Towards more accurate microbial source tracking via non-negative matrix factorization (NMF)

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https://yannisun.github.io/
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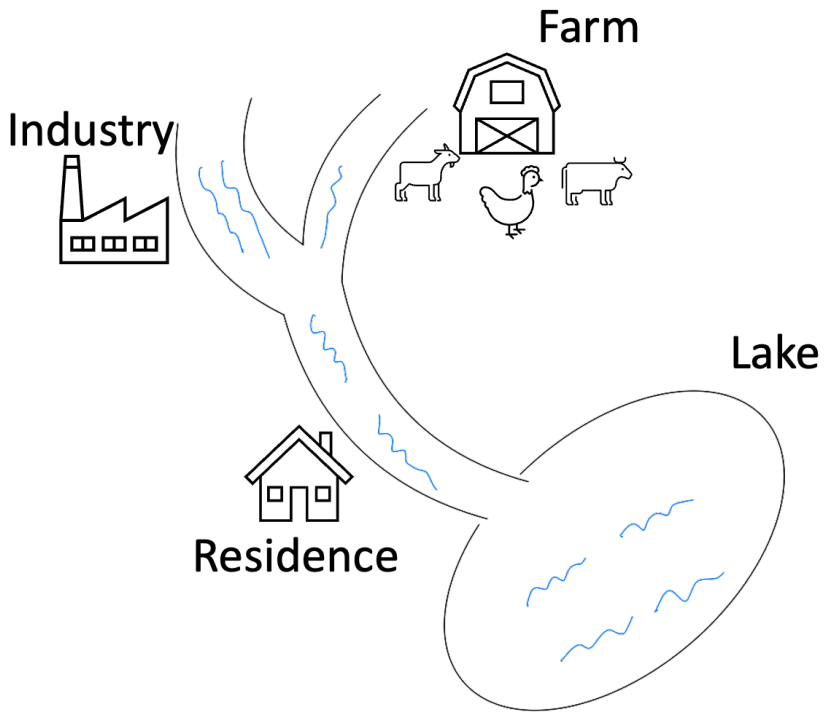
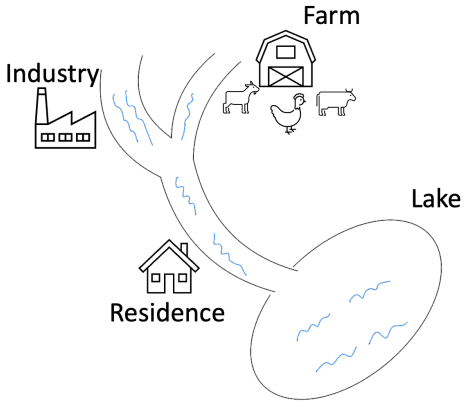
Sources of Lake Pollution: Who is Responsible?



- **Issue**: Poor water quality due to microbial pollution
- **Potential Polluters**: Industry, farms, residences
- **Action**: Sampling lake and surrounding sources
- **Goal**: Identify pollution sources (microbial source tracking, MST)

Microbial Source Tracking (MST): overview



Microbial Source Tracking

- Input: a **target/sink** sample and multiple **source** samples from other microbial communities

  Goal: to determine the **contribution of each source to the target**.

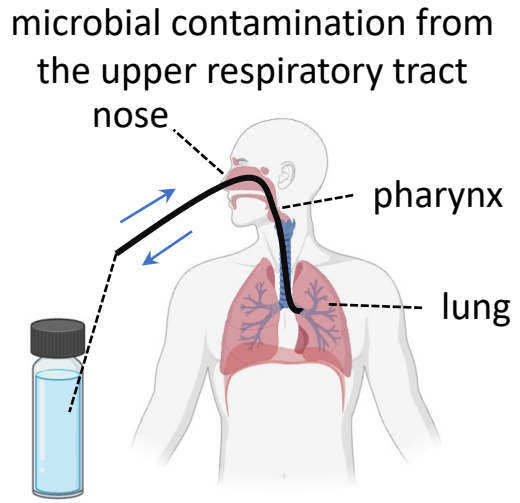
Applications

- Quantifying contamination

  - Laboratory contamination: the target sample may be contaminated by sampling procedures, reagents, indoor air, etc.

  - Water contamination

- Microbial interaction analysis
  - Microbial interaction between humans and the indoor environment



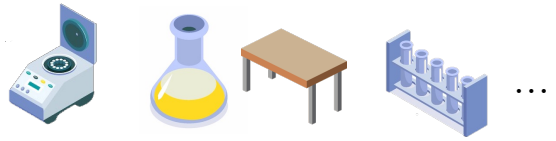
Pic source: https://app.biorender.com/

Input data: taxa abundance

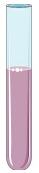
Example: Tracking laboratory contamination

Microbial Samples

Potential (reference) sources



A sink sample



Sequencing

Taxonomic profiling

Taxa abundance

Potential (reference) sources

	10	0	3	0	…
	29	27	0	0	…
	0	45	33	0	…
	33	12	0	23	…
	17	13	0	57	…
	0	0	78	20	…
	22	0	12	…	…
…	…	…	…	…	…

Target sample

37
15
22
33
15
7
12
…

MST

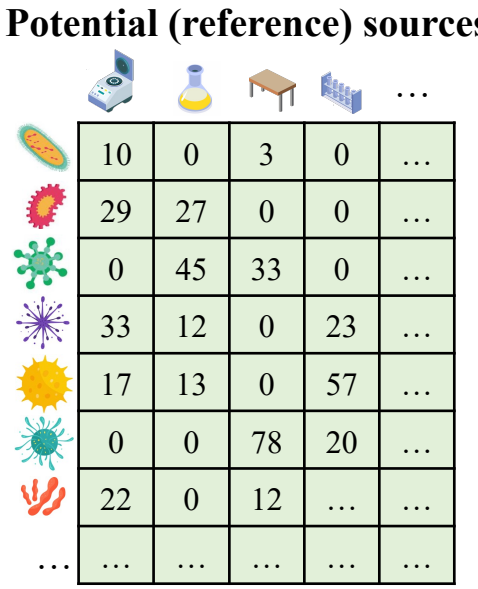
Source contributions

Figure sources: https://bioicons.com/

Challenges

Reference sources

- Irrelevant sources
- Unknown/unseen sources
- Similar sources
- Sequencing noises



State-of-the-art tools

- SourceTracker[1]
- FEAST[2]

