Frequency of Significant Sequential Motifs Reveal Patterns in Pathway Data

Presented by

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Ingo Scholtes

Tina Eliassi-Rad

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Motivation

- **Motifs** are meso-scale structures that characterize complex networks. They have long been studied for **static** networks.

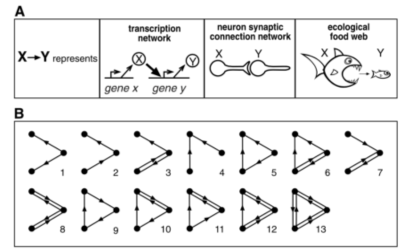

Fig. 1. (**A**) Examples of interactions represented by directed edges between nodes in some of the networks used for the present study. These networks go from the scale of biomolecules (transcription factor protein X binds regulatory DNA regions of a gene to regulate the production rate of protein Y), through cells (neuron X is synaptically connected to neuron Y), to organisms (X feeds on Y). (**B**) All 13 types of three-node connected subgraphs.

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Milo et al. Network Motifs: Building Blocks of Complex Networks. Science, 2002.

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- More recently, motifs in **temporal** and **dynamic** networks have been analyzed, as well as their role in **dynamics on networks**

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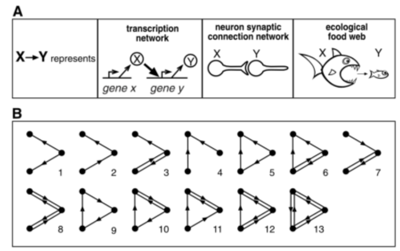

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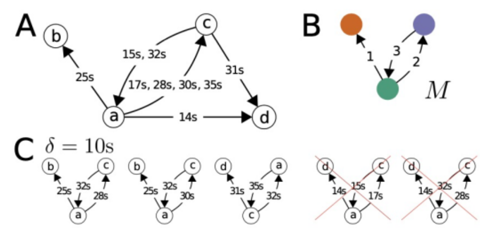

Figure 1: Temporal graphs and δ-temporal motifs. A: A temporal graph with nine temporal edges. Each edge has a timestamp (listed here in seconds). B: Example 3-node, 3-edge δ-temporal motif M. The edge labels correspond to the ordering of the edges. C: Instances of the δ-temporal motif M in the graph for δ = 10 seconds. The crossed-out patterns are not instances of M because either the edge sequence is out of order or the edges do not all occur within the time window δ.

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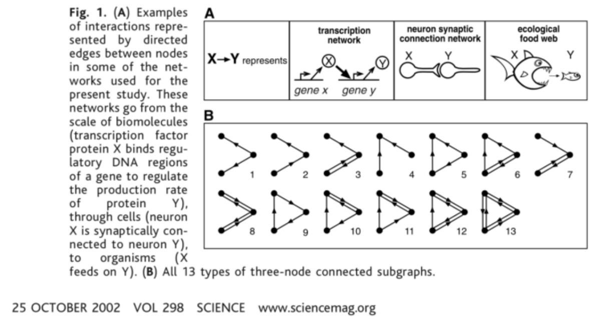
- **Today:** Network data often comes in the form of **pathways** or **sequences**. This data has different characteristics that require specific methodology.



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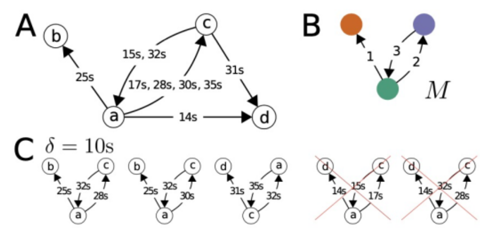

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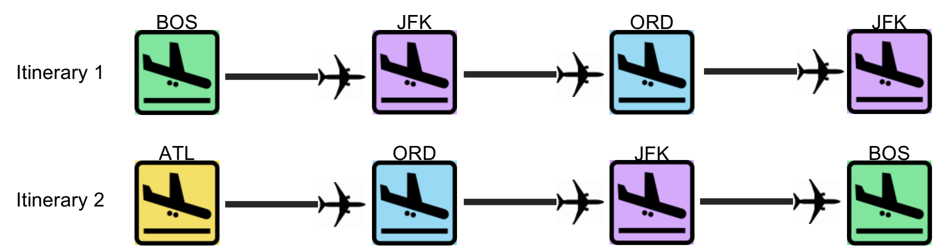

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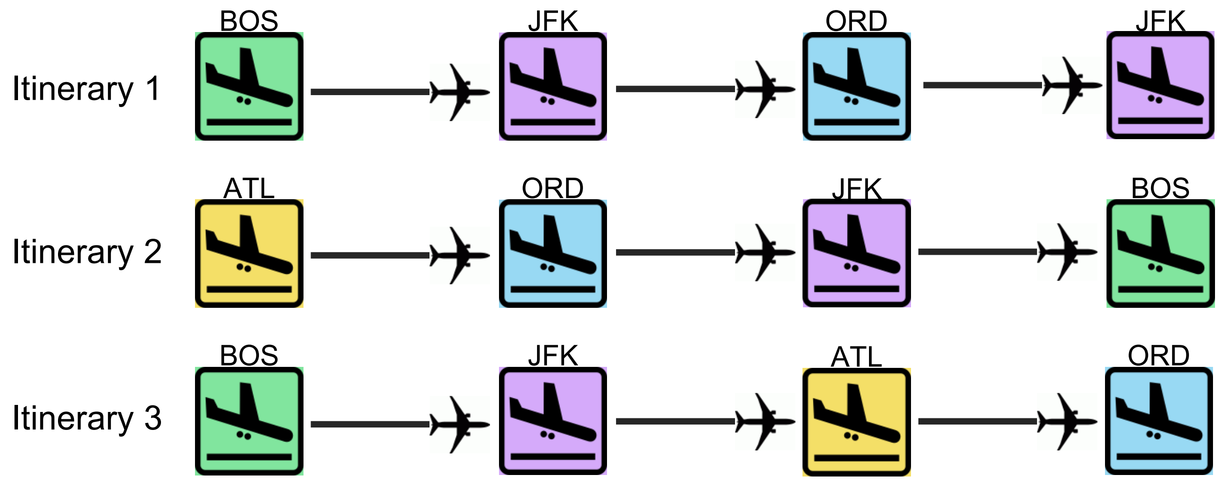
Motivating Example: Flight Data

Given: Flight itinerary data, where each itinerary is a sequence of airports visited by a passenger on a trip

High-level Goal: Characterize the airport network based on the *frequency* and *significance* of substructures found in the itinerary data



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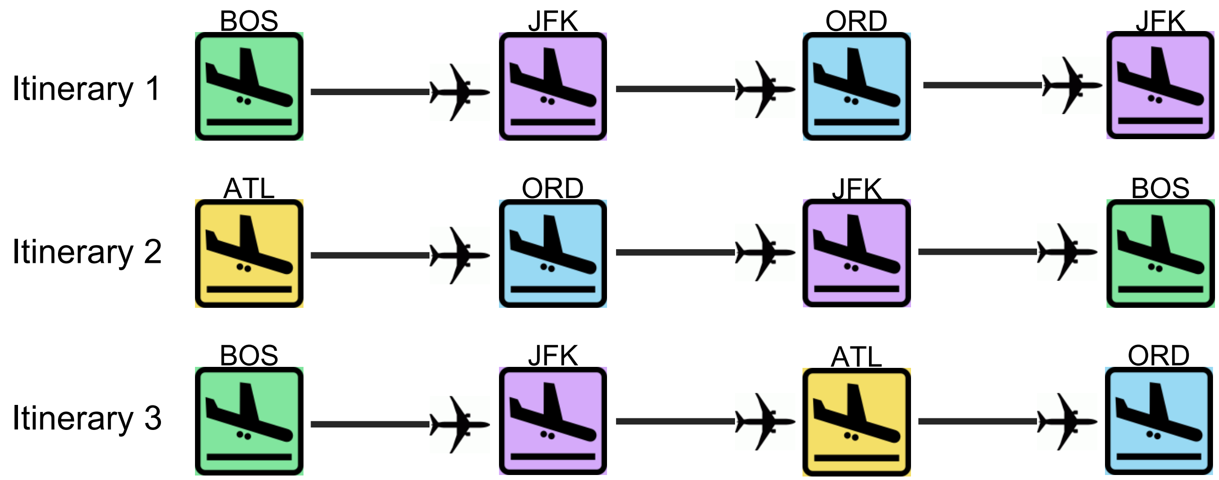

Note: We use people traveling through an airport network as motivation, but any network that individual items move through can be studied.

