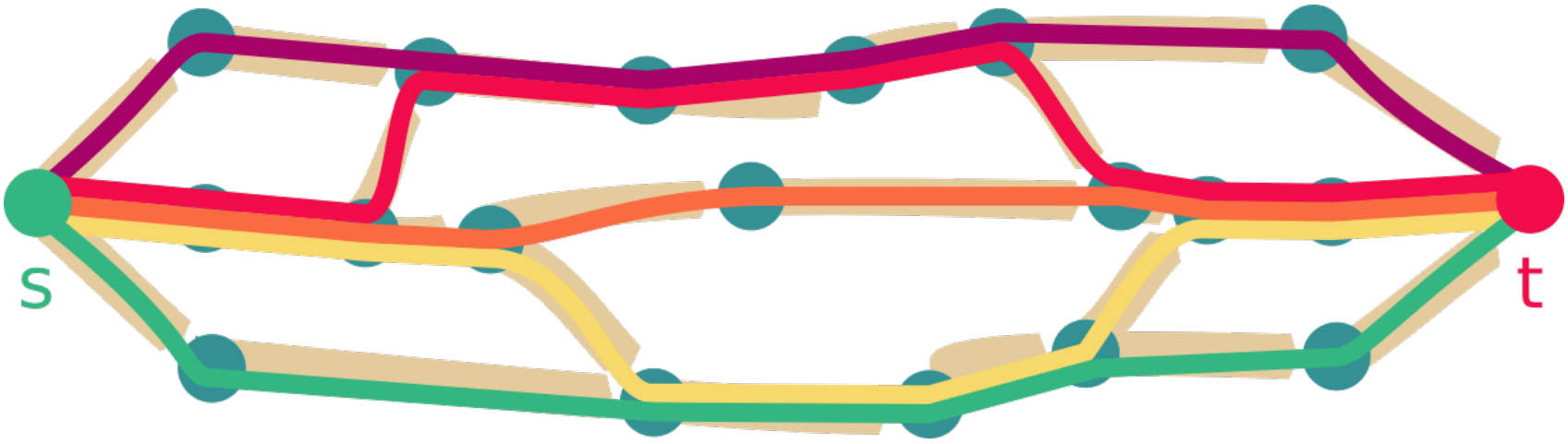


Connecting overlapping segments and counting their frequencies yields a DAG and a flow

The Problem



The problem is to split the flow int the least amount of s-t-paths, to recover the original DNA/RNA strands.

The Problem

k-Flow Decomposition (k-FD)

Input: (G, f, k) with G an s-t–DAG, f a flow on G, and k a positive integer.

Problem: Is there an integral *flow decomposition* of (G, f) using at most k paths?

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Problem is NP-hard even for weights $\{1, 2, 4\}$

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FPT

Definition

A parameterized problem L is *linear fixed-parameter tractable* if the question "$(x, k) \in L$?" can be decided in $f(k)\, O(|x|)$.

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3. Output decompositions (not only decision problem).
   $\rightarrow$ reliably recover **domain-specific solution**.

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Theorem

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- Usable in practice (*so we claim*)

Preliminaries

Related Work

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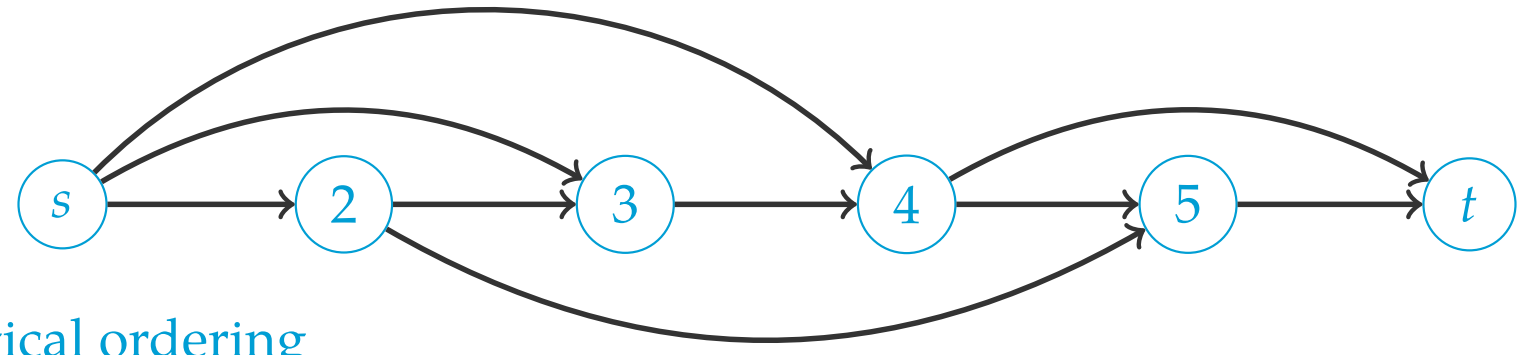
So far no exact algorithm

Definitions



topological ordering

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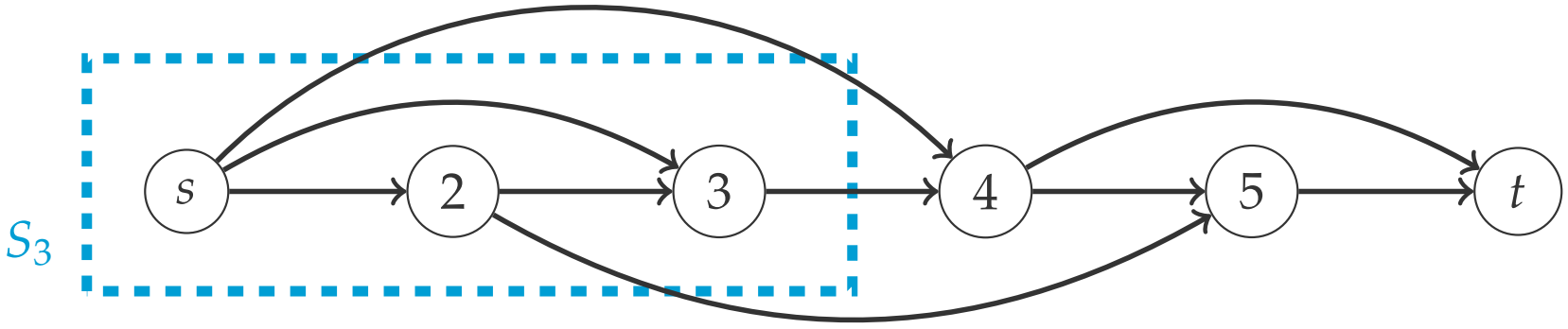