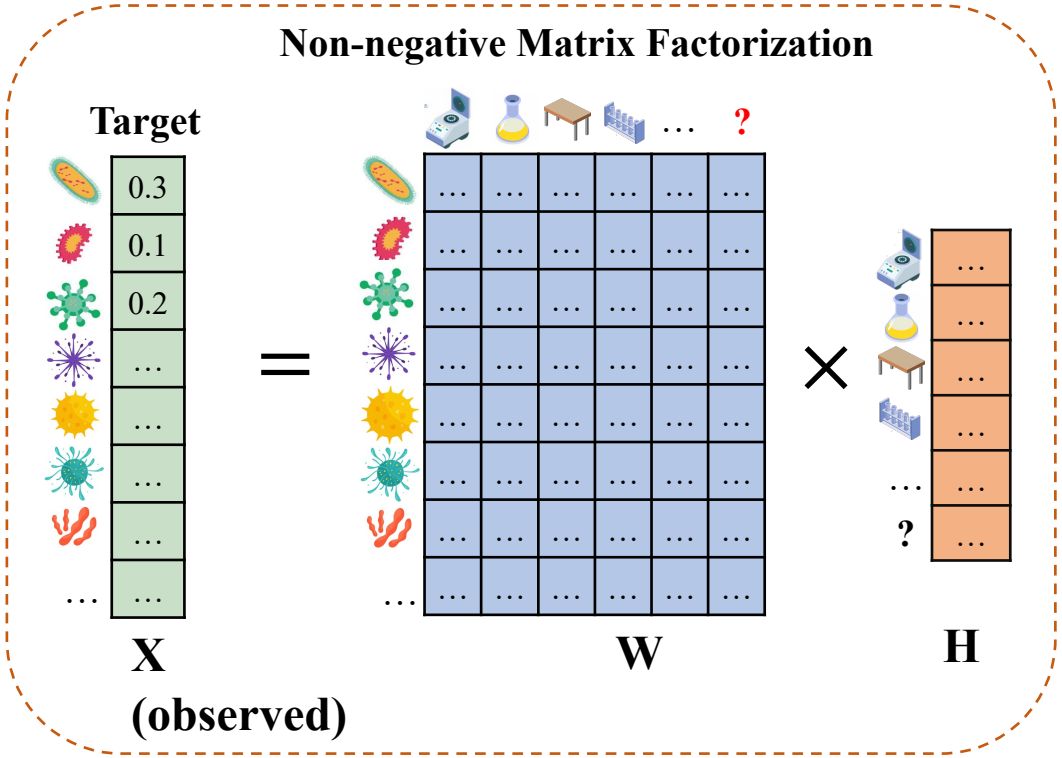
[1] Knights, Dan, et al. "Bayesian community-wide culture-independent microbial source tracking." *Nature methods* 8.9 (2011): 761-763.
[2] Shenhav, Liat, et al. "FEAST: fast expectation-maximization for microbial source tracking." *Nature methods* 16.7 (2019): 627-632.

Method

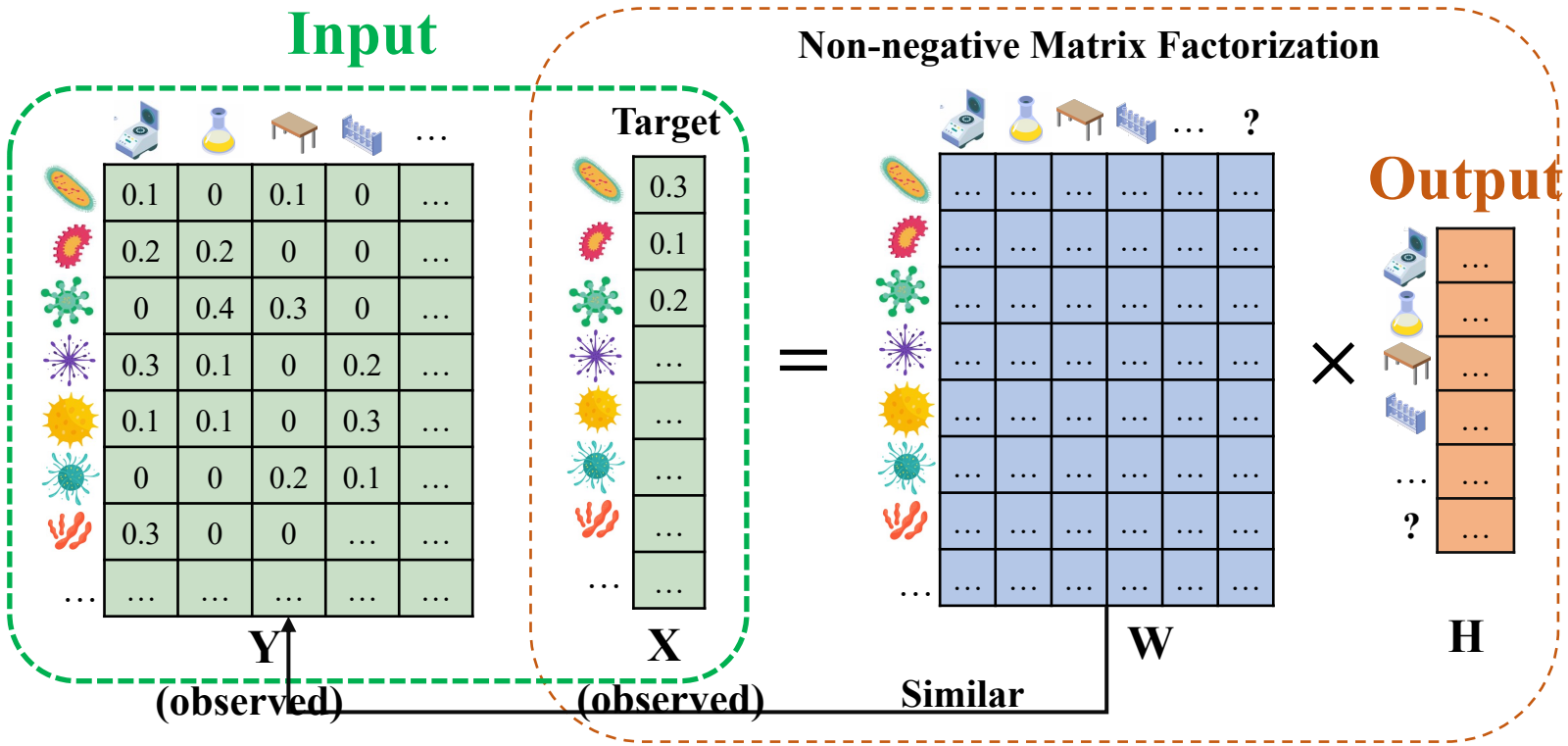
Non-negative Matrix Factorization (NMF)

- X: relative taxa abundance of the target sample
- W: relative taxa abundance matrix of sources
- H: proportion (contribution) of sources
- ? : Unknown sources

X is given.
Our goal: find W and H

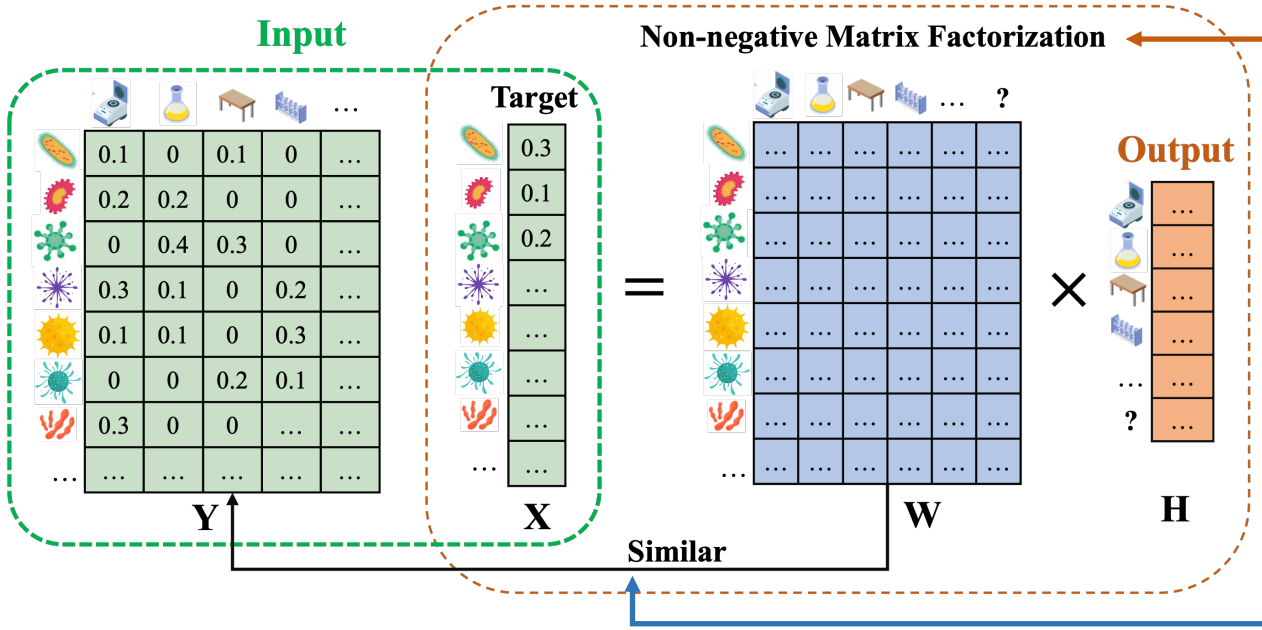


Adding reference sources



- Y: observed taxa abundance of reference sources

SourceID-NMF: optimization objective



Optimization Problem

$$\underset{W,H}{\operatorname{argmin}} \frac{1}{2}\|X - WH\|_F^2 + \frac{1}{2}\|A \circ (W - Y)\|_F^2$$

$$s.t. W \geq 0, H \geq 0, \sum_j H_j = 1, \sum_i W_{ij} = 1 (for\ j = 1{:}K+1)$$