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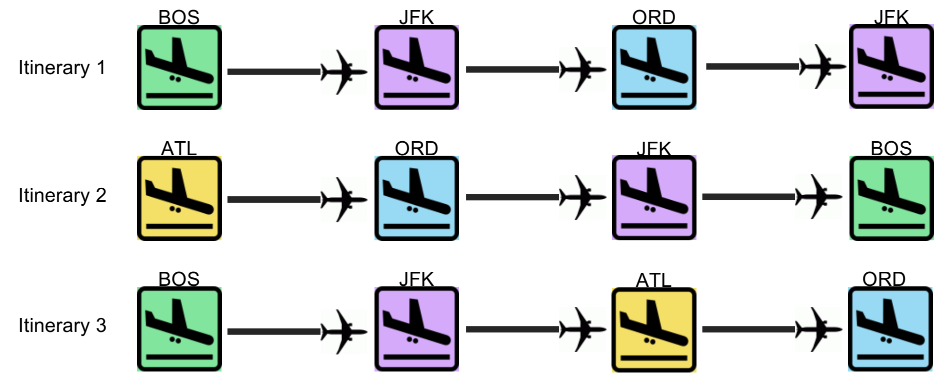
Potential Solution 1



Input Data

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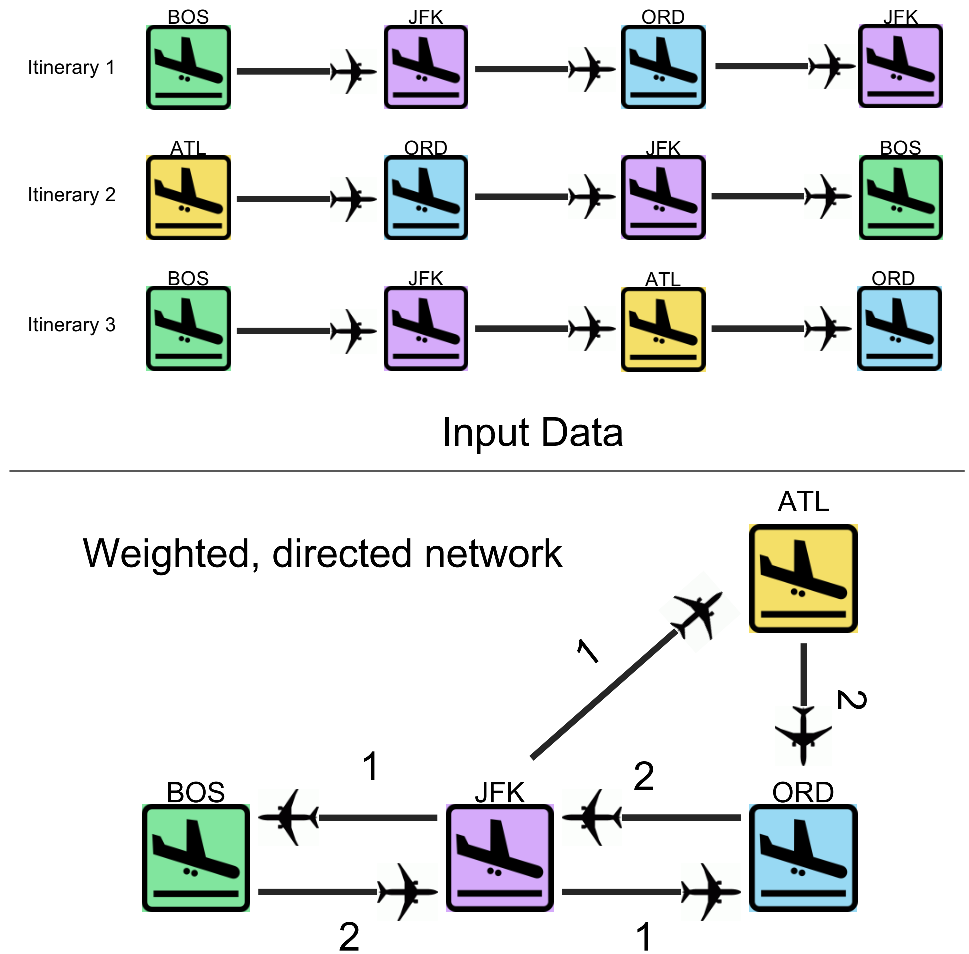
Potential Solution 1

Why not construct a weighted and directed network, then count motifs?



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- We have methods to do this, e.g.
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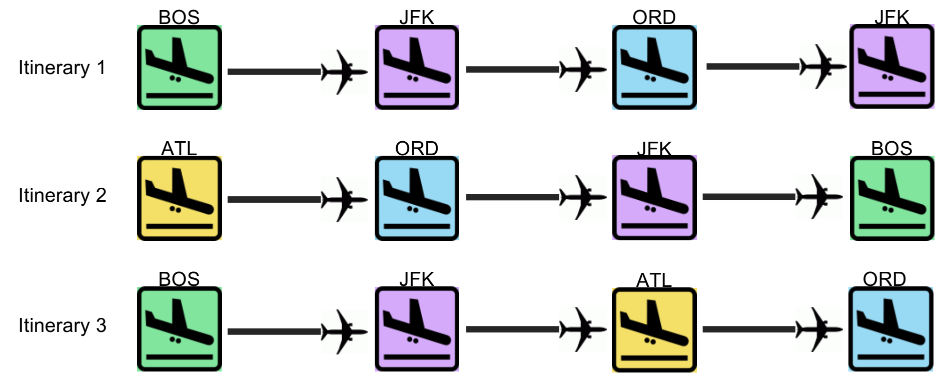
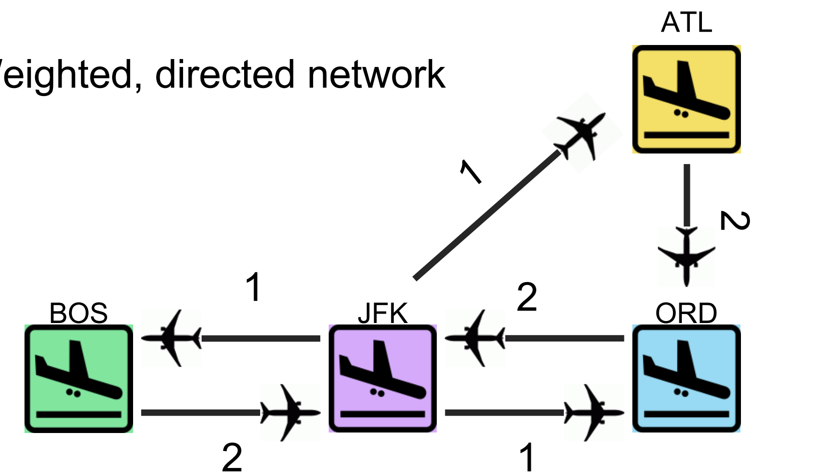
  - Saramäki et al. Characterizing Motifs in Weighted Complex Networks. AIP Conference Proceedings, 2005.
  - Alon. Network Motifs: Theory and Experimental Approaches. Nature Reviews Genetics. 2007.
  - Underwood et al. Motif-based spectral clustering of weighted and directed networks. Applied NetSci, 2020.



Input Data

Weighted, directed network



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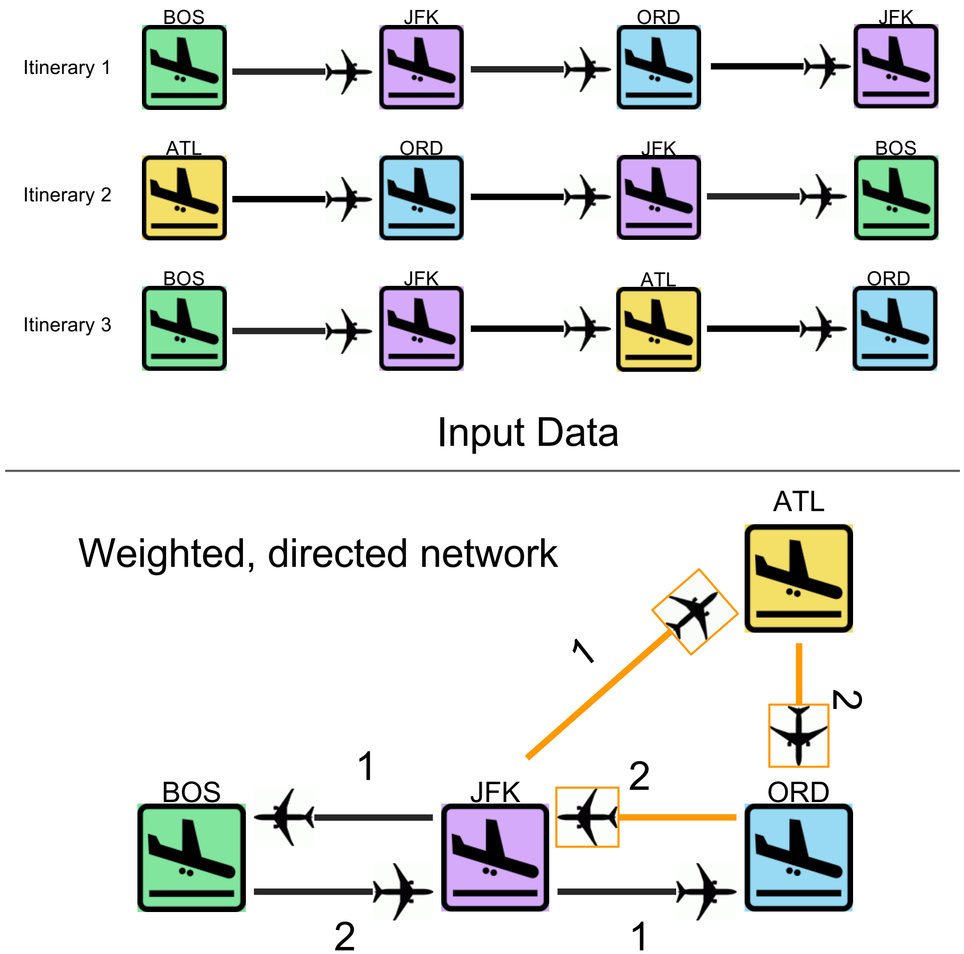
Why not construct a weighted and directed network, then count motifs?