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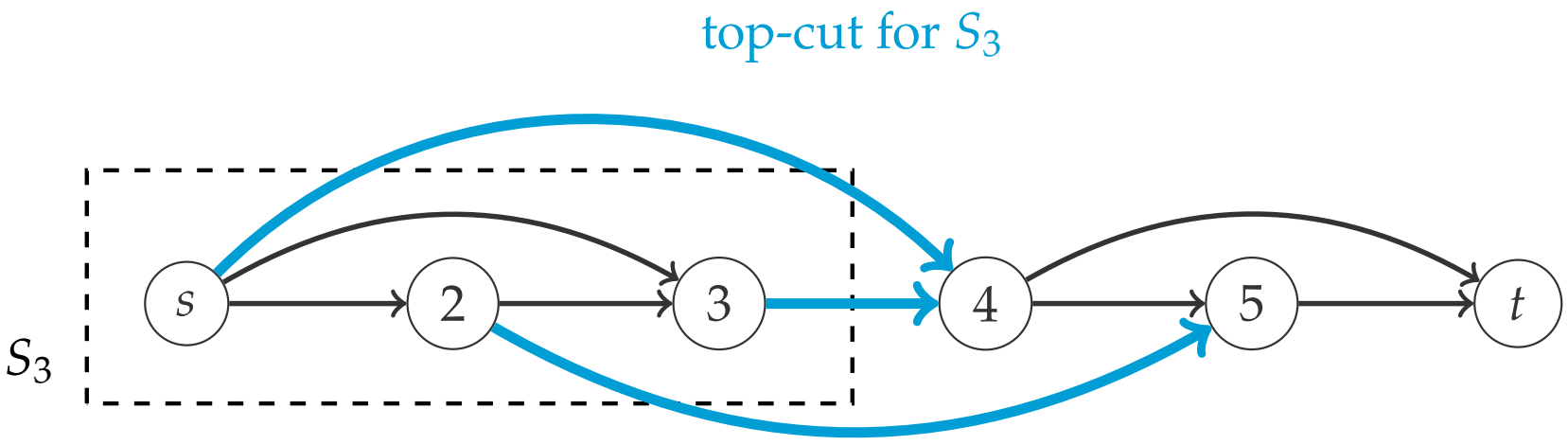
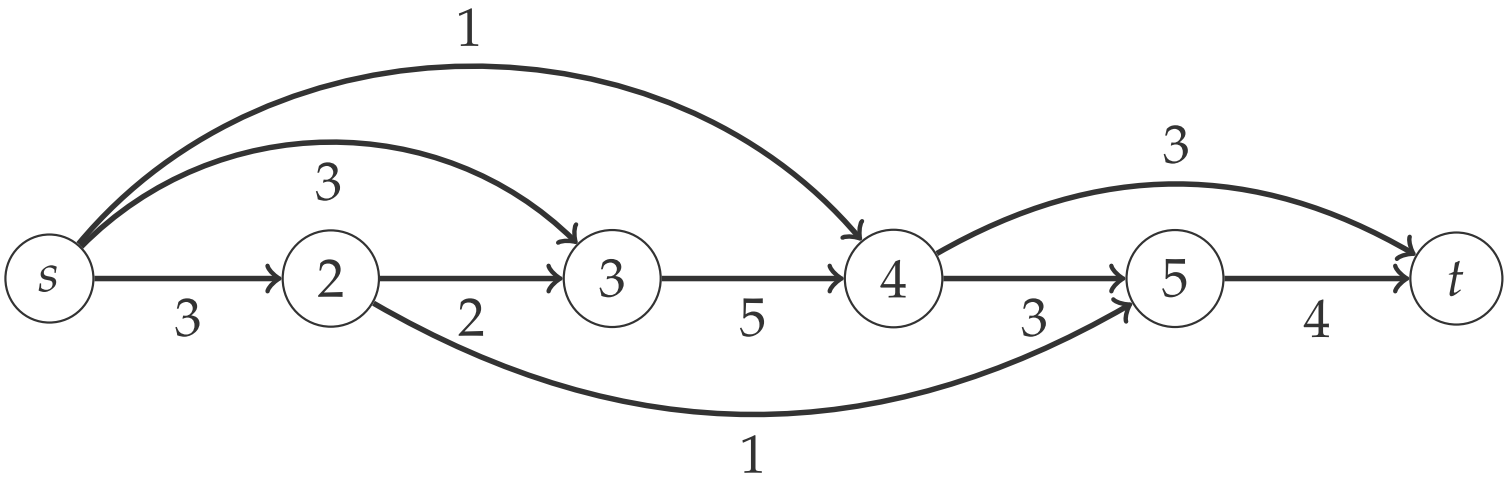


