ResearchMate

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by Paraskevi Tassopoulou, Zewen Yang & Vladimir Angirov

PubMed

Database providing access to biomedical literature

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doi: 10.1146/annurev-biophys-062215-010822. Epub 2017 Mar 30.

CRISPR-Cas9 Structures and Mechanisms

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Affiliations + expand
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Abstract

Many bacterial clustered regularly interspaced short palindromic repeats (CRISPR)-CRISPR-associated (Cas) systems employ the dual RNA-guided DNA endonuclease Cas9 to defend against invading phages and conjugative plasmids by introducing site-specific double-stranded breaks in target DNA. Target recognition strictly requires the presence of a short protospacer adjacent motif (PAM) flanking the target site, and subsequent R-loop formation and strand scission are driven by complementary base pairing between the guide RNA and target DNA, Cas9-DNA interactions, and associated conformational changes. The use of CRISPR-Cas9 as an RNA-programmable DNA targeting and editing platform is simplified by a synthetic single-guide RNA (sgRNA) mimicking the natural dual trans-activating CRISPR RNA (tracrRNA)-CRISPR RNA (crRNA) structure. This review aims to provide an in-depth mechanistic and structural understanding of Cas9-mediated RNA-guided DNA targeting and cleavage. Molecular insights from biochemical and structural studies provide a framework for rational engineering aimed at altering catalytic function, guide RNA specificity, and PAM requirements and reducing off-target activity for the development of Cas9-based therapies against genetic diseases.

Keywords: CRISPR; Cas9; genome engineering; mechanism; off-target; structure.

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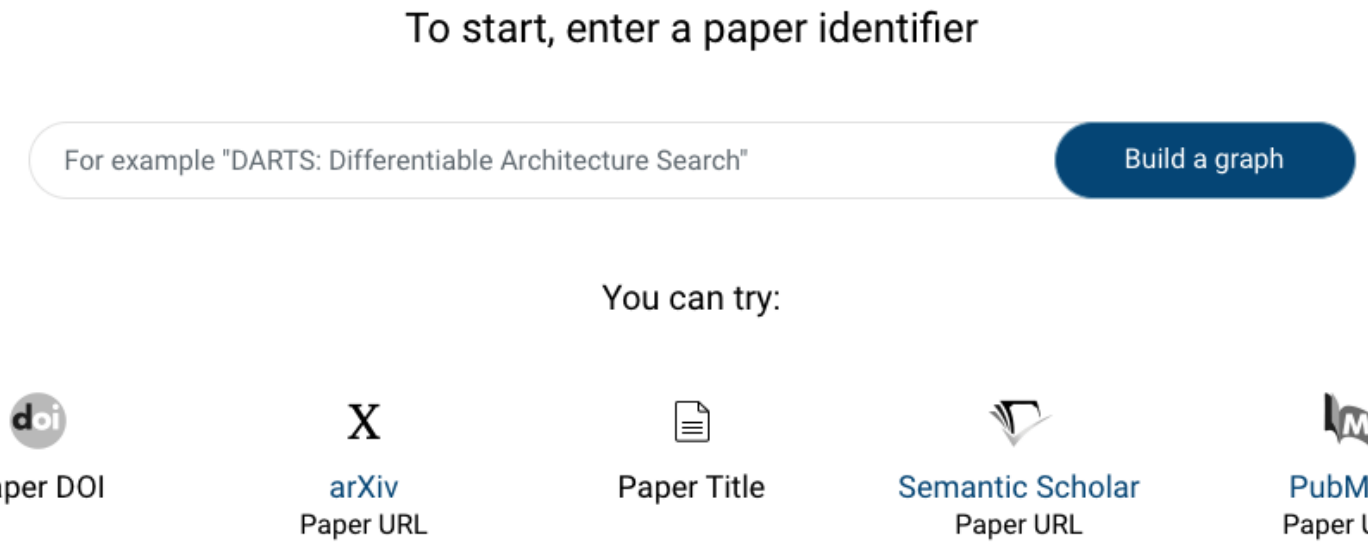