Consider the directed cycle on the 3 edges between JFK, ATL, and ORD.



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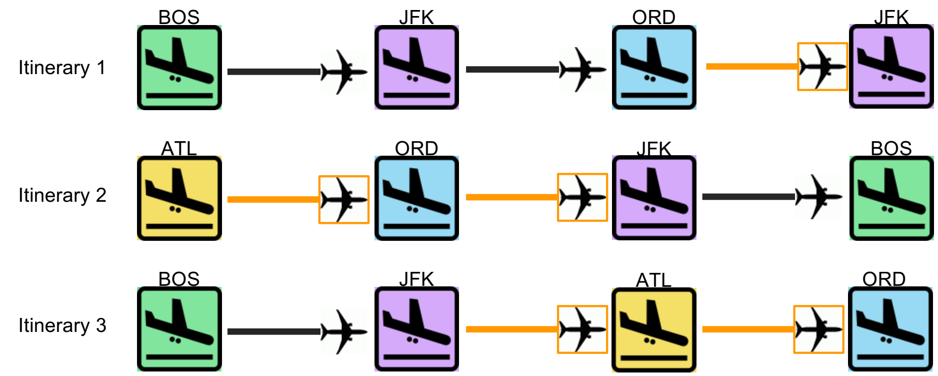

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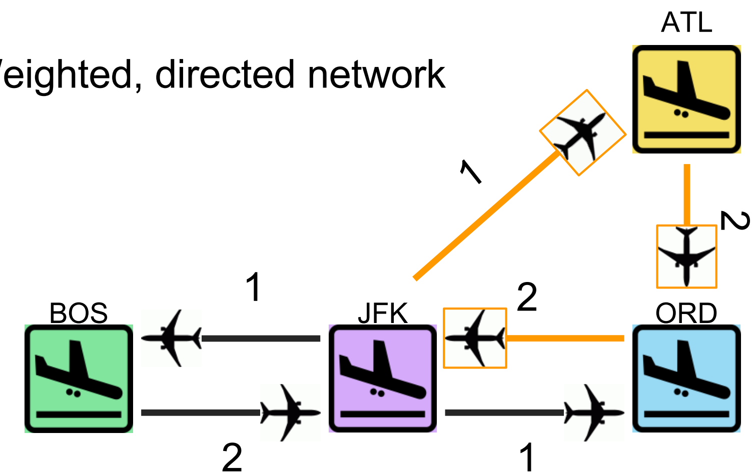

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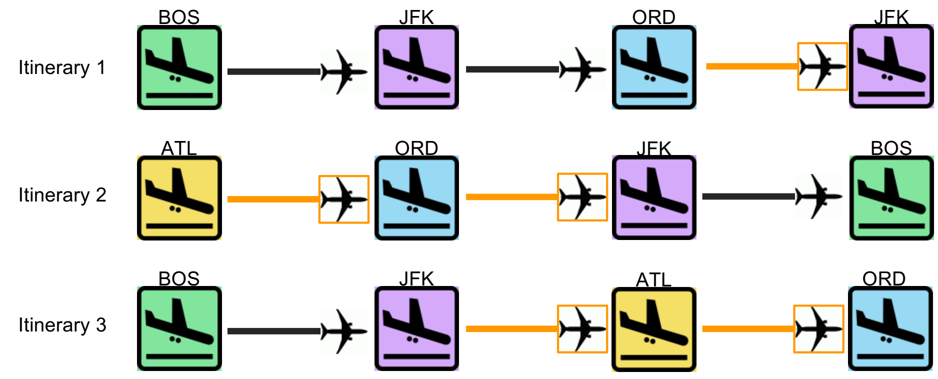

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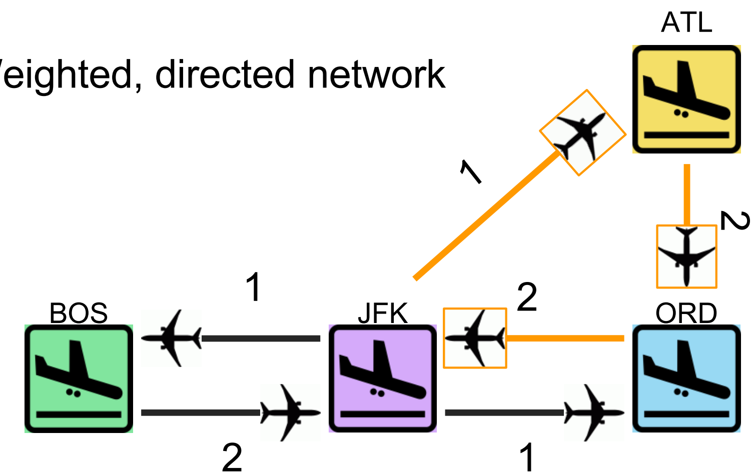

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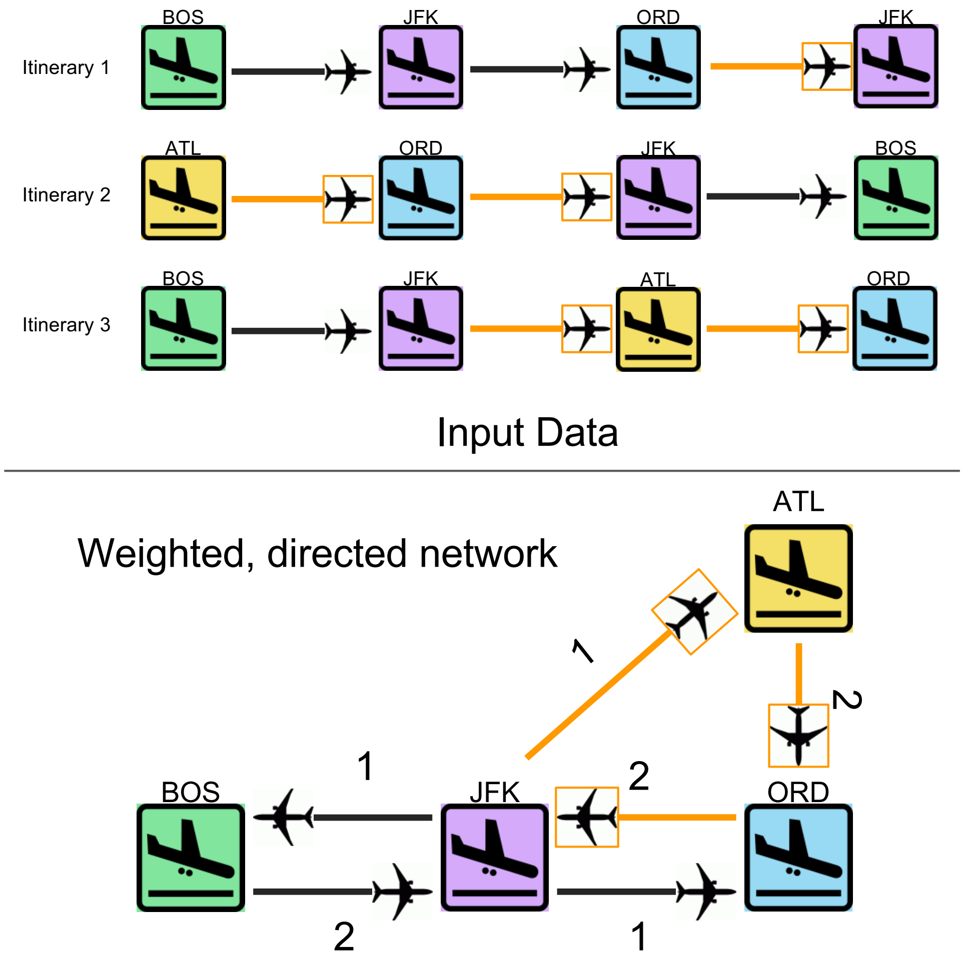
2. How should we include edge weight information?
   - Combining edge weights does not correspond to what we want to count!



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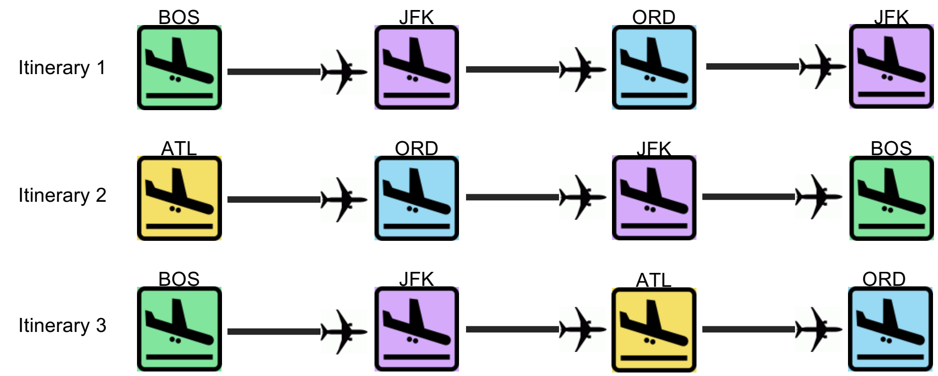
Potential Solution 2



Input Data

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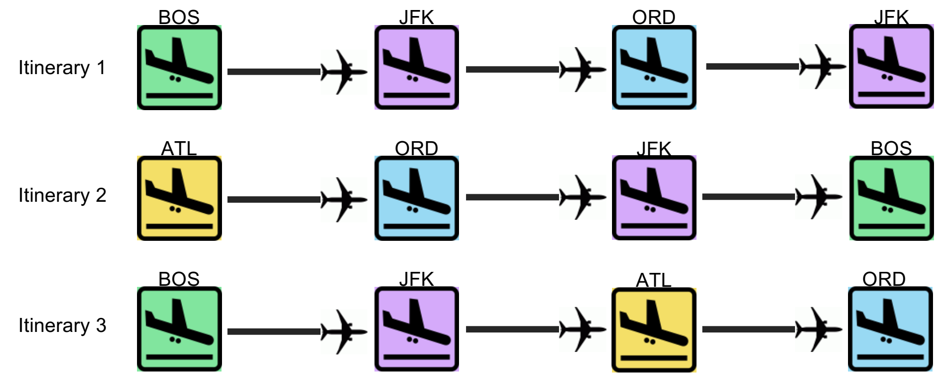
Potential Solution 2

Why not adopt methods for temporal and/or dynamic network data?