Algorithm

The Idea



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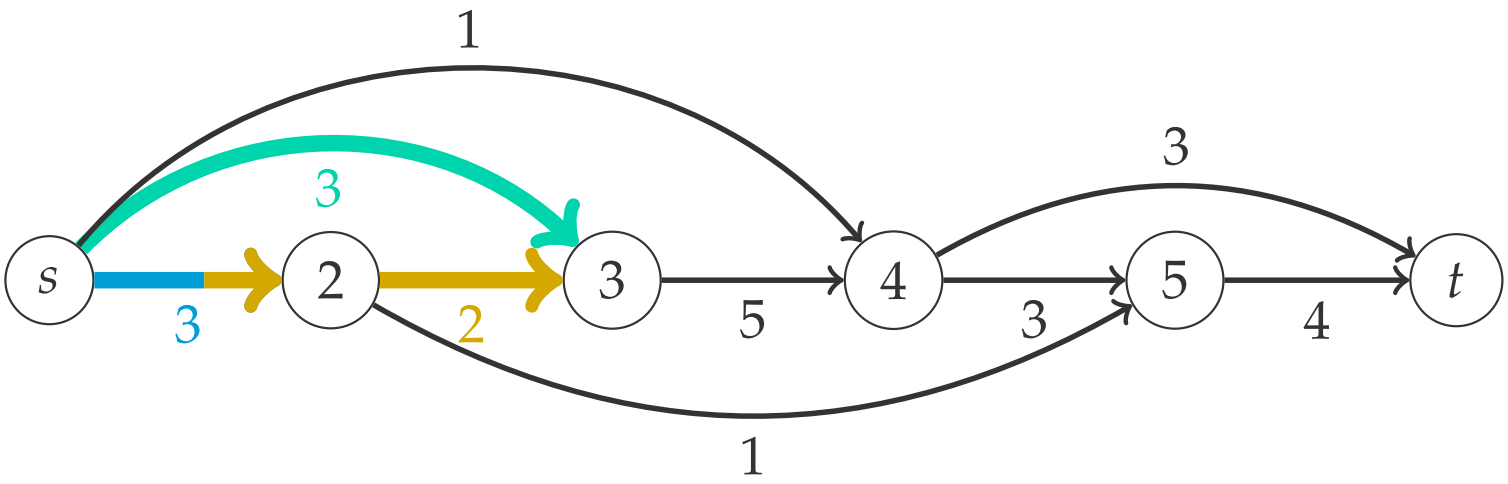

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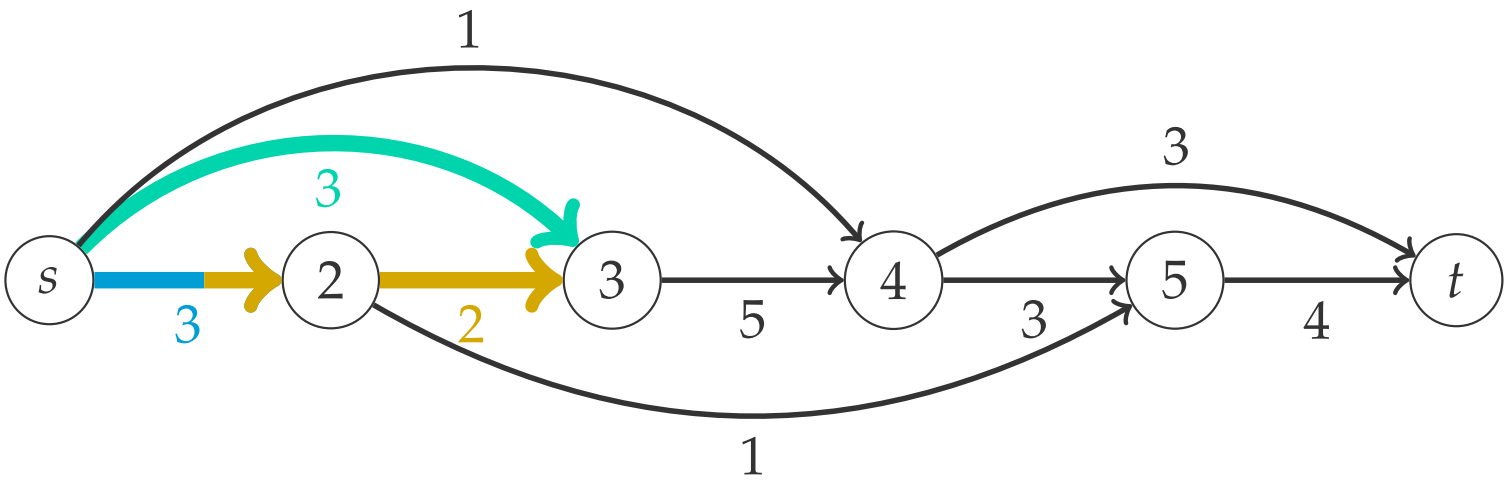

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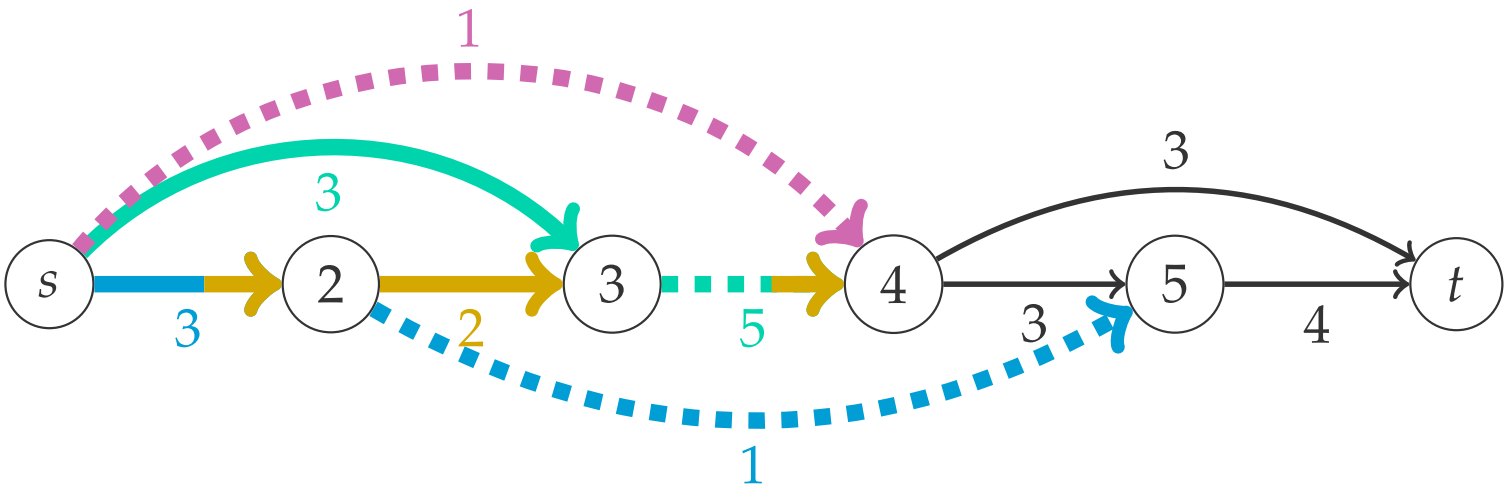