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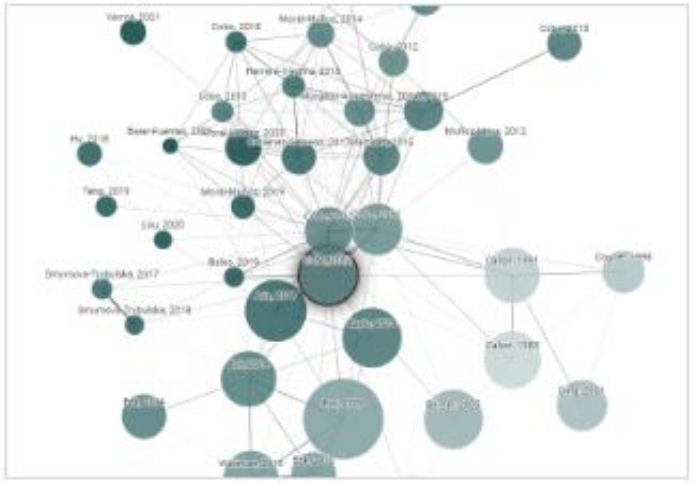
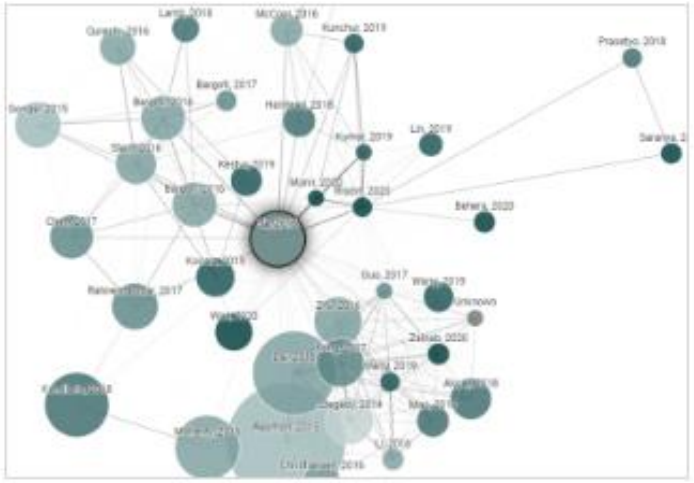
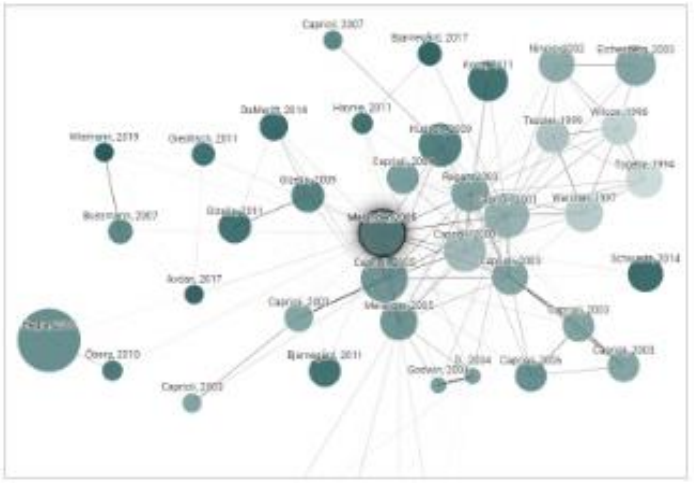


Science mapping software tools: Review, analysis, and cooperative study among tools (Cobo, 2011)



DeepFruits: A Fruit Detection System Using Deep Neural Networks (Sa, 2016)



Gender Equality and Intrastate Armed Conflict (Melander, 2005)