- X: taxa abundance of a sample
- Y: observed taxa abundance of reference sources
- W: taxa abundance of sources (to be estimated)
- H: mixing proportion of sources (to be estimated)
- ? : Unknown sources
- A: the last column is all 0 and other elements are 1

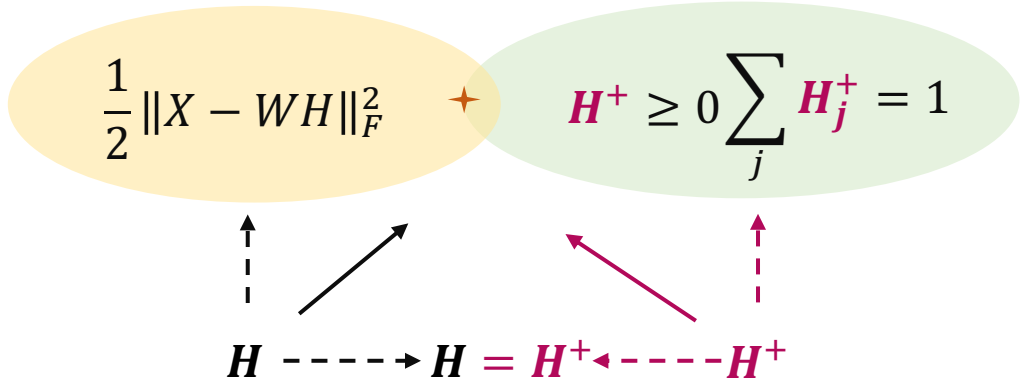
SourceID-NMF: optimization method (ADMM)

Optimization Problem

$$\underset{W,H}{\operatorname{argmin}} \frac{1}{2}\|X - WH\|_F^2 + \frac{1}{2}\|A \circ (W - Y)\|_F^2$$

$$s.t. W \geq 0, H \geq 0, \sum_j H_j = 1, \sum_i W_{ij} = 1 (\, for\ j = 1{:}K+1)$$

Optimization process of $\boldsymbol{H}$ and $\boldsymbol{H^+}$



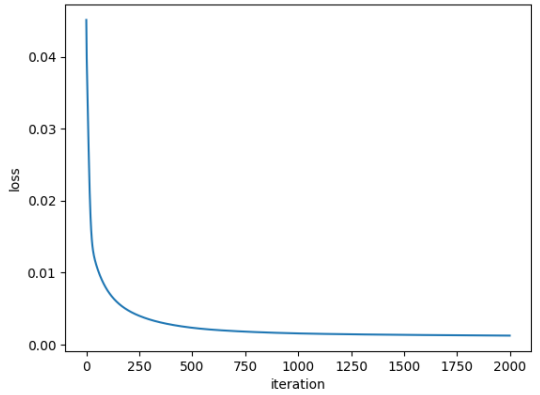
Alternating Direction Method of Multipliers (ADMM)[1]

$$\underset{\boldsymbol{W^+},\boldsymbol{H^+},W,H}{\operatorname{argmin}} \frac{1}{2}\|X - WH\|_F^2 + \frac{1}{2}\|A \circ (\boldsymbol{W^+} - Y)\|_F^2$$

$$s.t. \boldsymbol{W} = \boldsymbol{W^+}, \boldsymbol{H} = \boldsymbol{H^+}$$

$$\boldsymbol{W^+} \geq 0, \boldsymbol{H^+} \geq 0, \sum_j \boldsymbol{H_j^+} = 1, \sum_i \boldsymbol{W_{ij}^+} = 1 (\, for\ j = 1{:}K+1)$$

auxiliary variables: $\boldsymbol{W^+}, \boldsymbol{H^+}$



[1] Boyd, S. *et al.* (2011). Distributed optimization and statistical learning via the alternating direction method of multipliers. *Foundations and Trends® in Machine learning*, 3(1), 1–122.

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Result

Experiment design

Testing SourceID-NMF on different datasets

- Simulated data
  - ➢ Inter-source similarity ➢ Irrelevant sources ➢ Unknown sources ➢ Sources with noises
- Real data
  - ➢ Indoor environmental samples ➢ Infant's fecal samples

Metrics: contribution of sources (H)

Jensen-Shannon Divergence (JSD): the difference of true H and the estimated H
Pearson Correlation (PCC): the correlation between H and the estimated H

Compare with two state-of-the-art tools

- SourceTracker[1]
- FEAST[2]

[1] Knights, Dan, et al. "Bayesian community-wide culture-independent microbial source tracking." *Nature methods* 8.9 (2011): 761-763.

[2] Shenhav, Liat, et al. "FEAST: fast expectation-maximization for microbial source tracking." *Nature methods* 16.7 (2019): 627-632.

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Simulated data settings

Simulated data process: how to obtain X (target) and Y (observed sources)

Taxa abundance (reads counts) of sources from the Earth's microbiome project[1]

	S_1	…	S_{K-F}	S_{K-F+1}	…	S_K	S_{K+1}	…	S_{K+U}
Taxon 1	15	…	600	88	…	130	234	…	12
Taxon 2	31	…	34	993	…	403	44	…	334
…	…	…	…	…	…	…	…	…	…
…	179	…	159	10	…	299	39	…	556
Taxon N	431	…	90	204	…	19	394	…	20

Multinomial sampling

Observed taxa abundance of K sources (Y)