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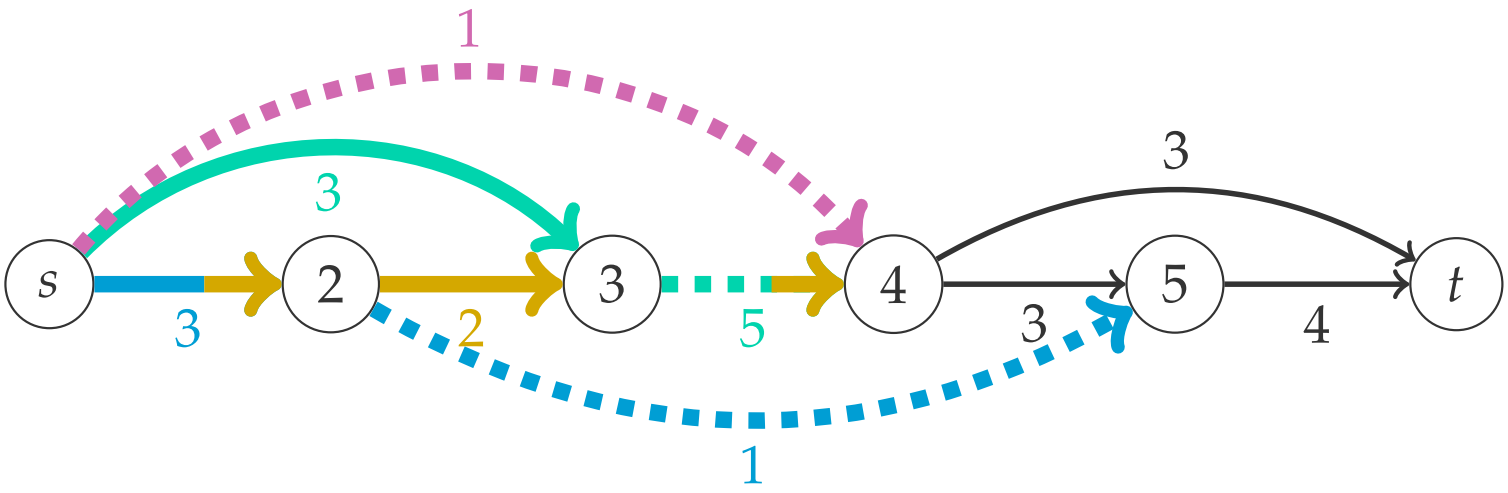

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Dynamic Programming Step

From S_i to S_{i+1} exactly one vertex (v_{i+1}) becomes internal. We need to push the incoming flows of v_i to the outgoing edges.

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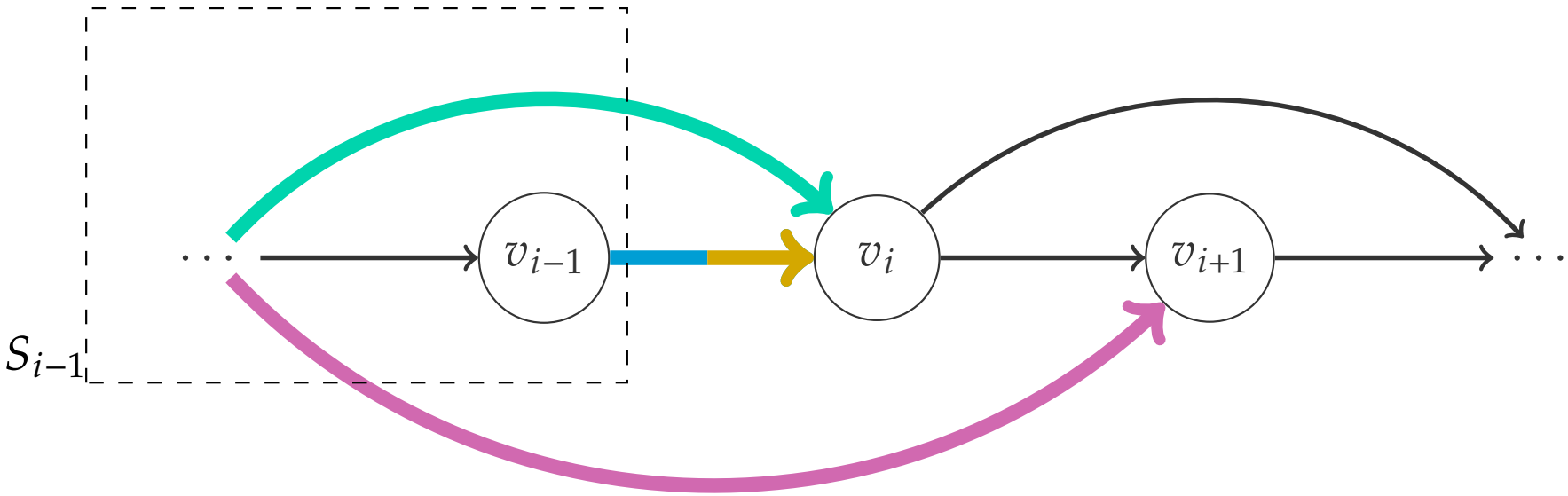