Input Data

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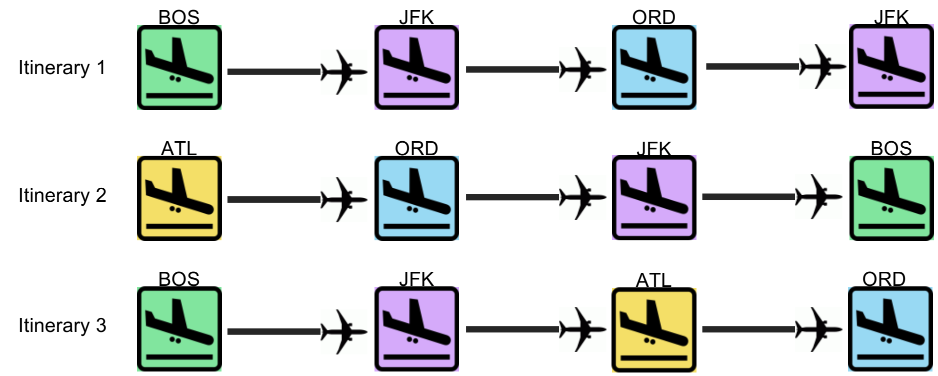
Why not adopt methods for temporal and/or dynamic network data?

- Again, we have methods to do this, e.g.
  - Kovanen et al. Temporal Motifs in time-dependent networks. Journal of Stat Mech, 2011.
  - Jurgens et al. Temporal Motifs Reveal the Dynamics of Editor Interactions in Wikipedia. ICWSM, 2012.
  - Kovanen et al. Temporal motifs reveal homophily, gender-specific patterns, and group talk in call sequences. PNAS 2015.
  - Xuan et al. Temporal motifs reveal collaboration patterns in online task-oriented networks. PRE, 2015.
  - Paranjape et al. Motifs in Temporal Networks. ICWSM, 2017.
  - Liu et al. Temporal Network Motifs: Models, Limitations, Evaluation. ArXiv Preprint, 2020.
- But...



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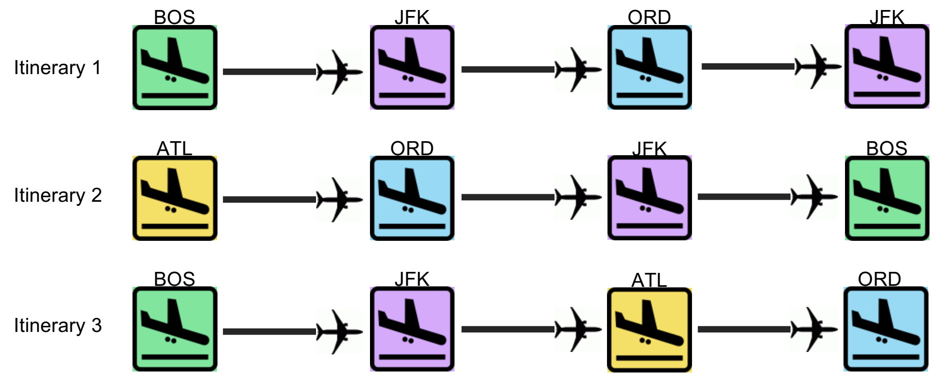
These types of input data are fundamentally different!



Input Data

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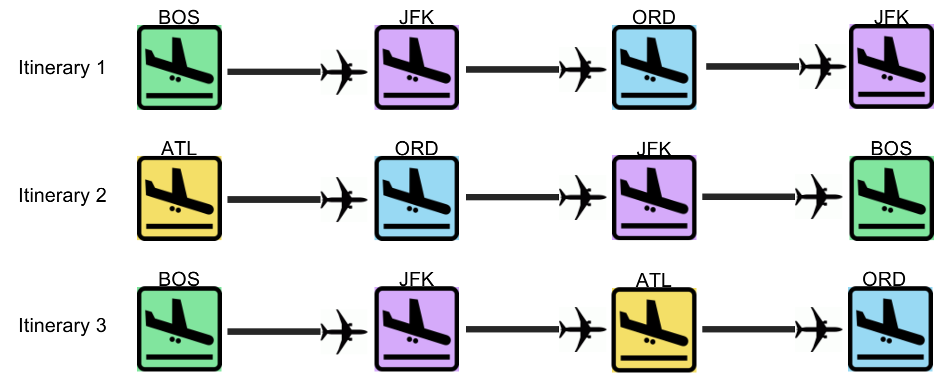
Why not adopt methods for temporal and/or dynamic network data?

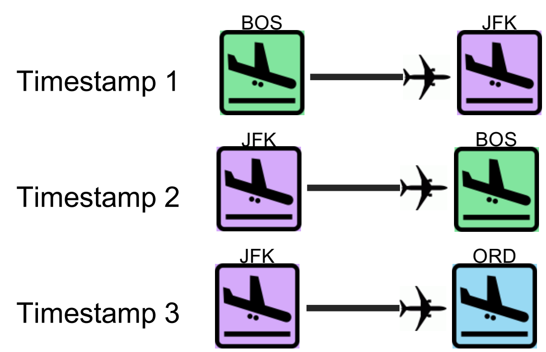
These types of input data are fundamentally different!

- Timestamped edge data is independent observations of individual edge events
    - Path data is **full path observations over multiple edges, typically without timestamps**



Input Data

Temporal Network Data



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- Timestamped edge data is independent observations of individual edge events
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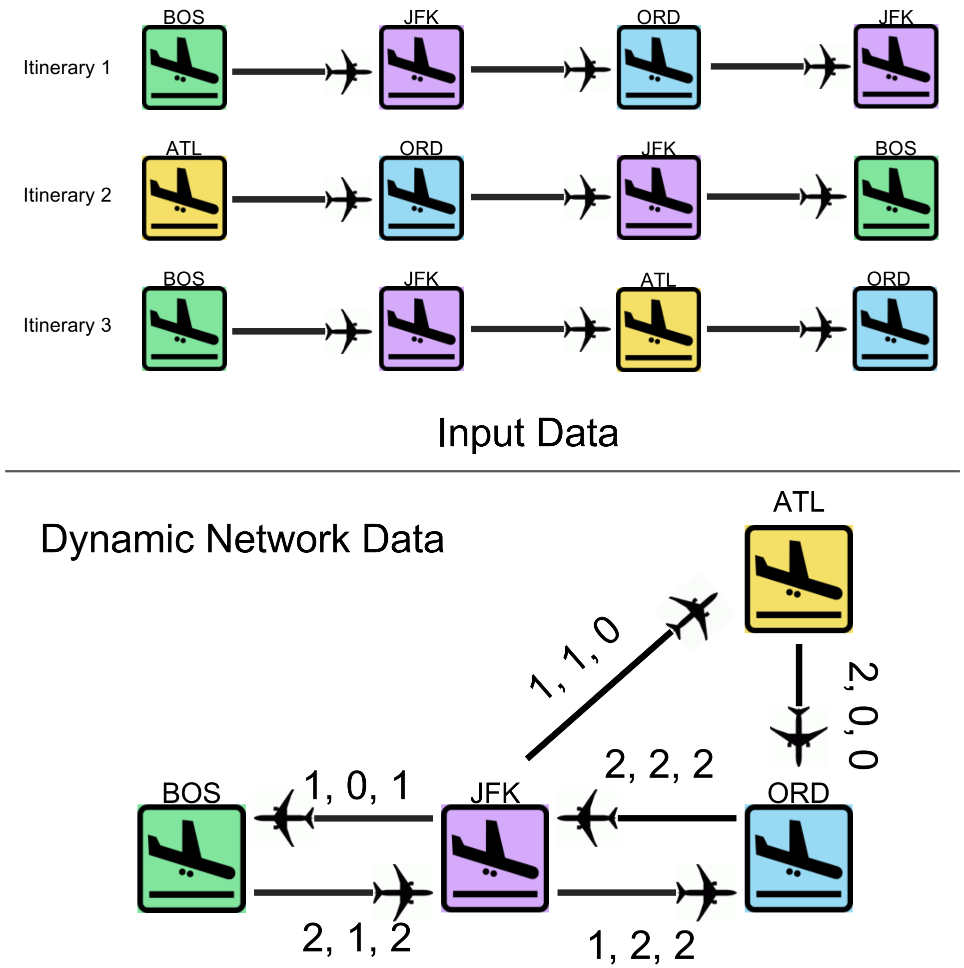
- Dynamic network data allows edge deletion between snapshots and assumes some synchronization of dynamics
  - Path data has **no edge deletion and a (typically) unknown and unsynchronized timescale**