S'_1	…	S'_{K-F}	S'_{K-F+1}	…	S'_K
10	…	589	78	…	123
38	…	50	948	…	430
…	…	…	…	…	…
168	…	143	12	…	278
456	…	98	231	…	14

Mixing proportions

P_1	…	P_{K-F}	P_{K-F+1}	…	P_K	P_{K+1}	…	P_{K+U}
0.05	…	0.16	0	…	0	0.2	…	0.3

$\sum_{j=1}^{j=K-F} P_j = 0.5$ Other sources proportions

0 Irrelevant sources proportions

$\sum_{j=K+1}^{j=K+U} P_j = 0.5$ Unknown sources proportion

Taxa abundance of X

	$\sum_{j=1}^{K+U} S_j \times P_j$
Taxon 1	104
Taxon 2	170
…	…
…	167
Taxon N	31

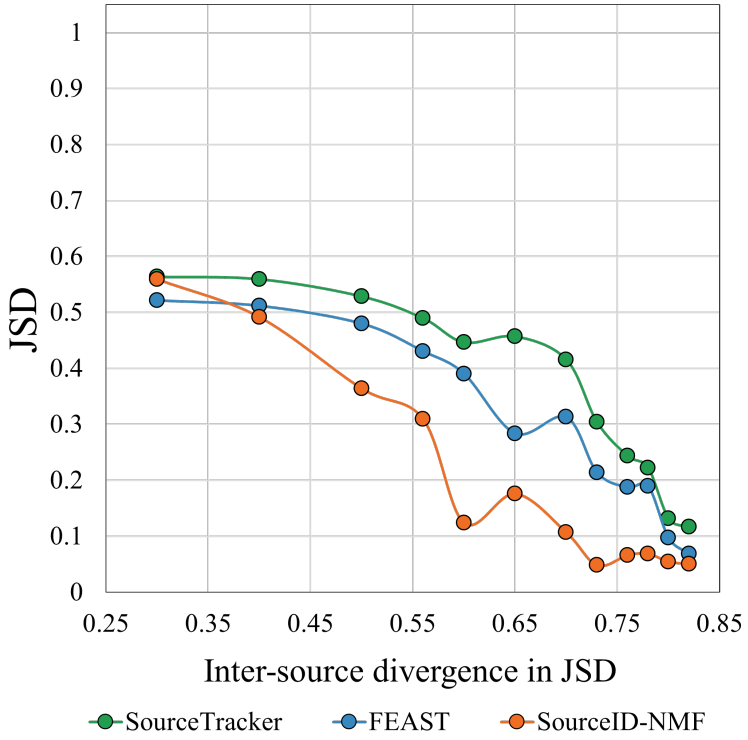
Simulated data settings

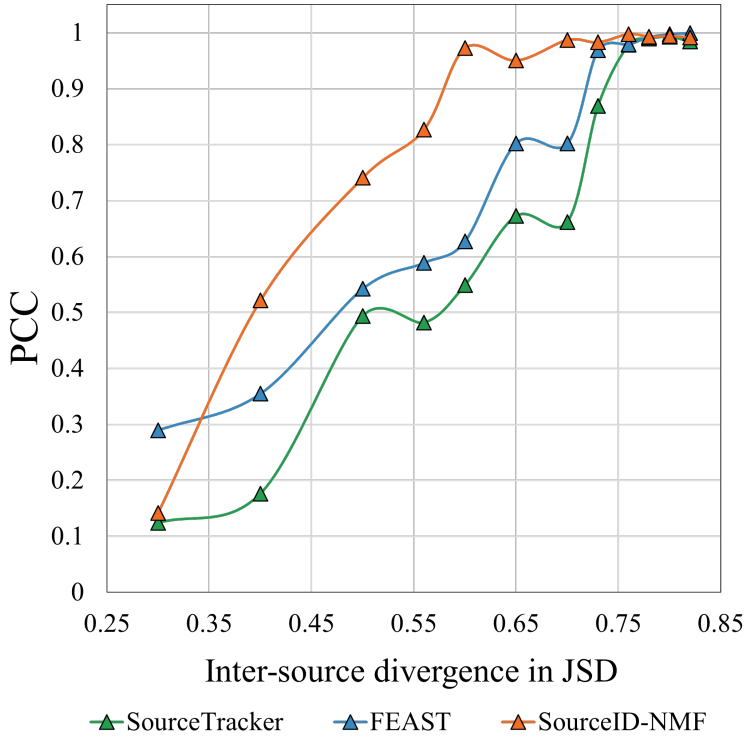
- K (15) + U (5) = 20 sources with different similarities
- Varying proportions of 5 unknown sources (0.1 to 0.9)
- 5 irrelevant sources in the 15 sources

[1] Thompson, L. R. *et al.* (2017). A communal catalogue reveals earth's multiscale microbial diversity. *Nature*, 551(7681), 457–463.

Simulated data experiment

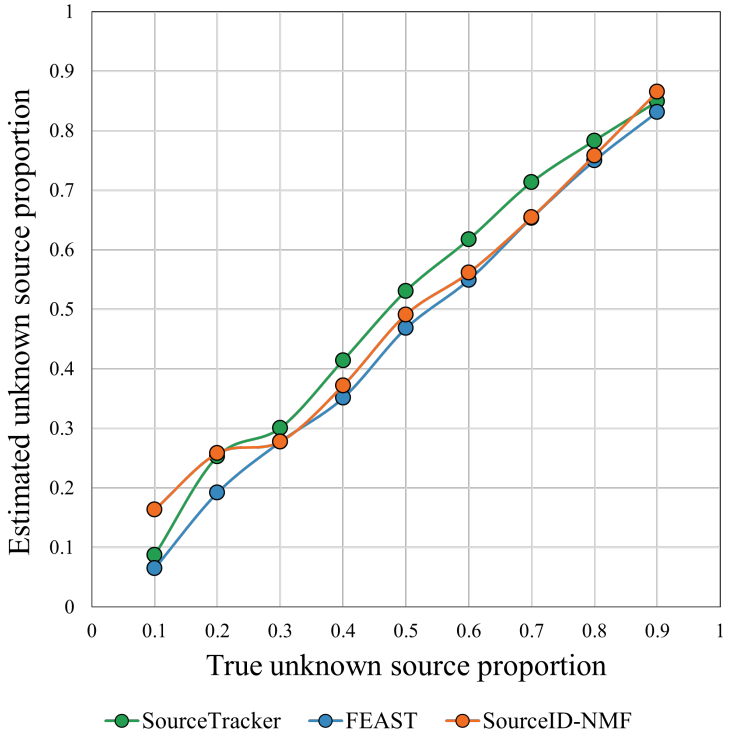
Impact of inter-source similarity on source tracking: estimated H and the true H