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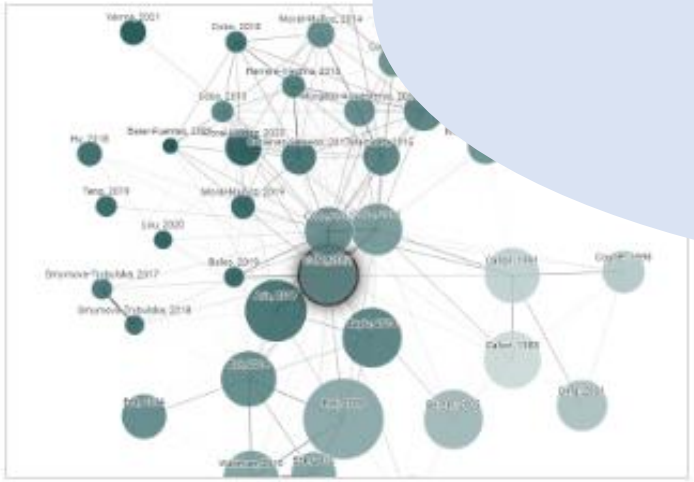

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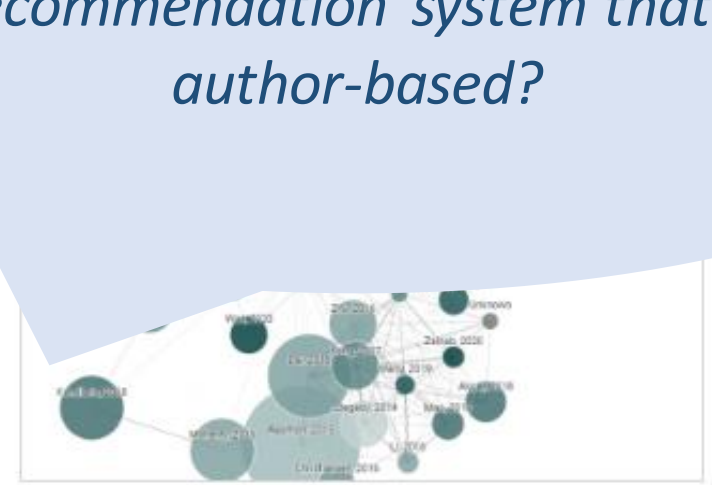

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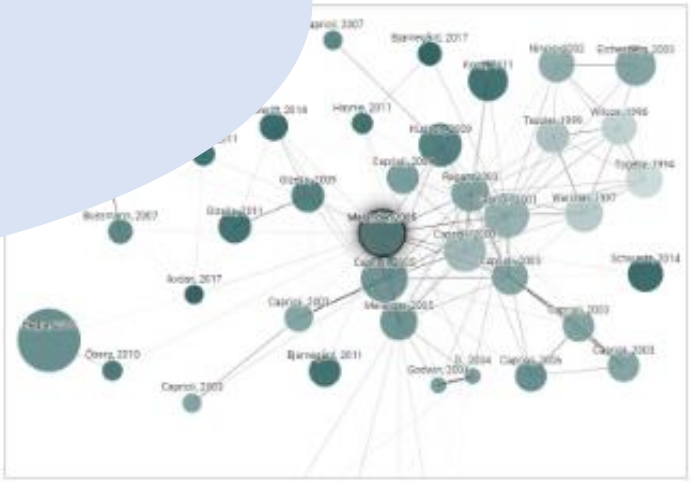