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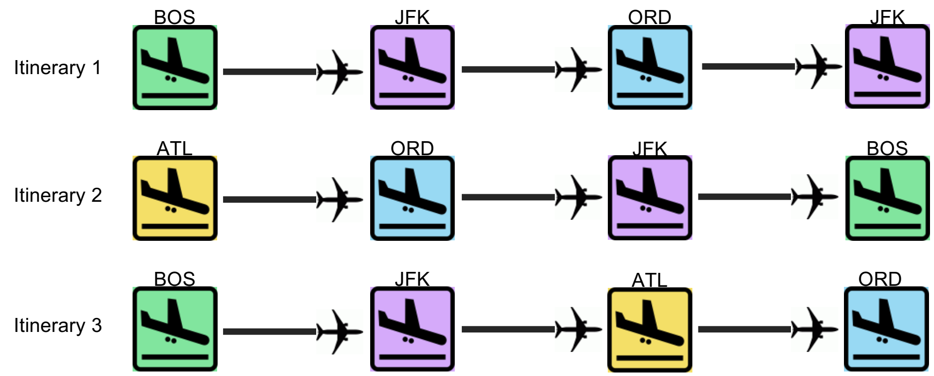
Potential Solutions



Input Data

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   - Existing methods may be misleading

2. **Adopt methods for temporal and/or dynamic data**
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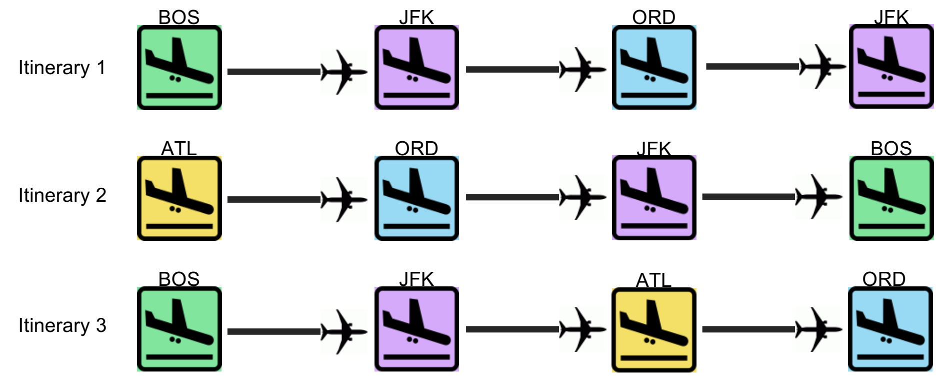

Input Data

<u>The bottom line:</u> Existing solutions are of limited use in this data, so new methodology is warranted!

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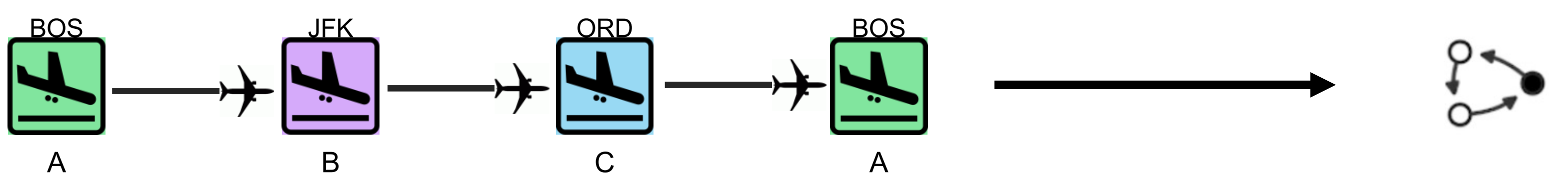
Sequential Motifs

Observation: Every *path* or *sequence* on *k* edges observed in a dataset corresponds to a *motif* of length *k*

We can move from specific paths to general motifs using a one-to-one mapping over an alphabet $\Sigma = (\sigma_1, \sigma_2, \ldots, \sigma_\ell)$, e.g. $\Sigma = (A, B, C)$



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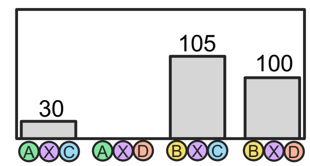
- **Next:** Corresponds to mapping the edges of a DeBruijn Graph to motifs

What is a DeBruijn Graph?

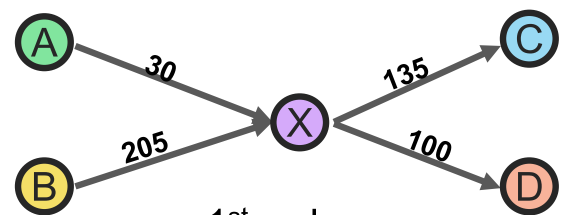
Natural graph representation for path and sequence data

A k^{th} order DeBruijn graph has nodes that represent paths of length $k-1$

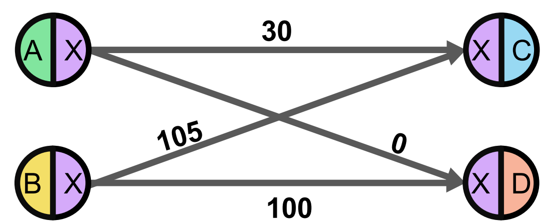
Higher-order nodes can connect if they overlap in $k-1$ first-order nodes, and each edge is a path of length k



Input Paths



1st-order
"DeBruijn" graph



2nd-order
DeBruijn graph

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HYPA = Higher Order Hypergeometric Path Anomaly

Why use a DeBruijn graph?

Leverage a null model for weighted DeBruijn graphs, HYPA

HYPA gives a probability of observing a smaller edge (path!) frequency according to a *k-1st* order model of the data

- Need to select threshold value α on this probability
- We use *1/M*, where *M* is the sum of all weights in the DeBruijn graph

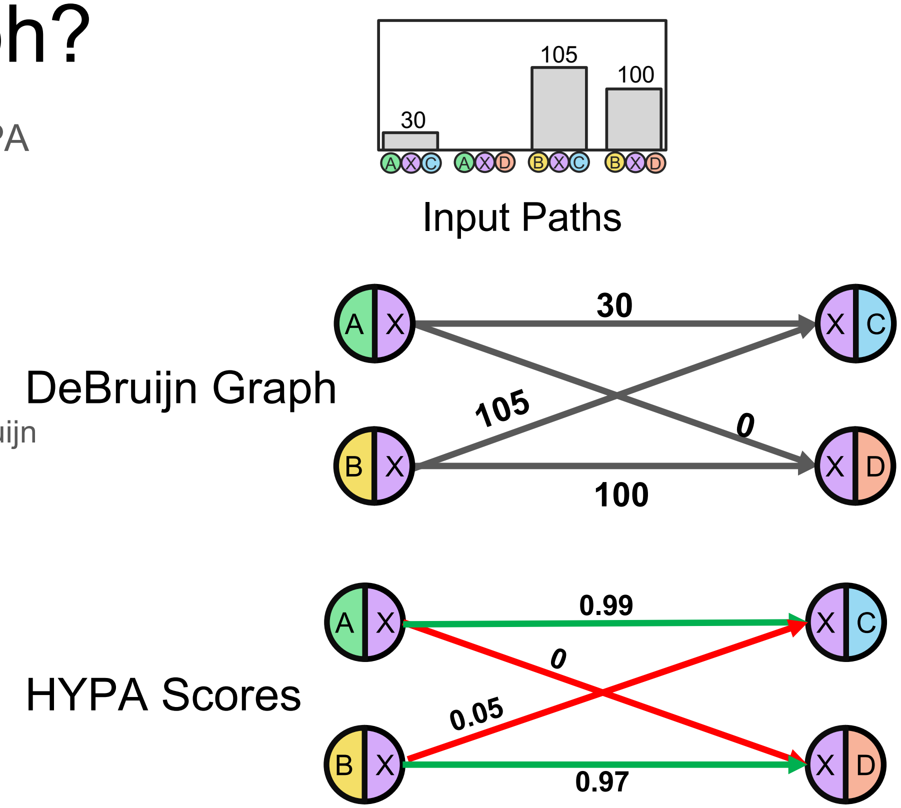
$$\mathrm{HYPA}^{(k)}(\vec{v}, \vec{w}) := \Pr\left(X_{\vec{v}\,\vec{w}} \leq f(\vec{v}, \vec{w})\right)$$

If $< \boldsymbol{\alpha}$ then the pathway is **underrepresented**.

If $\geq 1\text{-}\boldsymbol{\alpha}$, then pathway is **overrepresented**.