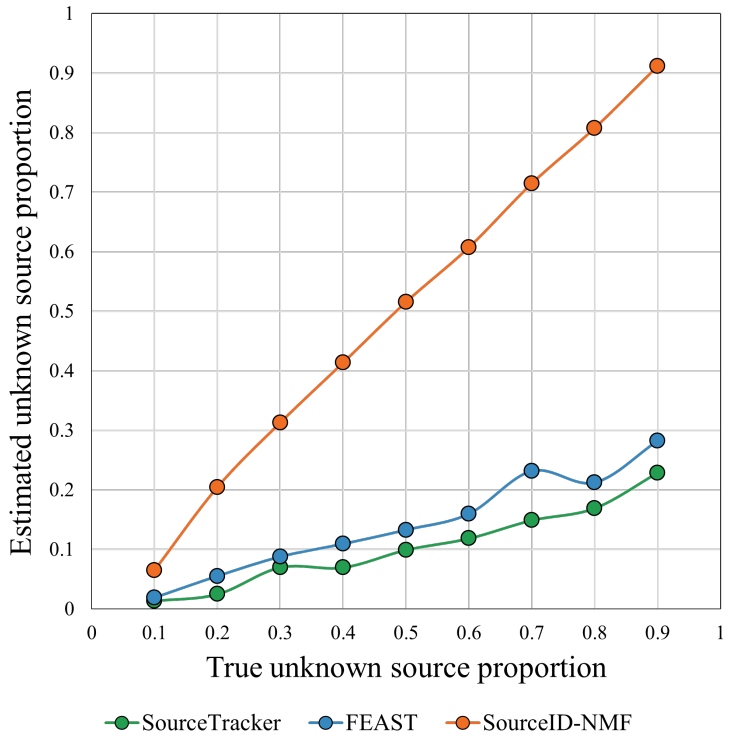


Simulated data experiment

SourceID-NMF has more accurate estimations of unknown sources' proportion



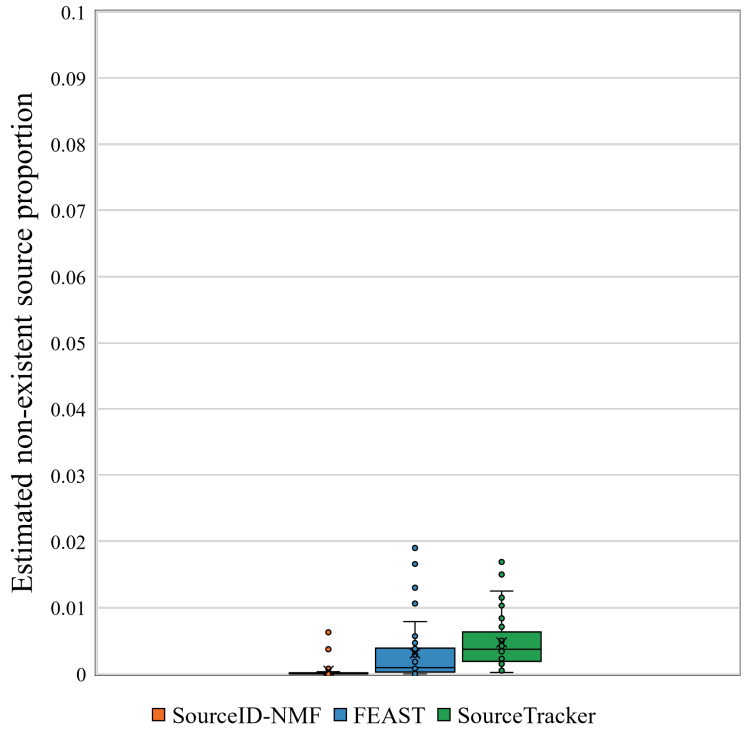
(b) 0.8 JSD



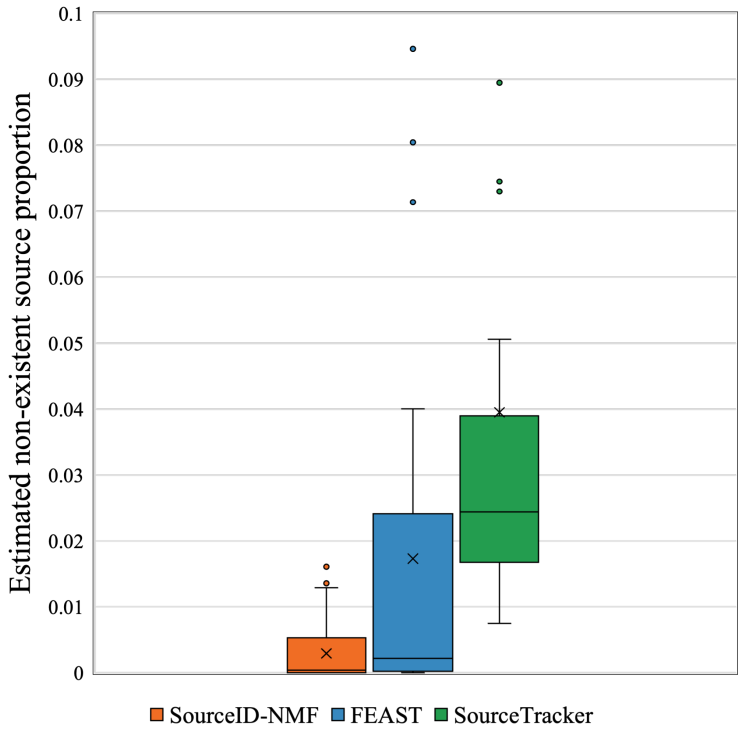
(a) 0.6 JSD

Simulated data experiment

More accurate identification of irrelevant sources (ideal value: 0)