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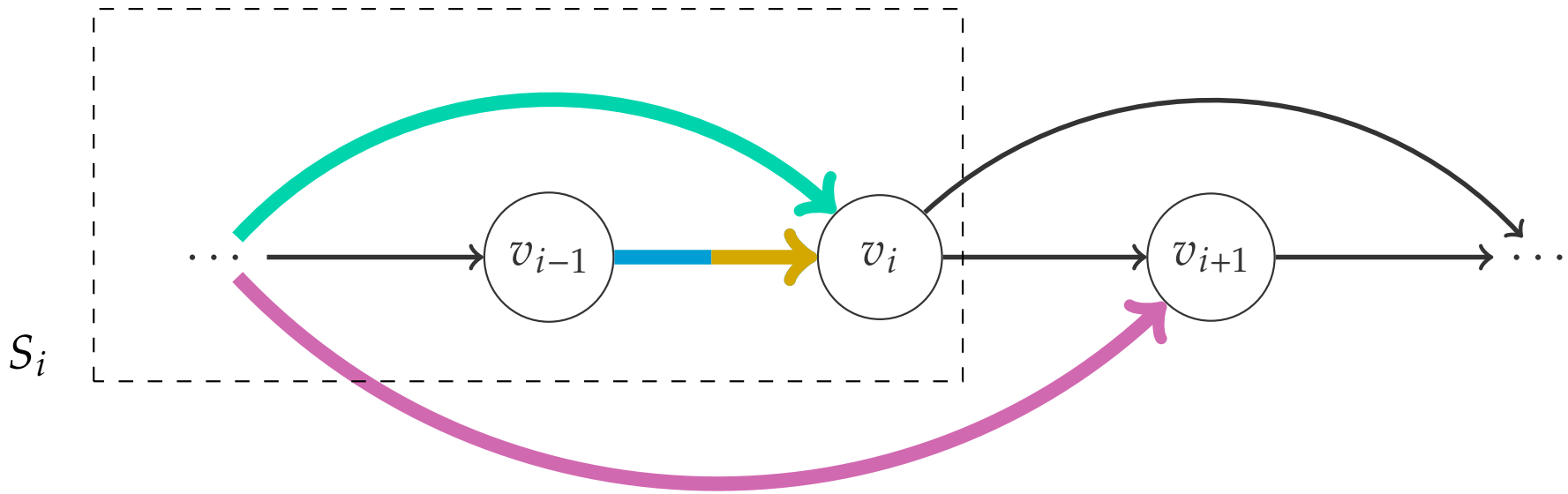

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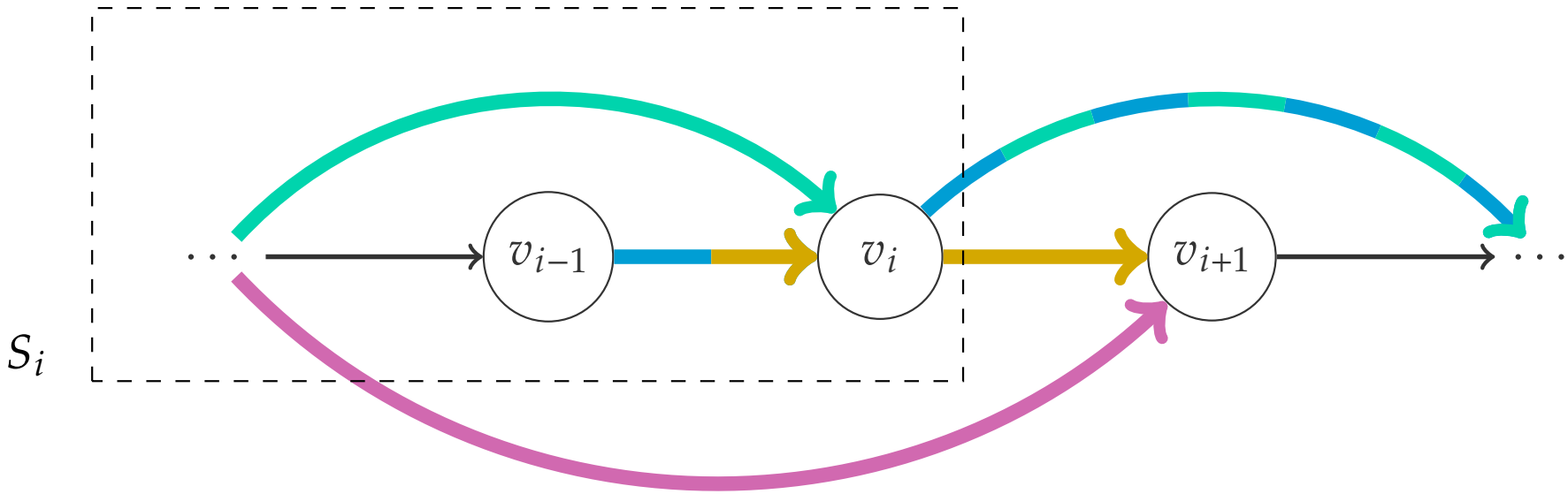