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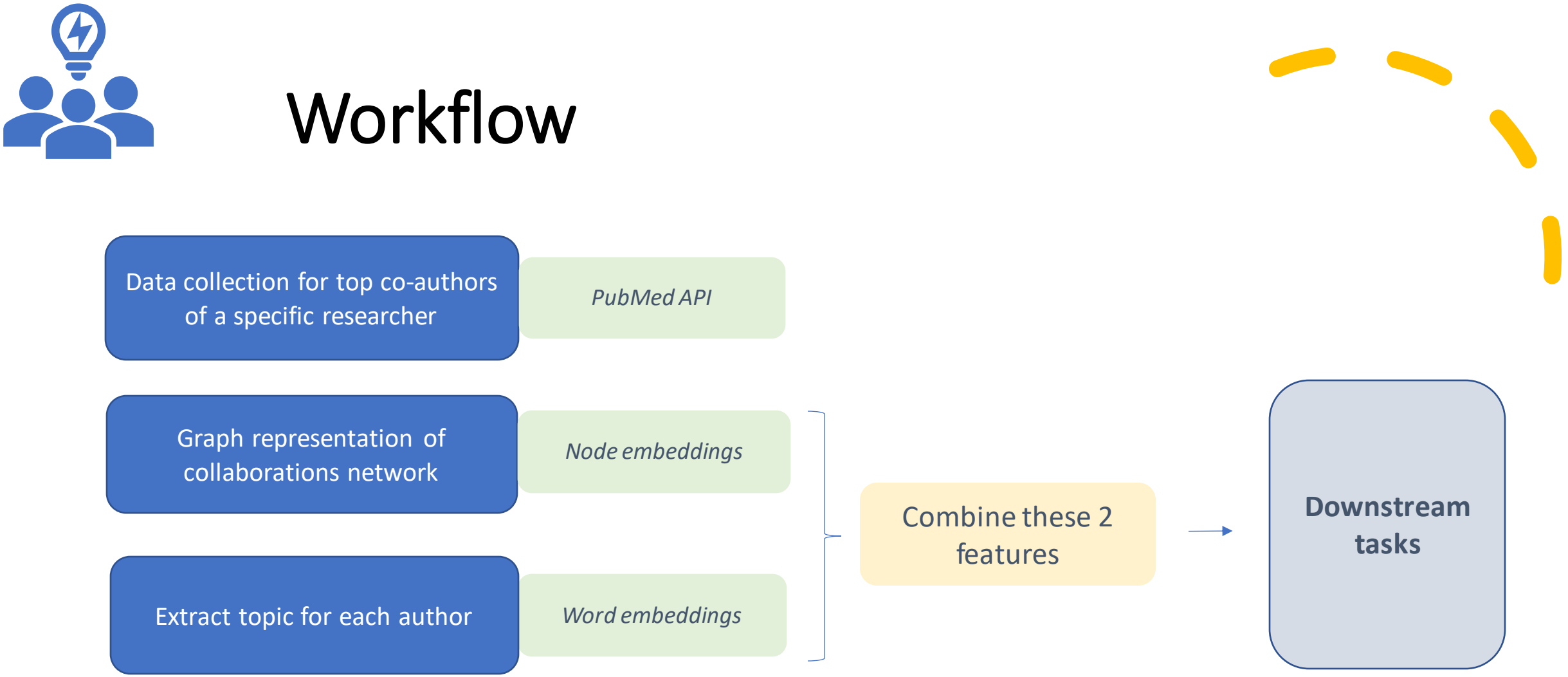
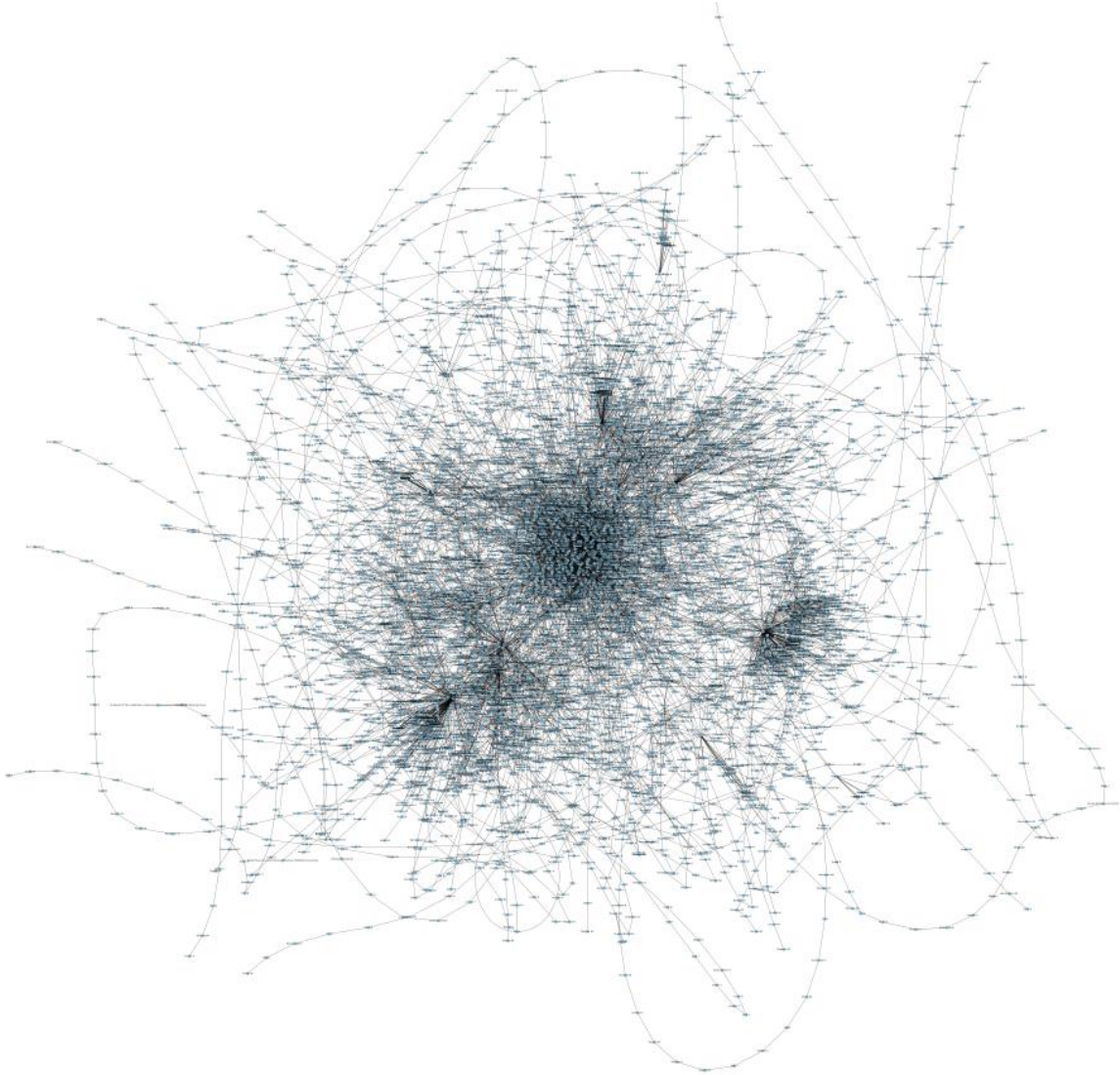
Workflow