For each motif, we keep track of the

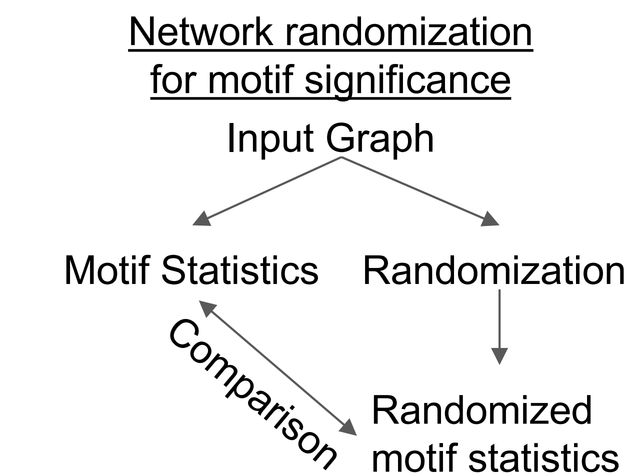
1. **total** number of edges that map to the motif
2. number of mapped edges that are **over** represented
3. Number of mapped edges that are **under** represented



LaRock et al. HYPA: Efficient Detection of Path Anomalies in Time Series Data on Networks. SDM, 2020. https://doi.org/10.1137/1.9781611976236.52

Some Subtlety in Significance

The method presented here **does not** measure the significance of motif frequency compared to a randomization of the first-order network structure (p-value per motif)



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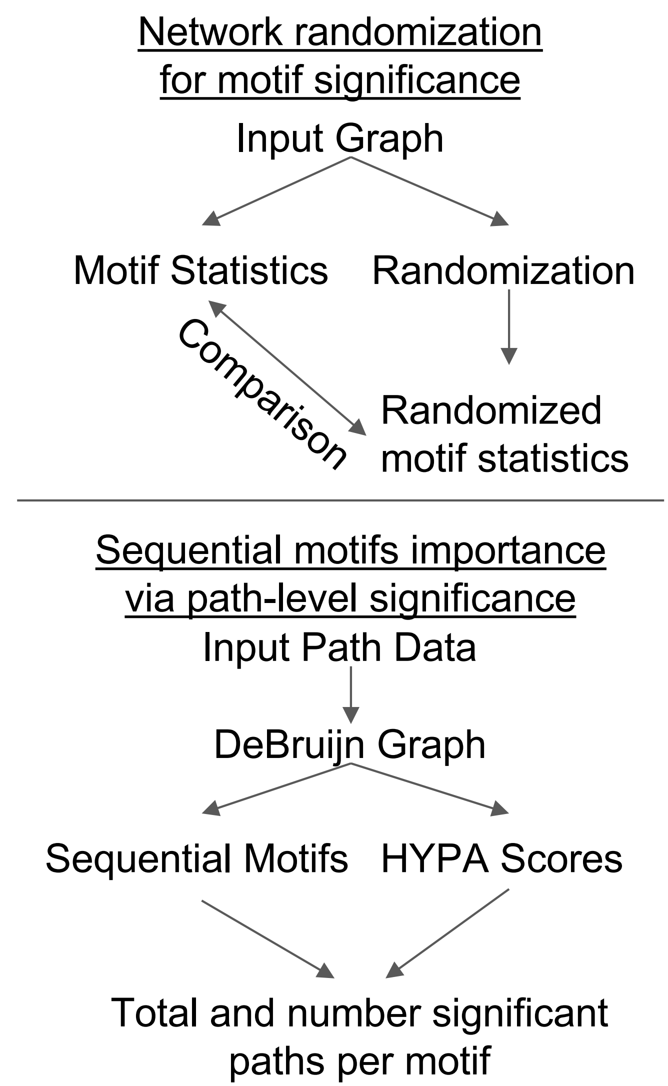
Instead, for each motif we count the **number of paths** mapping to that motif that are significantly over or under represented compared to a path-based null model (p-value per path, aggregated for each motif)



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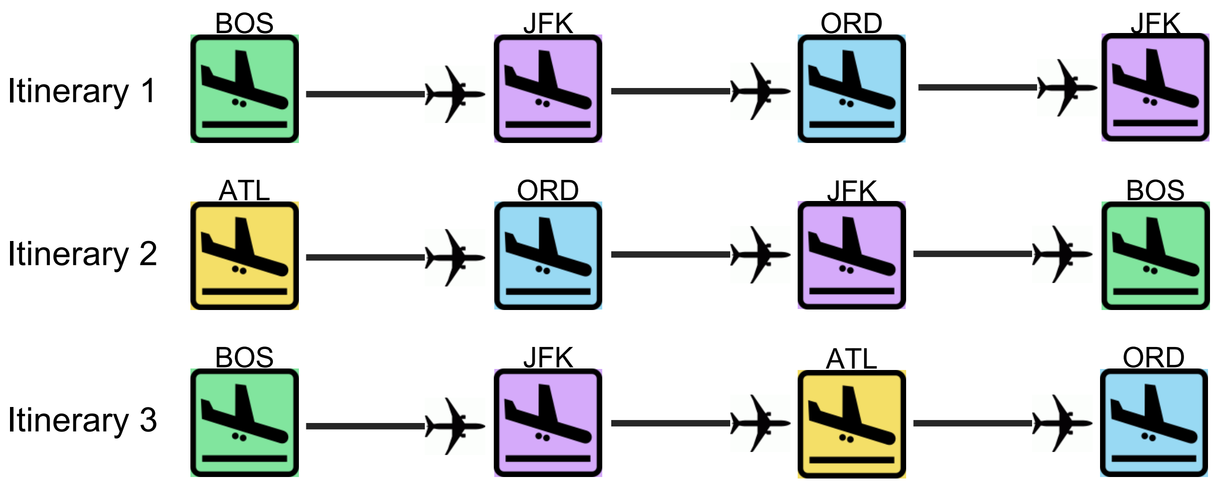
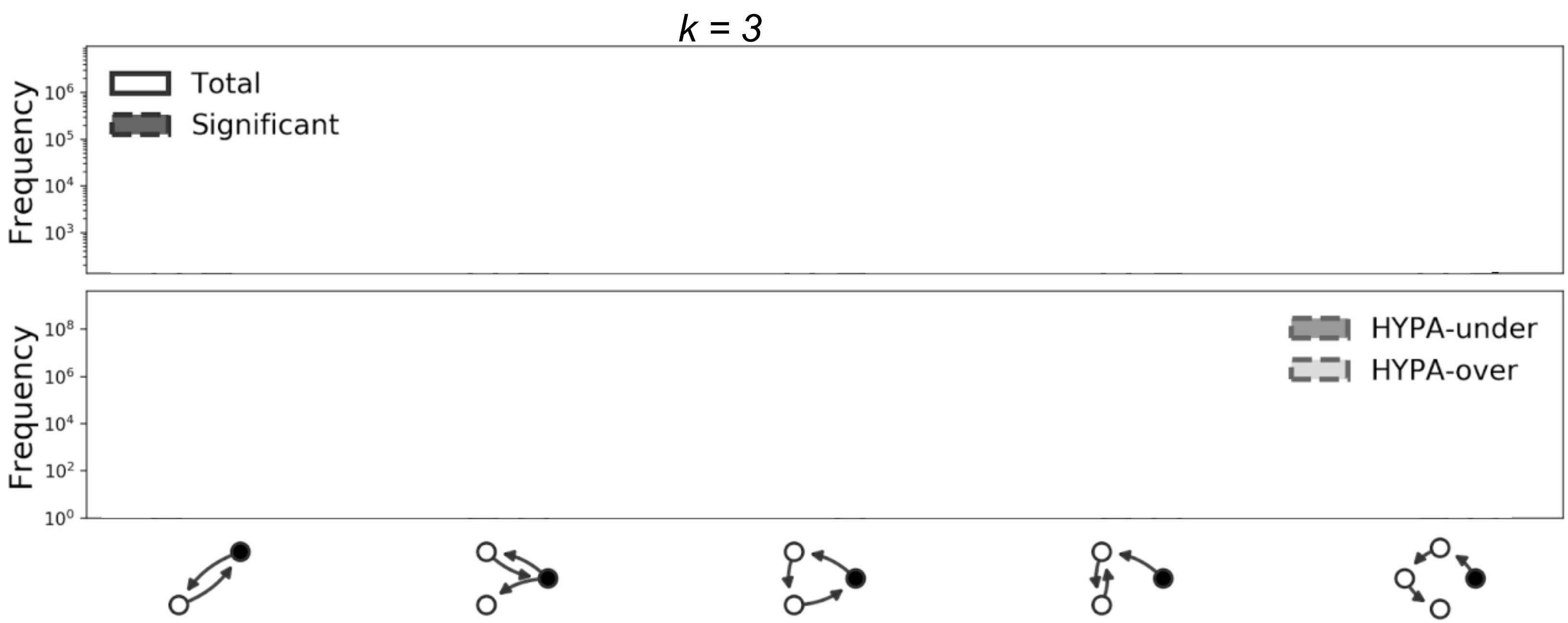
Dataset: Domestic Flights in the US

US passenger flight itineraries downloaded from https://transtats.bts.gov/

Data from quarter 1 of 2019 includes 3,981,589 itineraries with maximum length 12