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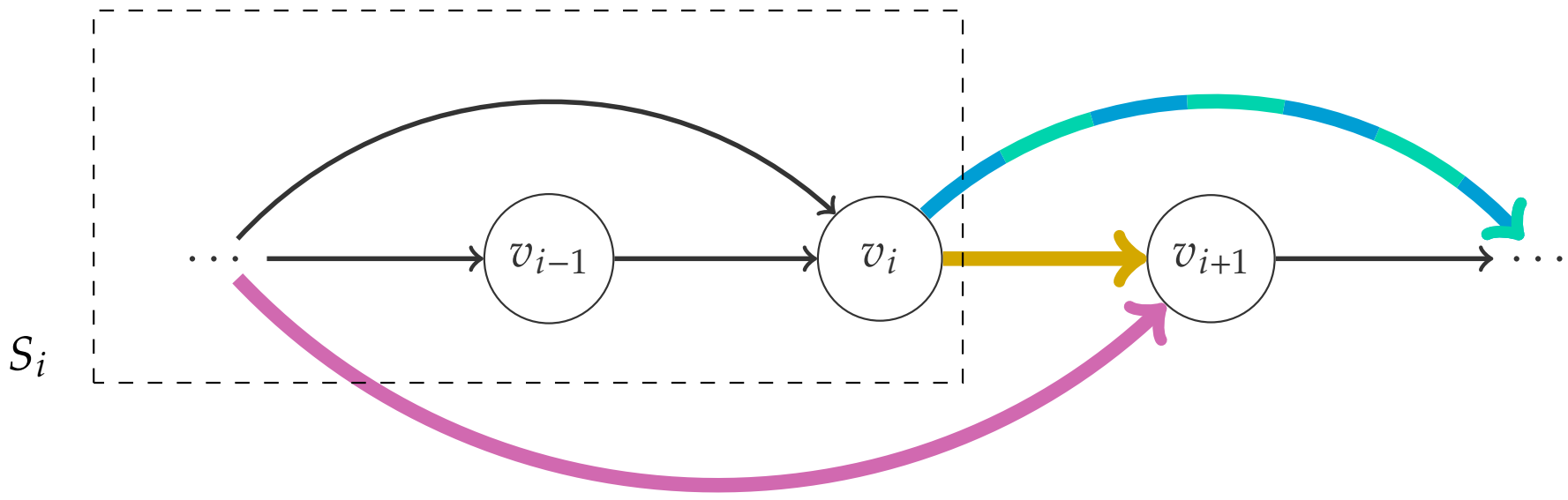

We can "forget" internal labels.

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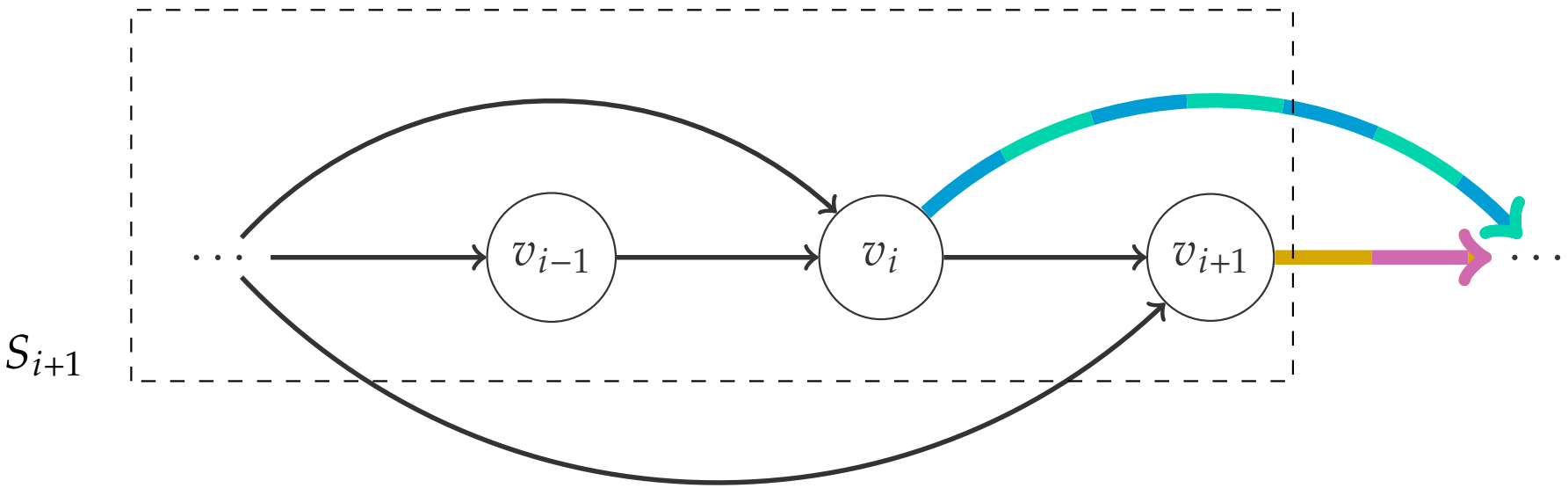

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- When we arrive at S_n we check each linear system for valid solution.

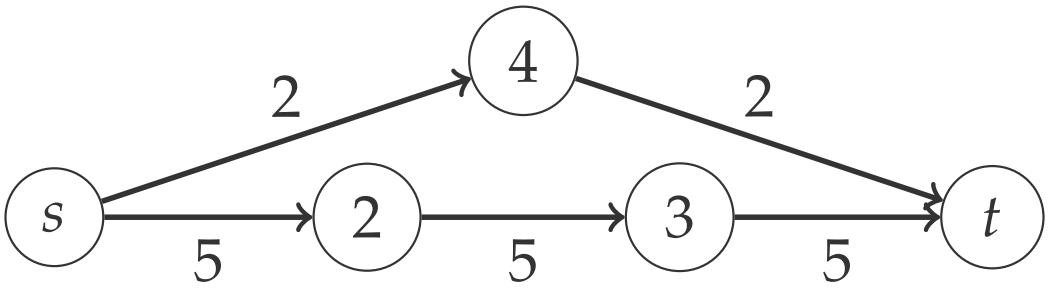
Always true?

Conjecture

If k is the minimum value for which (G, f) has a flow decomposition of size k, then every integer-weighted solution has a corresponding linear system L of rank k.