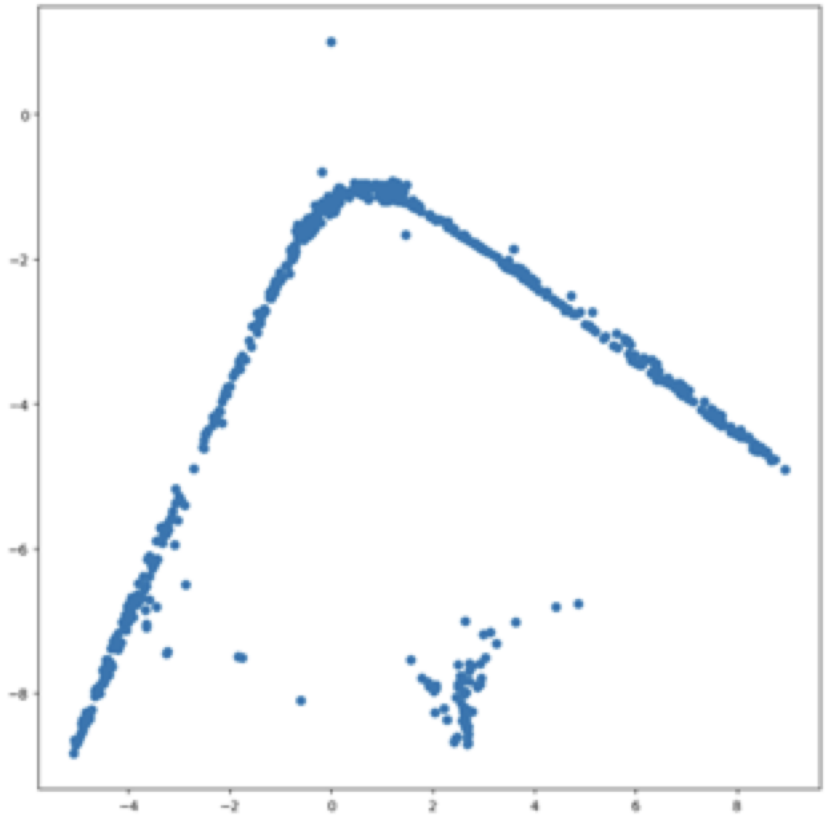

Data collection for top co-authors of a specific researcher
PubMed API
Graph representation of collaborations network
Node embeddings
Extract topic for each author
Word embeddings
Combine these 2 features
Downstream tasks