Sequential Motifs: Flights



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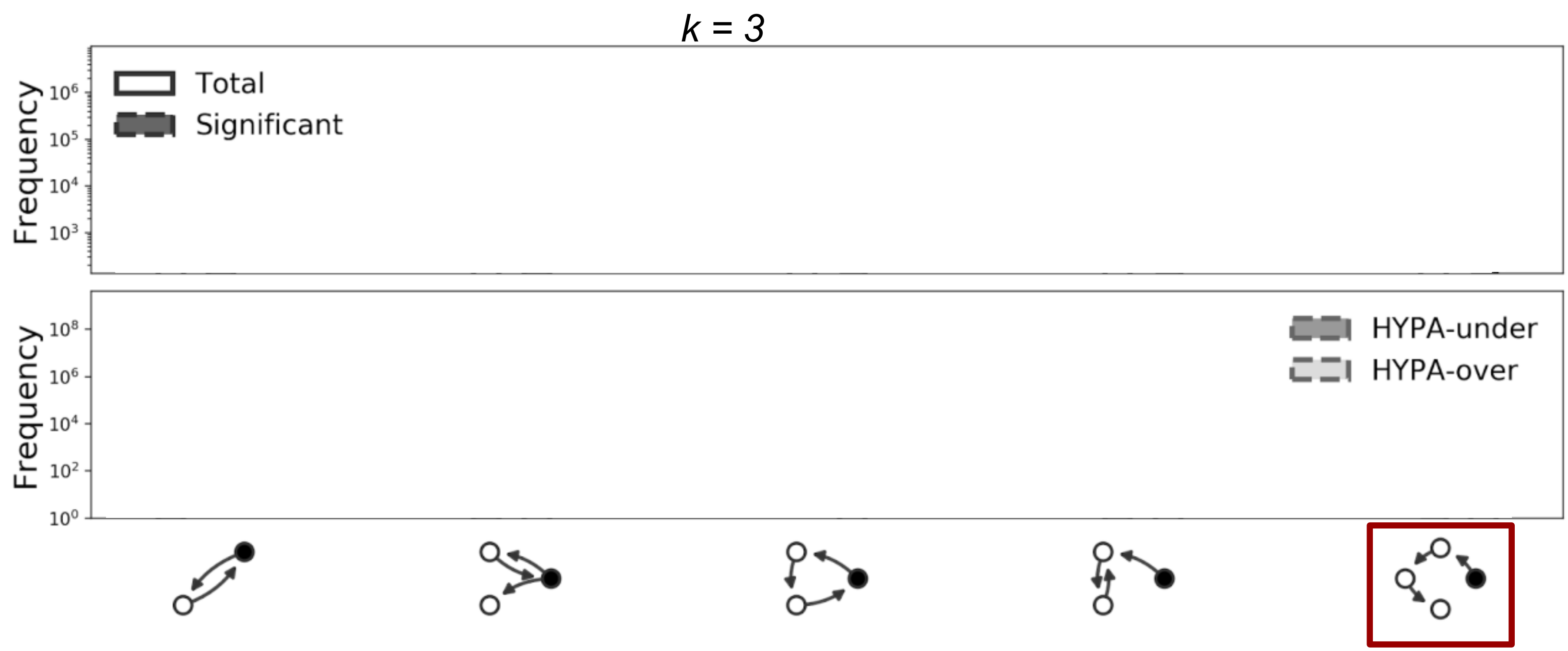

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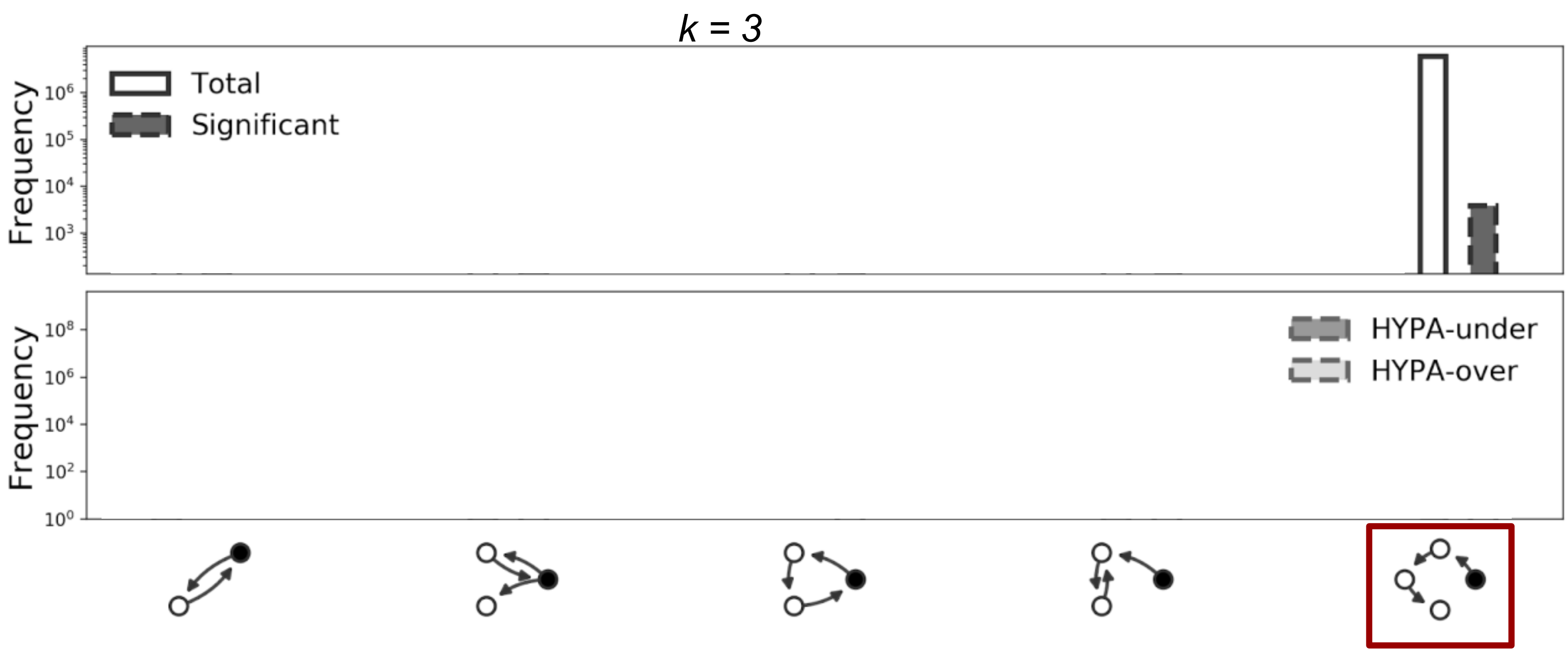

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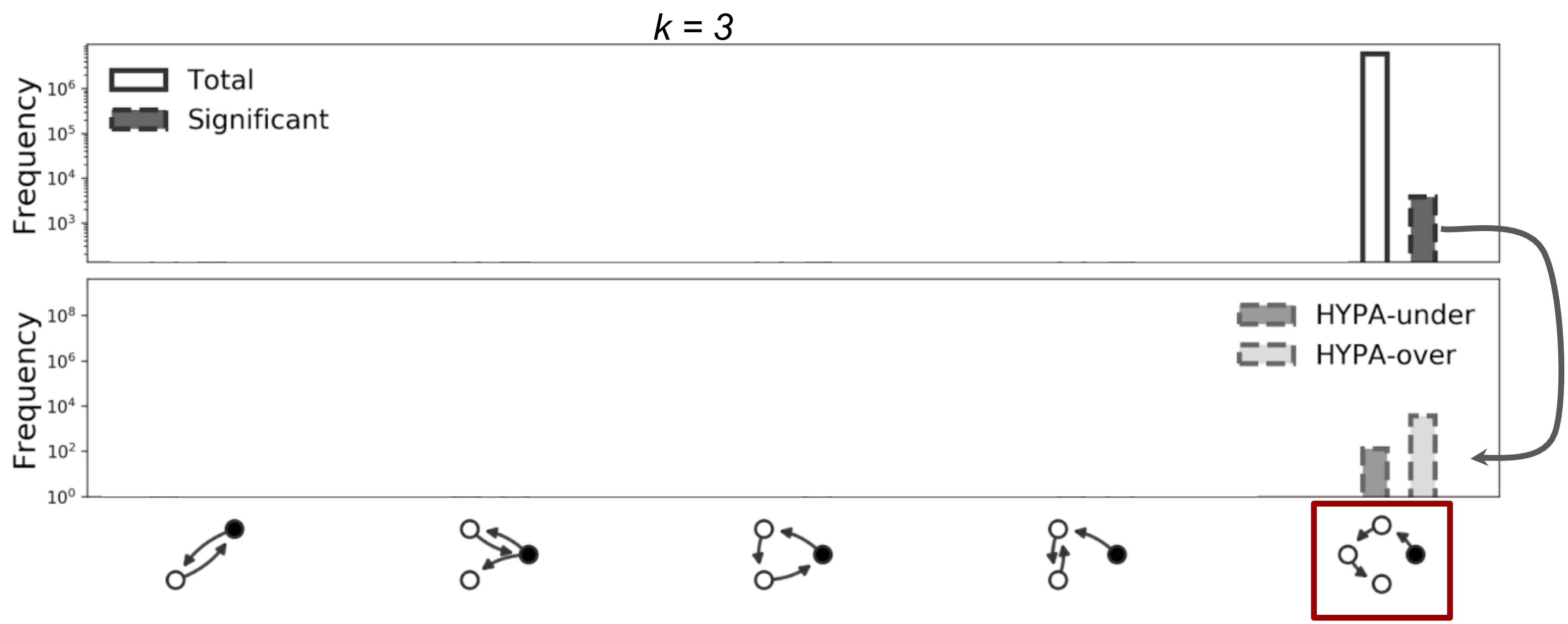