Implementation

Graph Reduction



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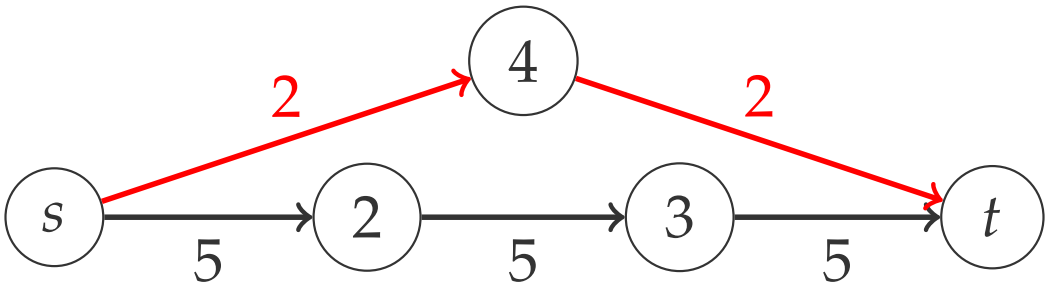

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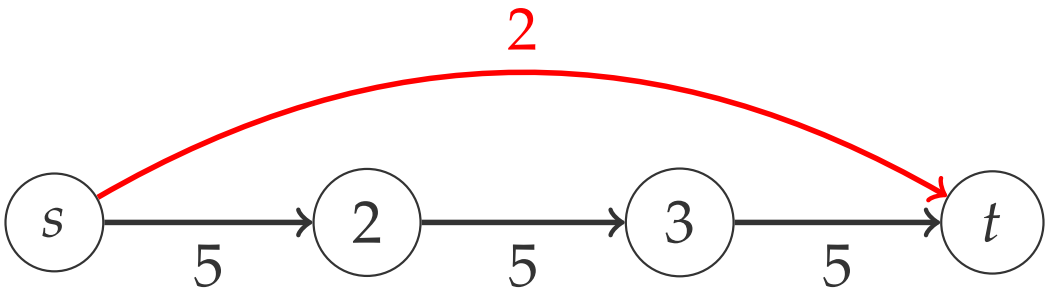

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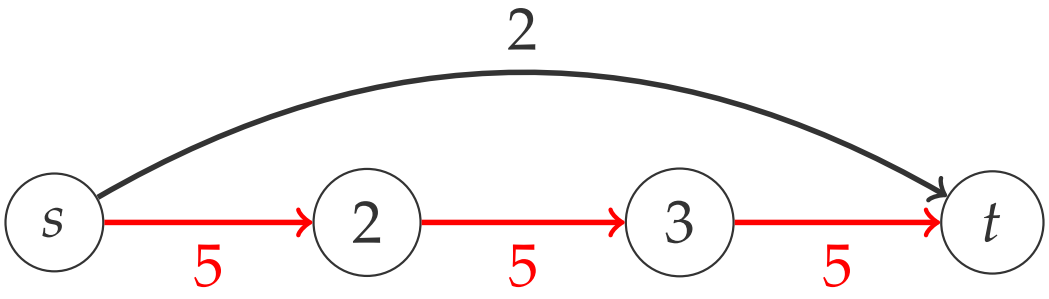

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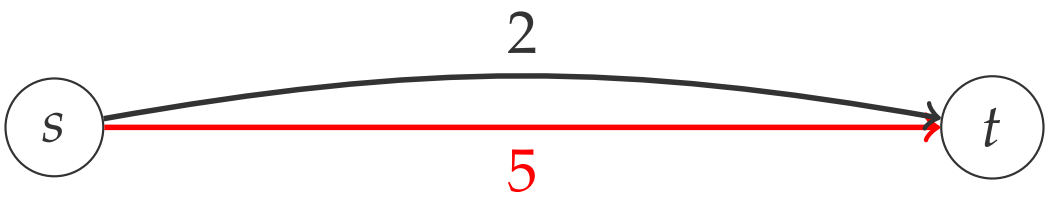

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Additional pruning is performed according to heuristics.

Repository

Python implementation is available on Github:

`https://github.com/theoryinpractice/toboggan`

Experiments

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Simulated RNA sequencing data for `human`, `mouse` and `zebrafish`, containing ground-truth.

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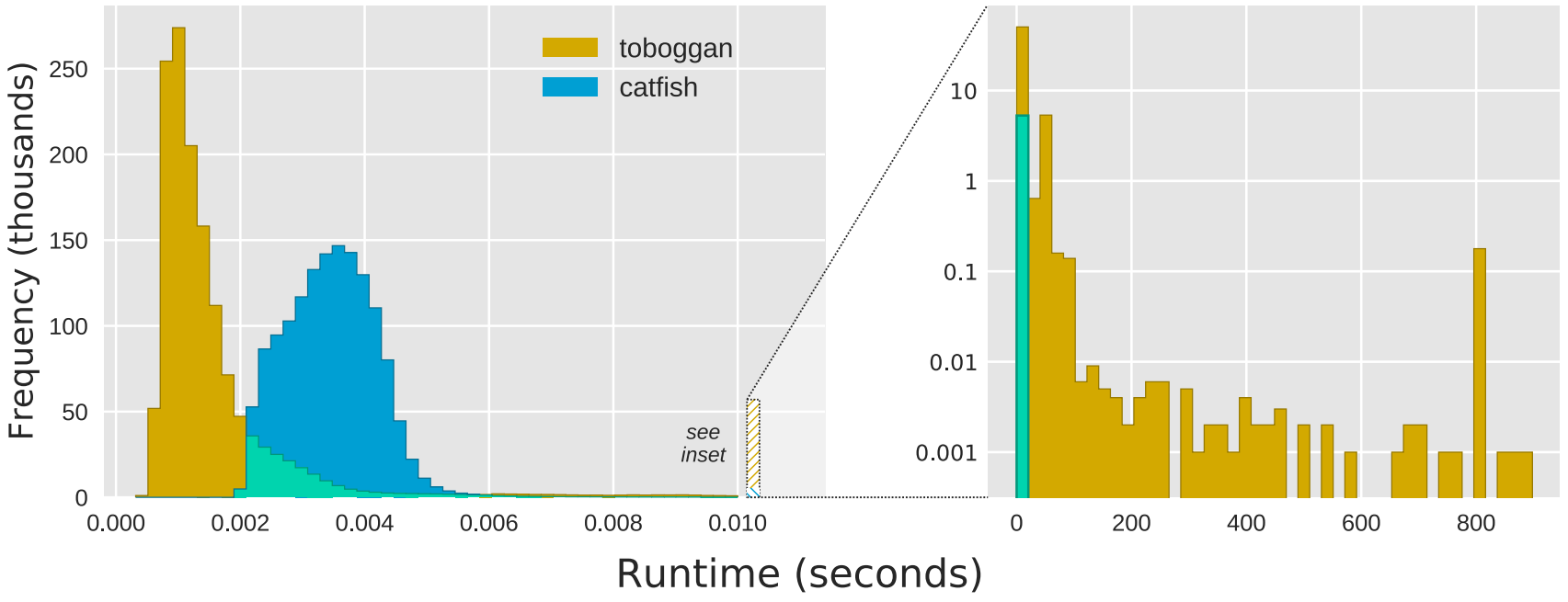
Toboggan had a 800 second timeout limit.

