

ResearchMate

Towards a collaborators recommendation system in biomedical research

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Database providing access to biomedical literature

Review > Annu Rev Biophys. 2017 May 22;46:505-529.

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

CRISPR-Cas9 Structures and Mechanisms

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Affiliations + expand

PMID: 28375731 DOI: 10.1146/annurev-biophys-062215-010822

Abstract

Many bacterial clustered regularly interspaced short palindromic repeats (CRISPR)-CRISPRassociated (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 RNAguided 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 Cas9based therapies against genetic diseases.

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

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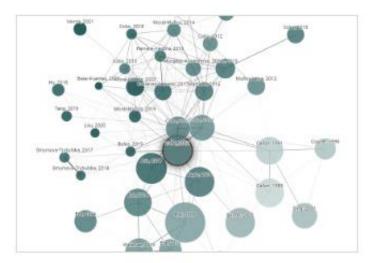
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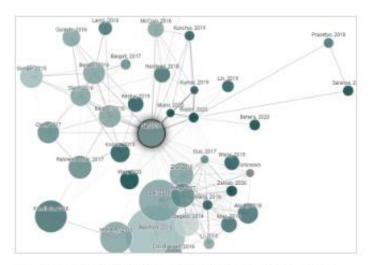


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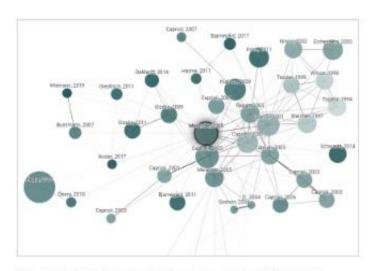
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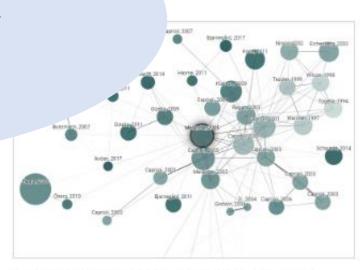
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Science mapping software tools: Review, analysis, and cooperative study among tools (Cobo, 2011)

Can we make a simple recommendation system that is author-based?



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



Gender Equality and Intrastate Armed Conflict (Melander, 2005)



Workflow

Data collection for top co-authors of a specific researcher

PubMed API

Graph representation of collaborations network

Node embeddings

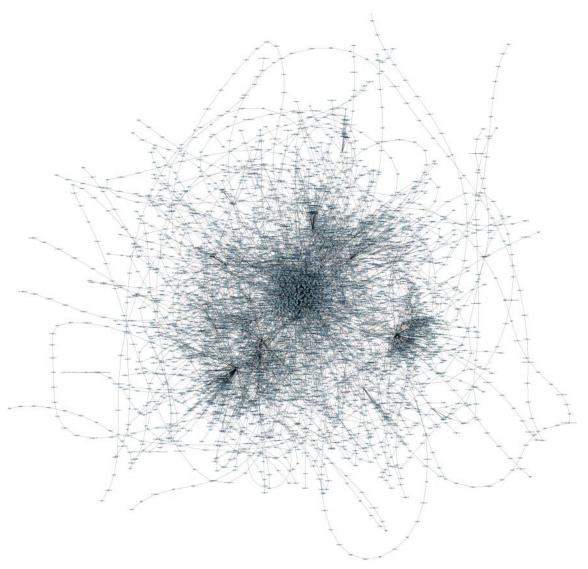
Extract topic for each author

Word embeddings

Combine these 2 features

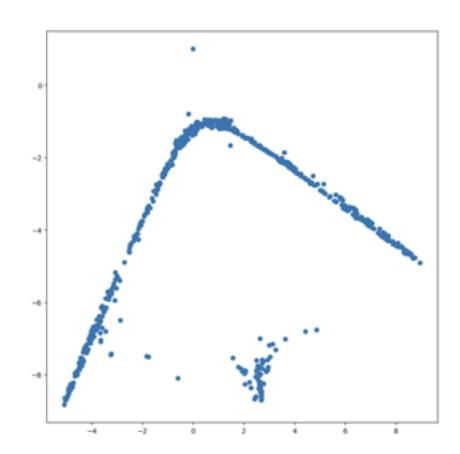
Downstream tasks

Graph of collaborations



Node embeddings: Node2Vec

- Node2Vec
- DeepWalk
- GraphSAGE
- GCN
- GAT
- ...



Research interests per Author

TITLE	ABSTRACT	KEYWORDS	
•	•	•	Fine
•	•	_	Generate keywords from Abstract
•	<u>—</u>	•	Generate keywords from Title

 Keywords used as indications for research interests/topics.

When absent: BERT or GPT-4?

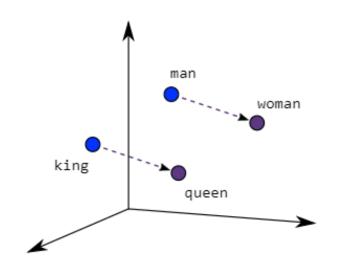


```
Generated keywords for index 243: RNA, protein, X-ray crystallography
Generated keywords for index 244: RNA-induced silencing complex, Argonaute protein, microRNA
Generated keywords for index 245: ribosome, protein synthesis, initiation
Generated keywords for index 246: RNA, Dicer, PAZ
Generated 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
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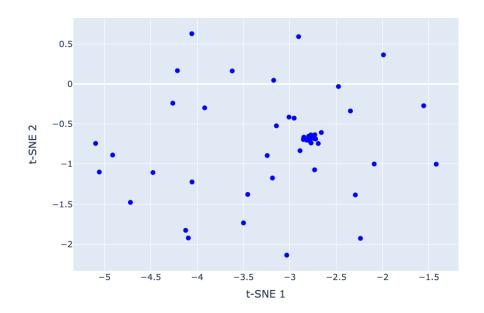
Word embeddings: Word2Vec

ML models for word embeddings:

- GloVe
- FastText
- BERT
- ..



t-SNE visualization of keyword embeddings per author

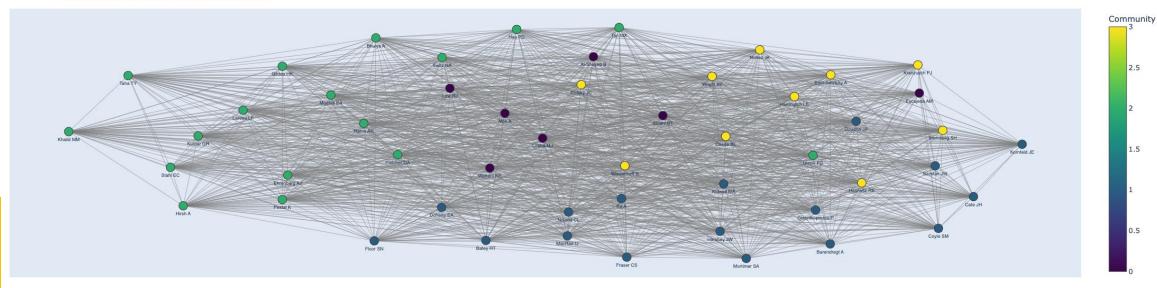


Similarity matrix

	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





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!