Graph of collaborations



Node embeddings: Node2Vec

- Node2Vec
- DeepWalk
- GraphSAGE
- GCN
- GAT
- …



Research interests per Author

TITLE	ABSTRACT	KEYWORDS	
•	•	•	Fine
•	•	—	Generate keywords from Abstract
•	—	•	Generate keywords from Title

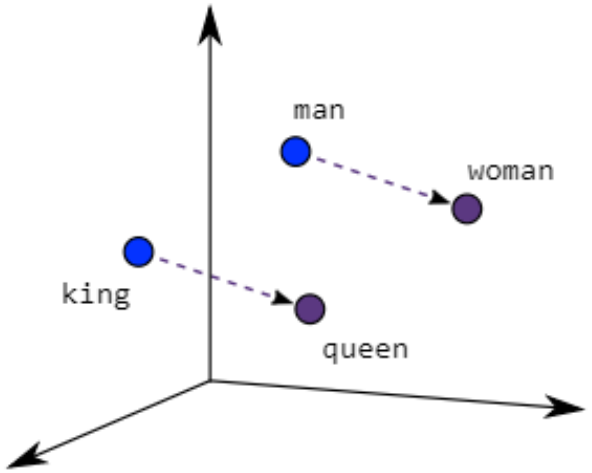
- Keywords used as indications for research interests/topics.
- When absent: BERT or GPT-4?

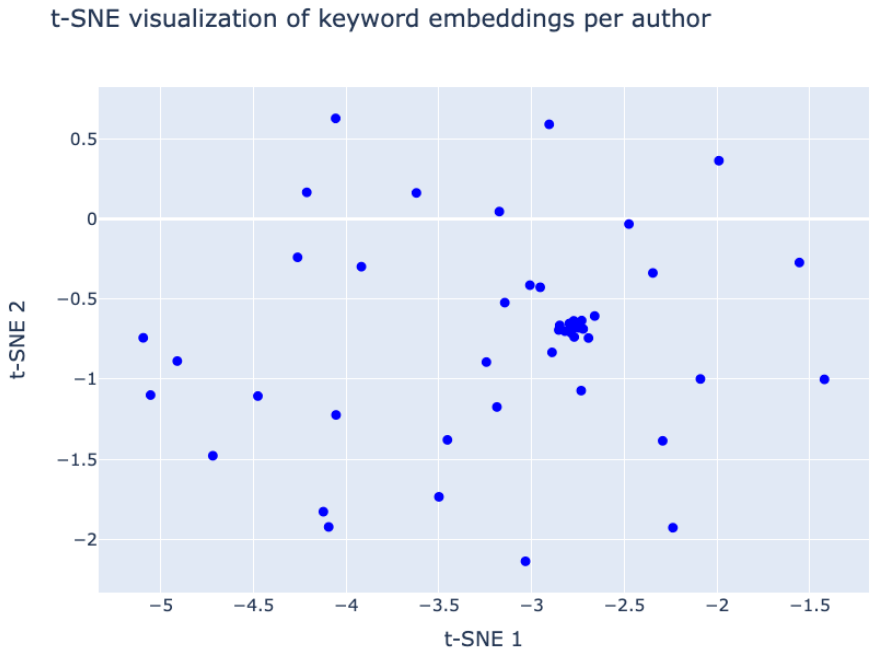

```
Generated keywords for index 243: RNA, protein, X-ray crystallography
Generated keywords for index 244: RNA-induced silencing complex, Argonaute protein, microRNA
Generated keywords for index 245: ribosome, protein synthesis, initiation
Generated keywords for index 246: RNA, Dicer, PAZ
Generated keywords for index 247: internal ribosome entry sites, mRNA, protein synthesis
Generated keywords for index 248: crystals, X-rays, twinning
Generated keywords for index 249: Protein synthesis, ribosomal subunit, mRNA
Generated keywords for index 250: degree, difficulty, higher.
Generated keywords for index 251: Dicer, RNAi, RNA
Generated keywords for index 252: hepatitis delta virus, ribozyme, active site
Generated keywords for index 253: protein synthesis, mammalian cells, initiation factor eIF3
Generated keywords for index 254: ribonuclease III, RNA, enzymes
Generated keywords for index 255: SRP, signal recognition particle, GTP
Generated keywords for index 256: RNA, regulate, biology.
Generated keywords for index 257: Hepatitis C virus, internal ribosome entry site, translation-start site
Generated keywords for index 258: antibody, phage display, ribonucleoprotein (RNP)
Generated keywords for index 259: Drosophila, P-element, somatic inhibitor protein
Generated keywords for index 260: Dicer, RNA interference, double-stranded RNA
Generated keywords for index 261: Small molecules
```