Execution Time



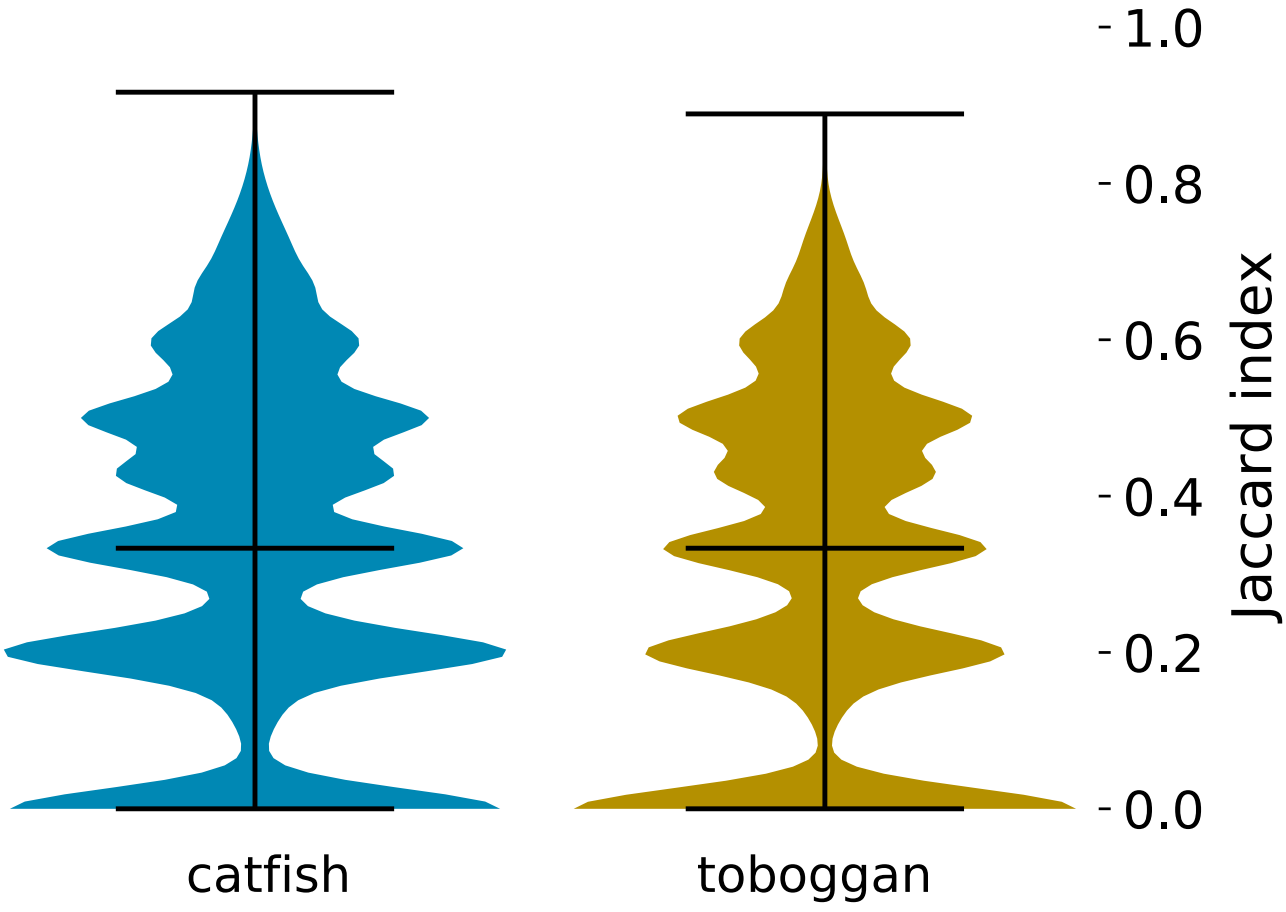
Ground Truth Validation

dataset	instances	non-trivial	optimal	non-optimal
`zebrafish`	1,549,373	445,880	99.907%	0.053%
`mouse`	1,316,058	473,185	99.401%	0.074%
`human`	1,169,083	529,523	99.490%	0.043%
all	4,034,514	1,448,588	99.589%	0.056%

Exact Recovery

k	instances	Catfish	Toboggan
2	63.2791%	0.992	**0.995**
3	22.0775%	0.967	**0.969**
4	8.5237%	**0.931**	0.930
5	3.4920%	0.886	0.886
6	1.5375%	**0.830**	0.828
7	0.6698%	**0.788**	0.780
8	0.2889%	**0.767**	0.766
9	0.1241%	0.740	**0.743**
10	0.0070%	0.752	**0.802**
11	0.0004%	0.500	0.500
all	100%	0.973	**0.975**

Solutions vs. Ground Truth



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paper: `https://arxiv.org/abs/1706.07851`

github: `https://github.com/theoryinpractice/toboggan`

Thank you!