(b) 0.8 JSD

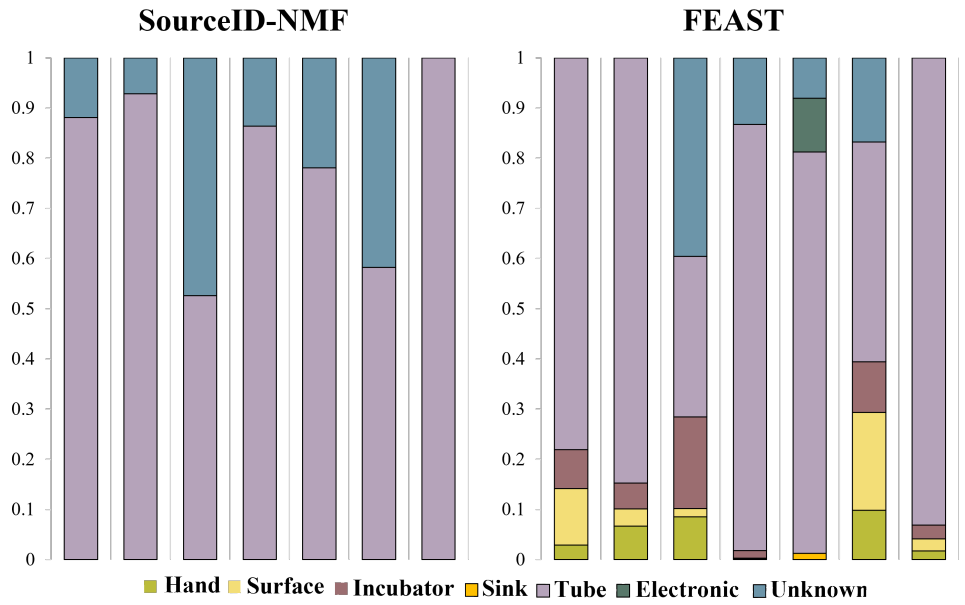


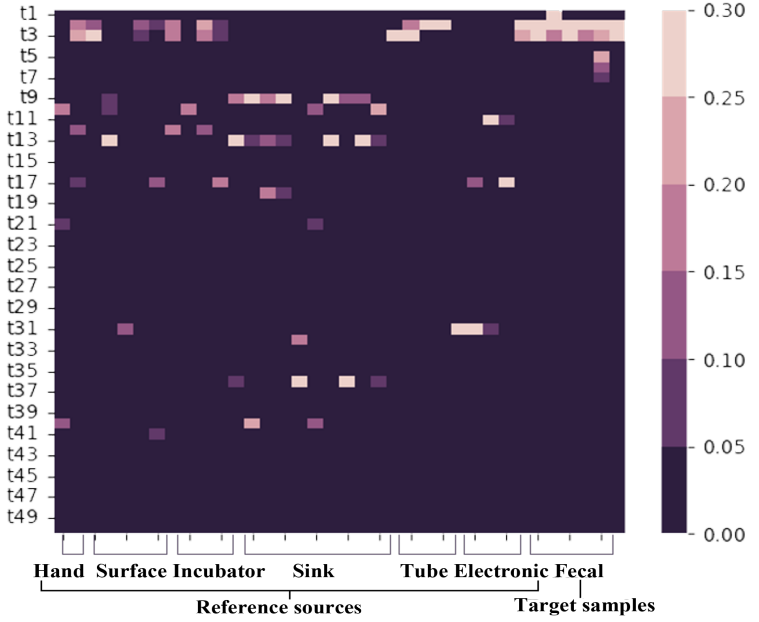
(a) 0.6 JSD

Real data experiment

Infants' fecal samples

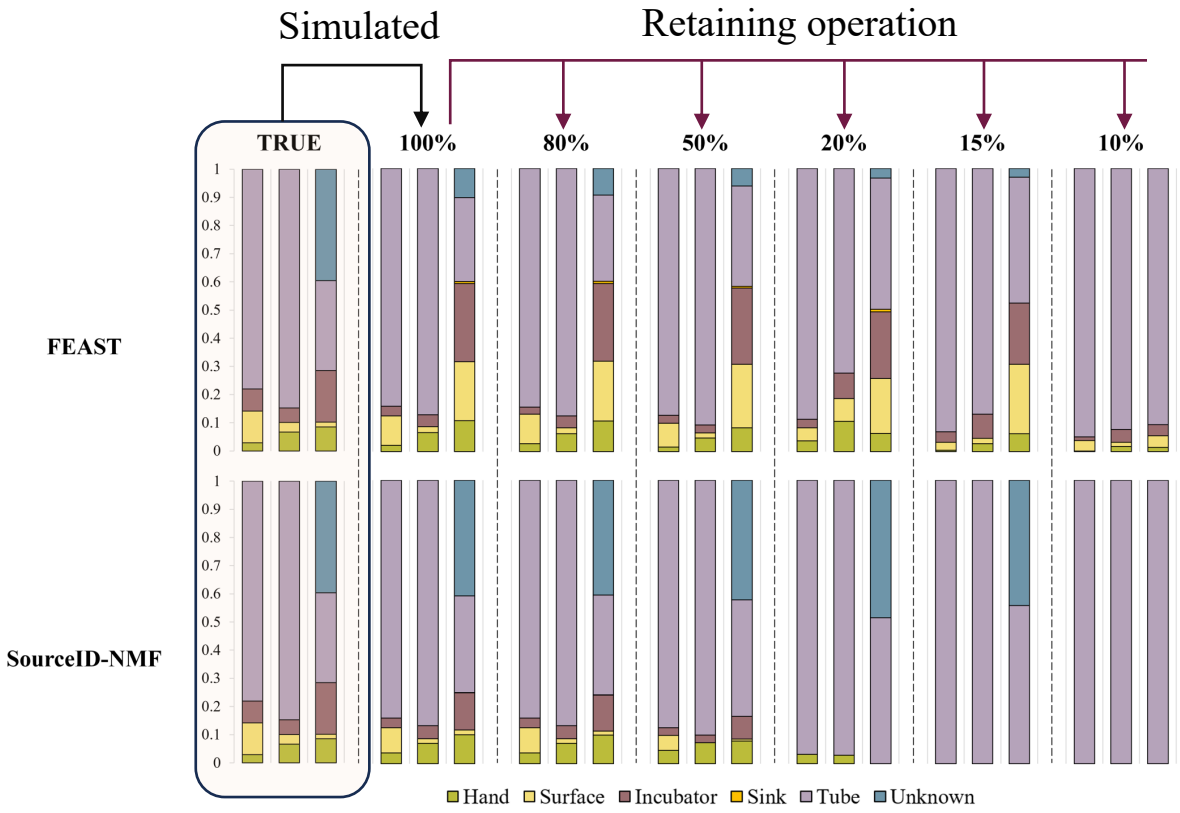
- Target samples: 7 fecal samples
- Reference sources: 29 samples from hands, environmental surfaces, incubators, sinks, tubes, and electronics

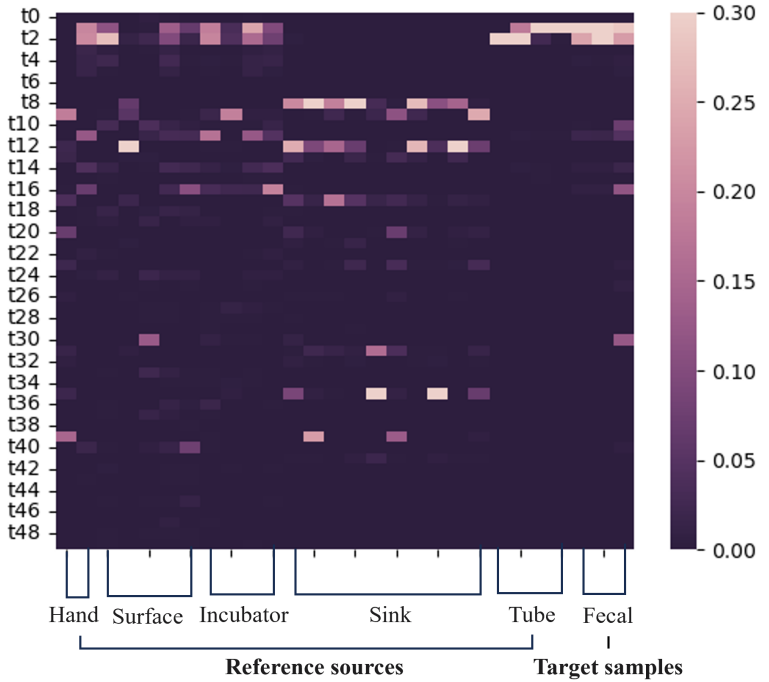




Investigate the reasons via simulation (I)

Retaining Top n% of Taxa in the Target Sample While Setting the Rest to Zero

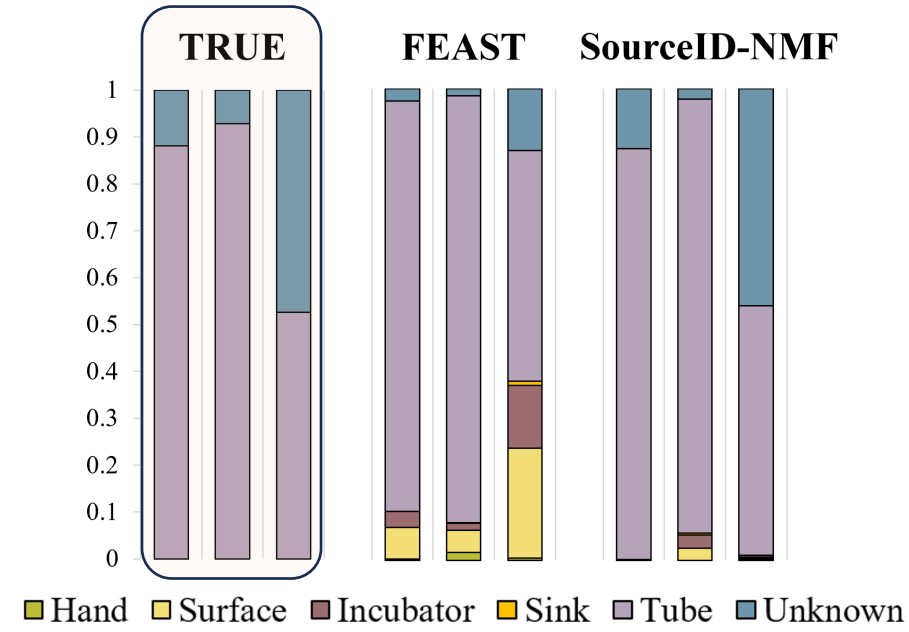




Heatmap of the taxa abundance when retaining 20% (highly similar to the real data)

Investigate the difference via simulation (II)

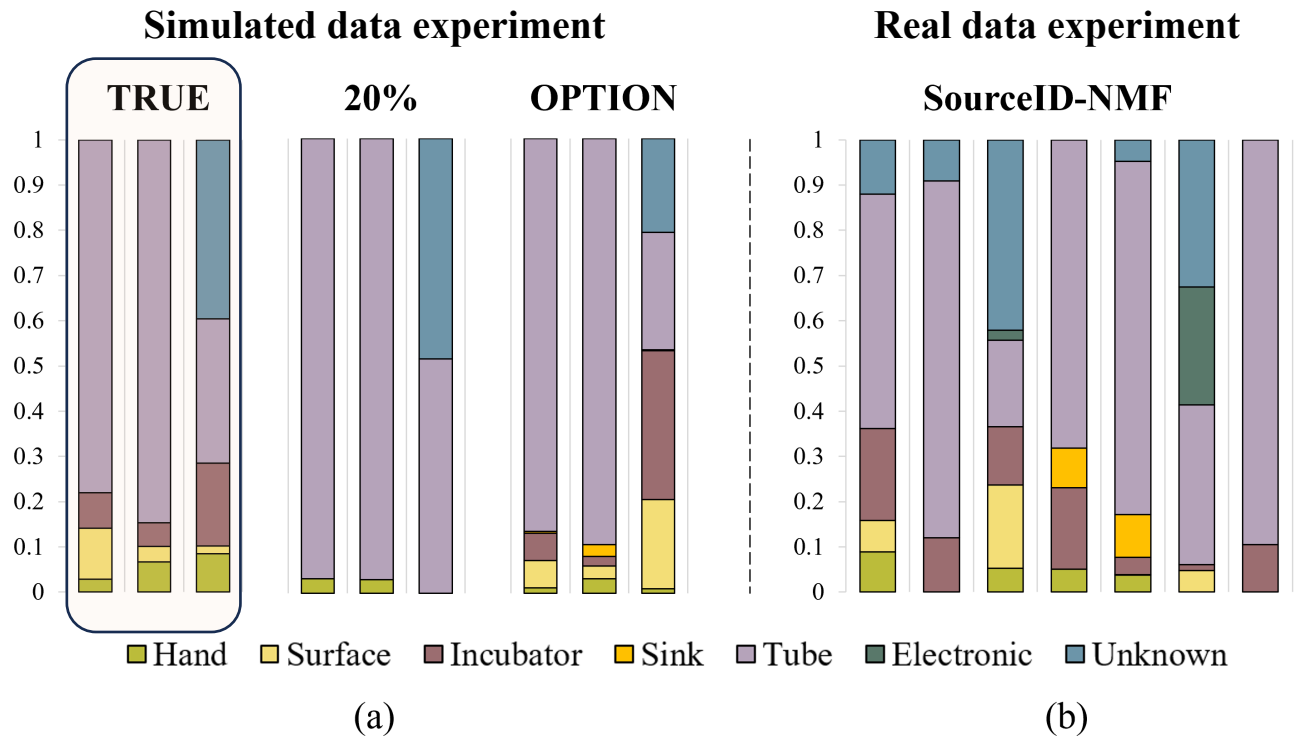
Re-generate the target sample using only tube and unknown sources