Word embeddings: Word2Vec

ML models for word embeddings:

- GloVe
- FastText
- BERT
- ...



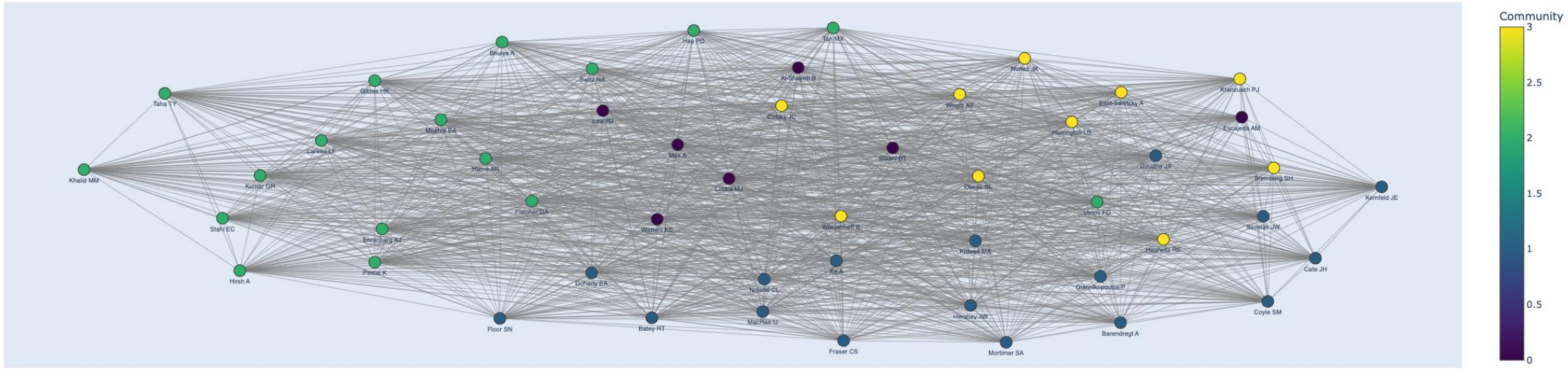


Similarity matrix

	Al-Shayeb B	Barendregt A	Batey RT	Bhuiya A	Cate JH
Al-Shayeb B	1.000000	0.221060	0.362840	0.331701	0.337607
Barendregt A	0.221060	1.000000	0.450579	0.229788	0.446754
Batey RT	0.362840	0.450579	1.000000	0.158361	0.545131
Bhuiya A	0.331701	0.229788	0.158361	1.000000	0.257348
Cate JH	0.337607	0.446754	0.545131	0.257348	1.000000

- Similarity between researchers
- Top candidates for collaboration
- [mini app]

Community detection in author networks



Future Goals

- Experiment with other models (eg. GAT)
- Include more features (citations, affiliations, gender etc)
- Generalize in other disciplines

Weak points

- Unlabelled dataset (unsupervised learning)
- Absence of a formal evaluation method for recommendations
- Ethical considerations (reinforcement of biases, Matthew's effect)

Discussion

Thank you all!