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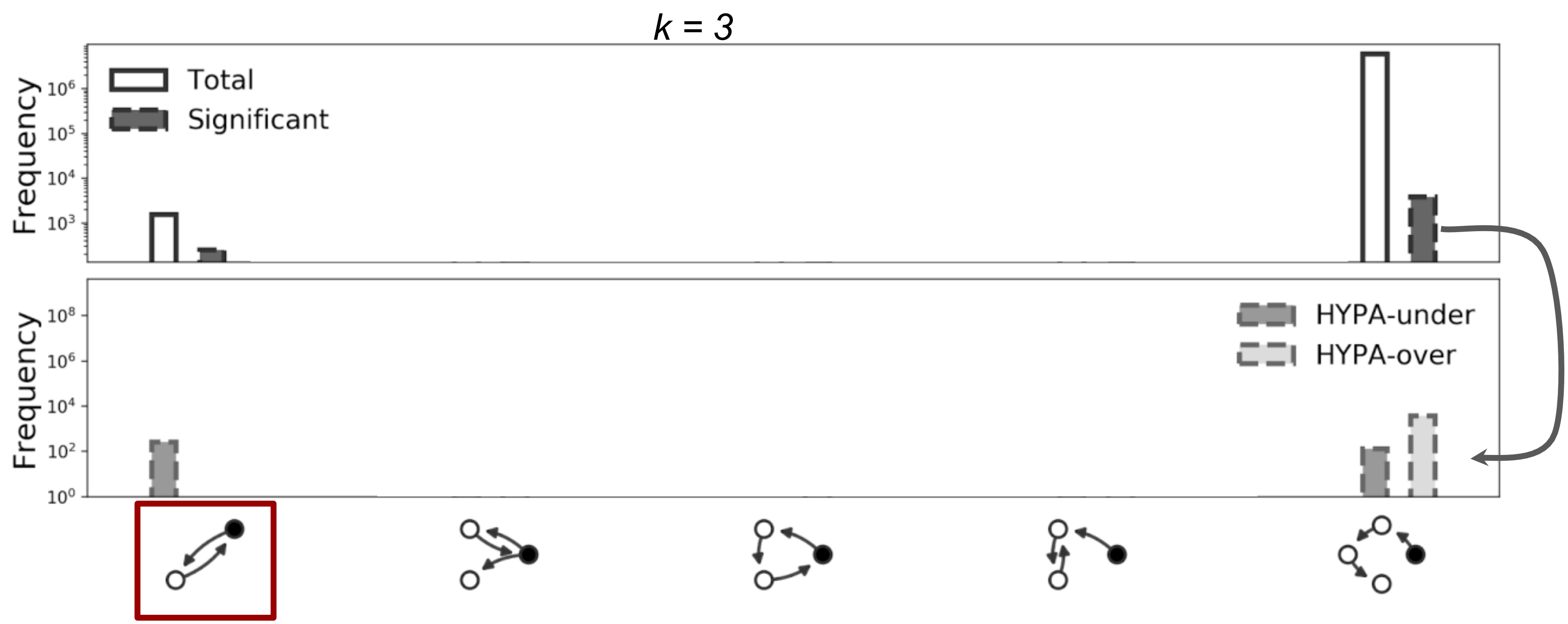

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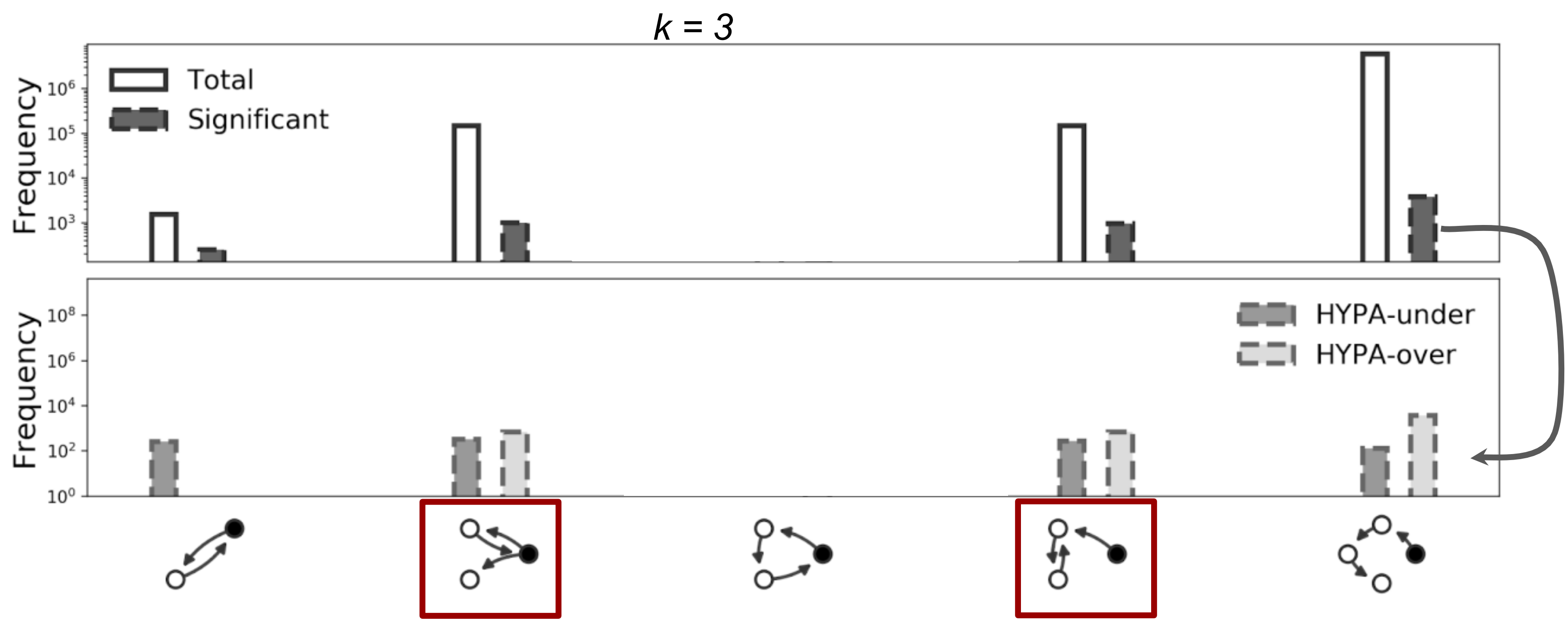

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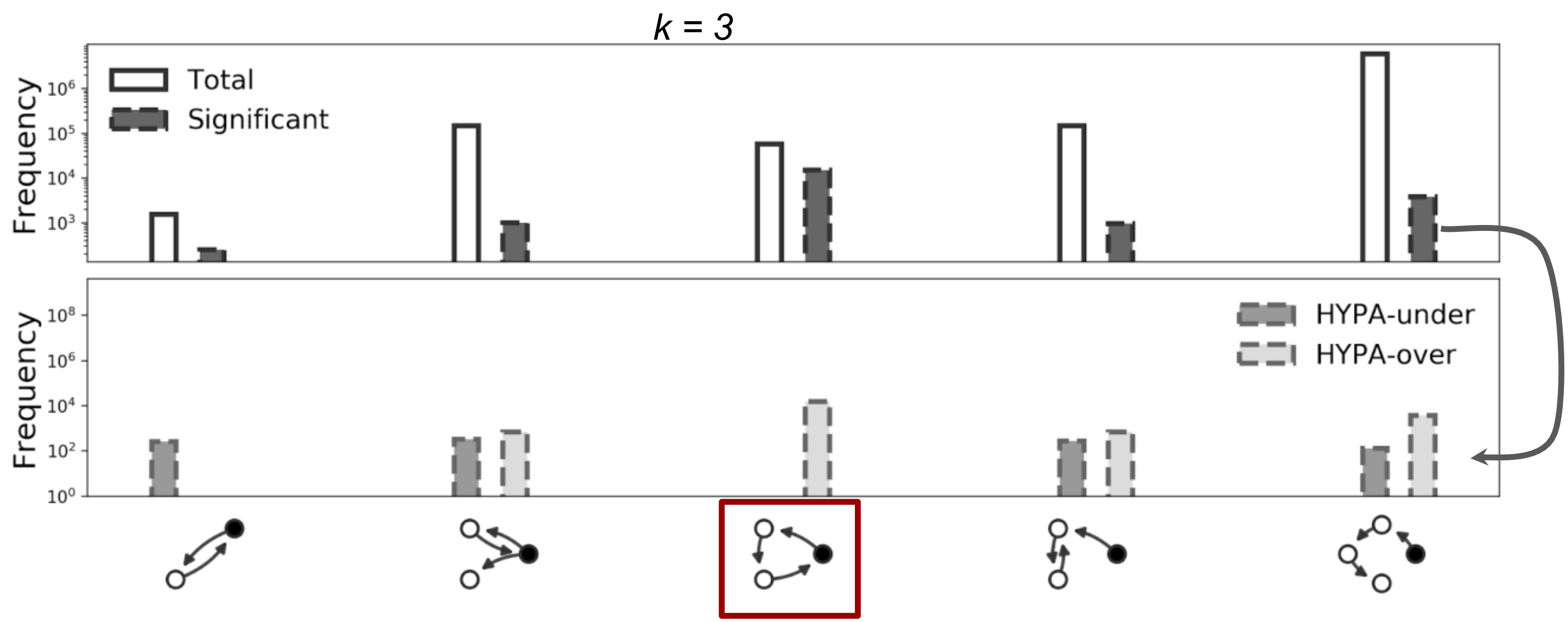

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Conclusions

- Existing motif counting methodology does not apply directly to pathway data
- Sequential motifs via DeBruijn graphs provide motif counting and an indication of significance via HYPA
- Analysis of sequential motifs in flight data identifies patterns that correspond to expectations

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Thank you!

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Preprint to come very soon!

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