FEAST can generate false positives, consistent with previous experimental results

An option to include more sources

Only use taxa observed in the target samples (OPTION)



Conclusions

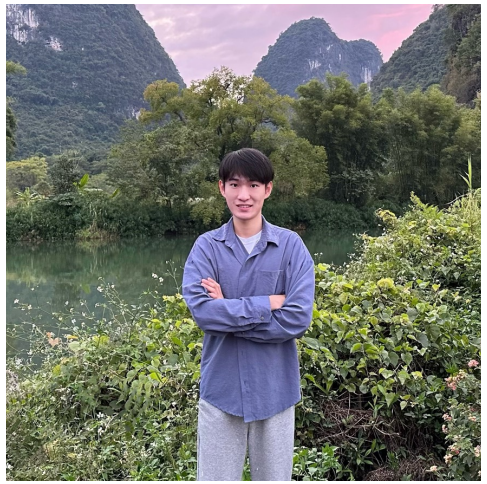
SourceID-NMF

- Goal: estimate the proportions of reference sources in a target microbial sample
- Input: taxa abundance of the target samples and reference sources
- Output: the proportion of reference sources and unknown source
- Good at estimating sources' proportions especially the unknown sources

Acknowledgement

Funding: GRF, ITF, and City University of Hong Kong

Ziyi Huang



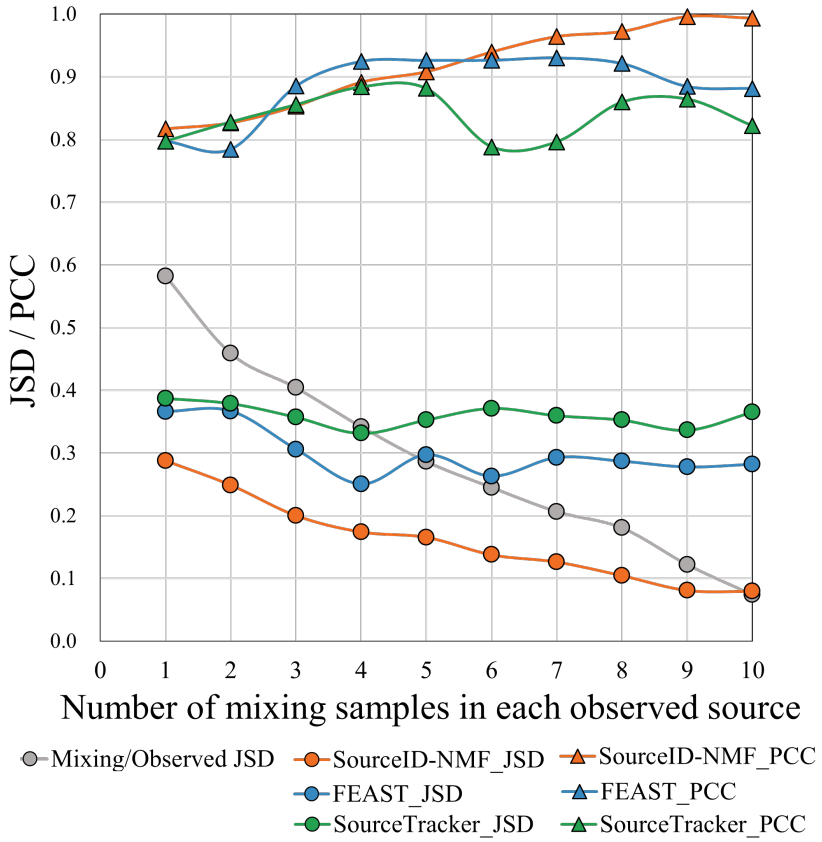
Dehan Cai

GitHub of SourceID:
https://github.com/ZiyiHuang0708/SourceID-NMF

Group Website:
https://yannisun.github.io/

Simulated data experiment

- Reference sources with noises

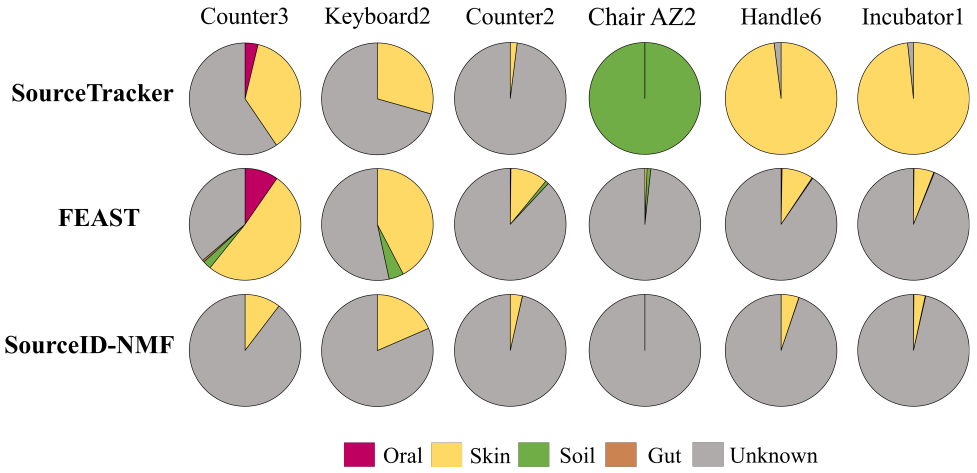


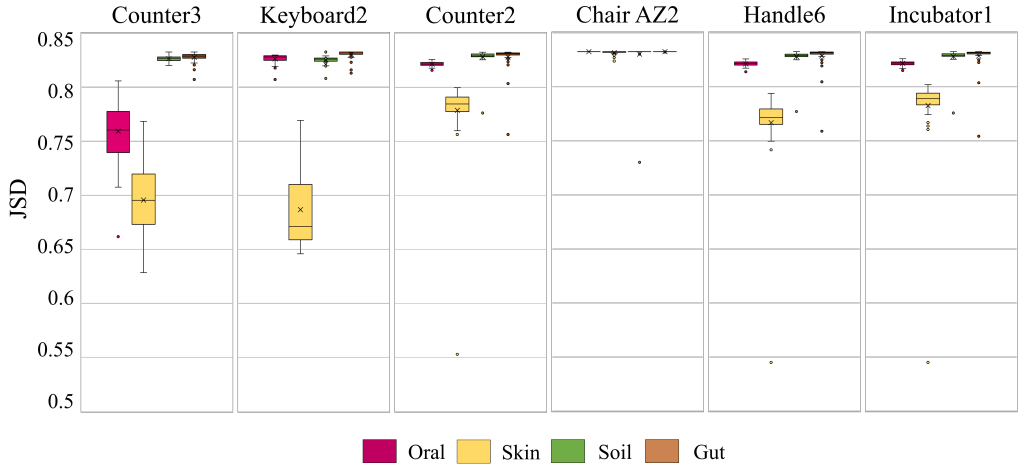
Real data experiment

Indoor environmental samples

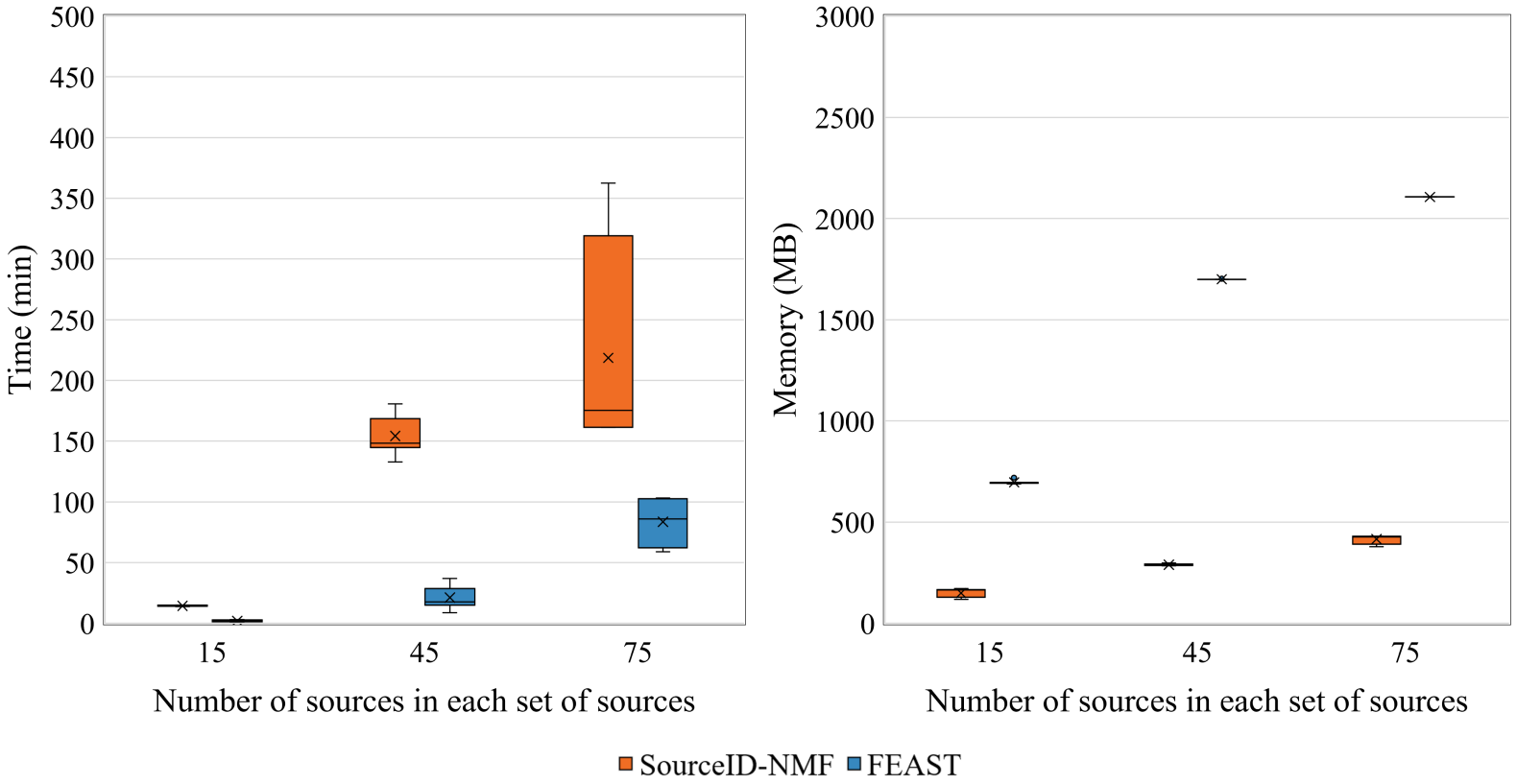
- Target samples: 6 Indoor environmental samples
- Reference sources: 180 microbial samples from from gut, oral, skin and soil (45 samples for each)

No space-time correlation

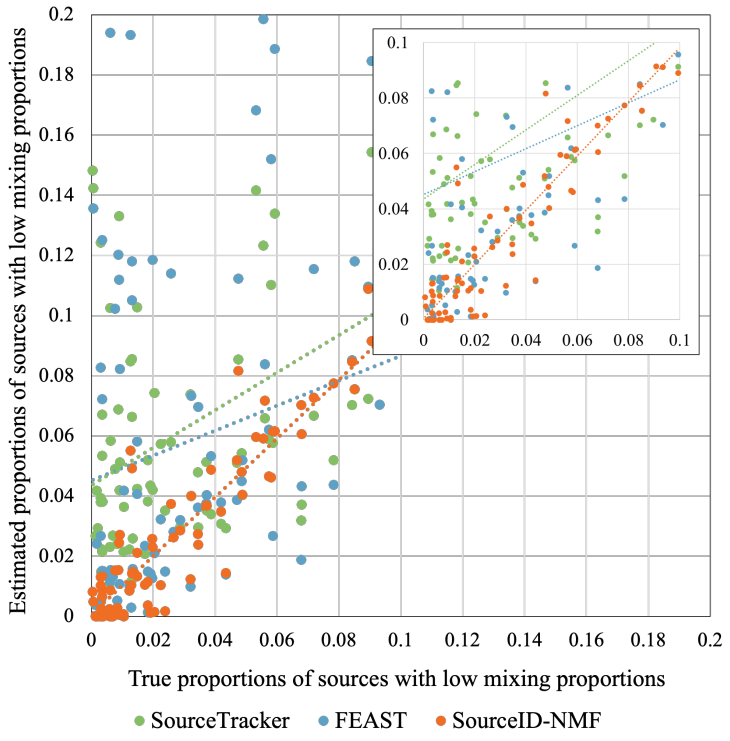




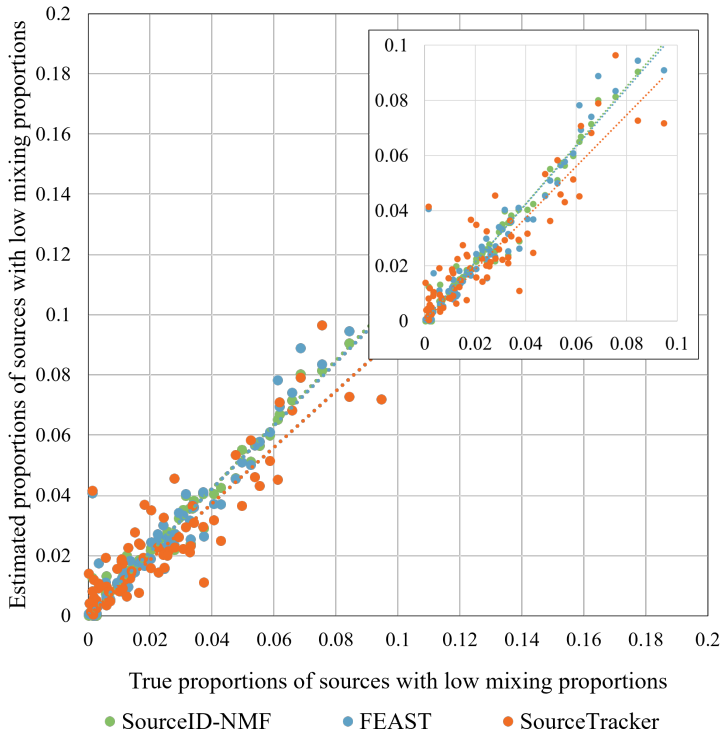
Running time and Memory Usage



Sources with small proportions



(a) 0.6 JSD



(b) 0.8 JSD