Gene attribute predictions through interpretable AI

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Danger of uninterpretable AI

When AI Fails, Lives Are at Risk

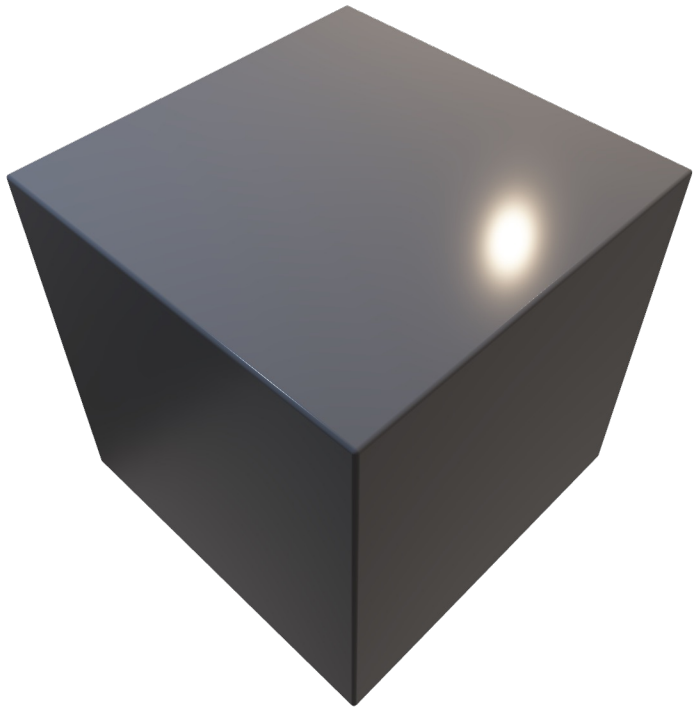
A significant number of AI failures are attributed to **interpretability** and **bias**.

London AJ. Artificial intelligence and black-box medical decisions: accuracy versus explainability. Hastings Cent Rep. 2019;49(1):15–21.

Transparency and fairness are crucial for AI adoption in genomics

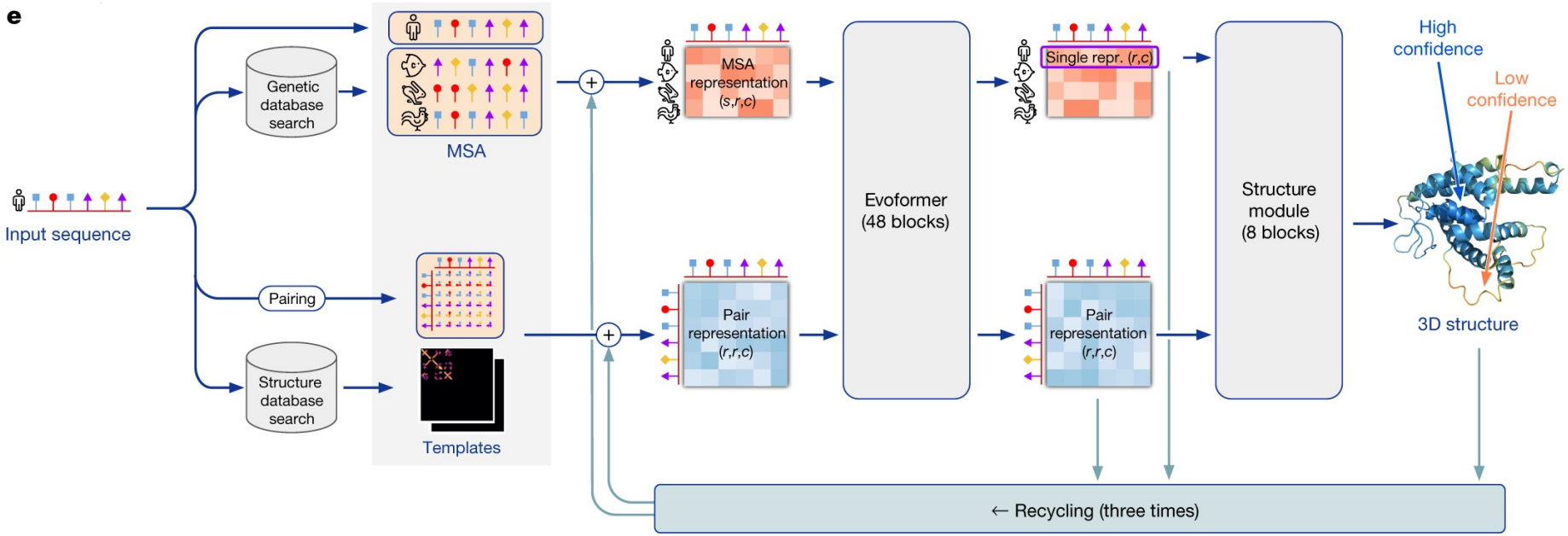
Interpretability

Bias



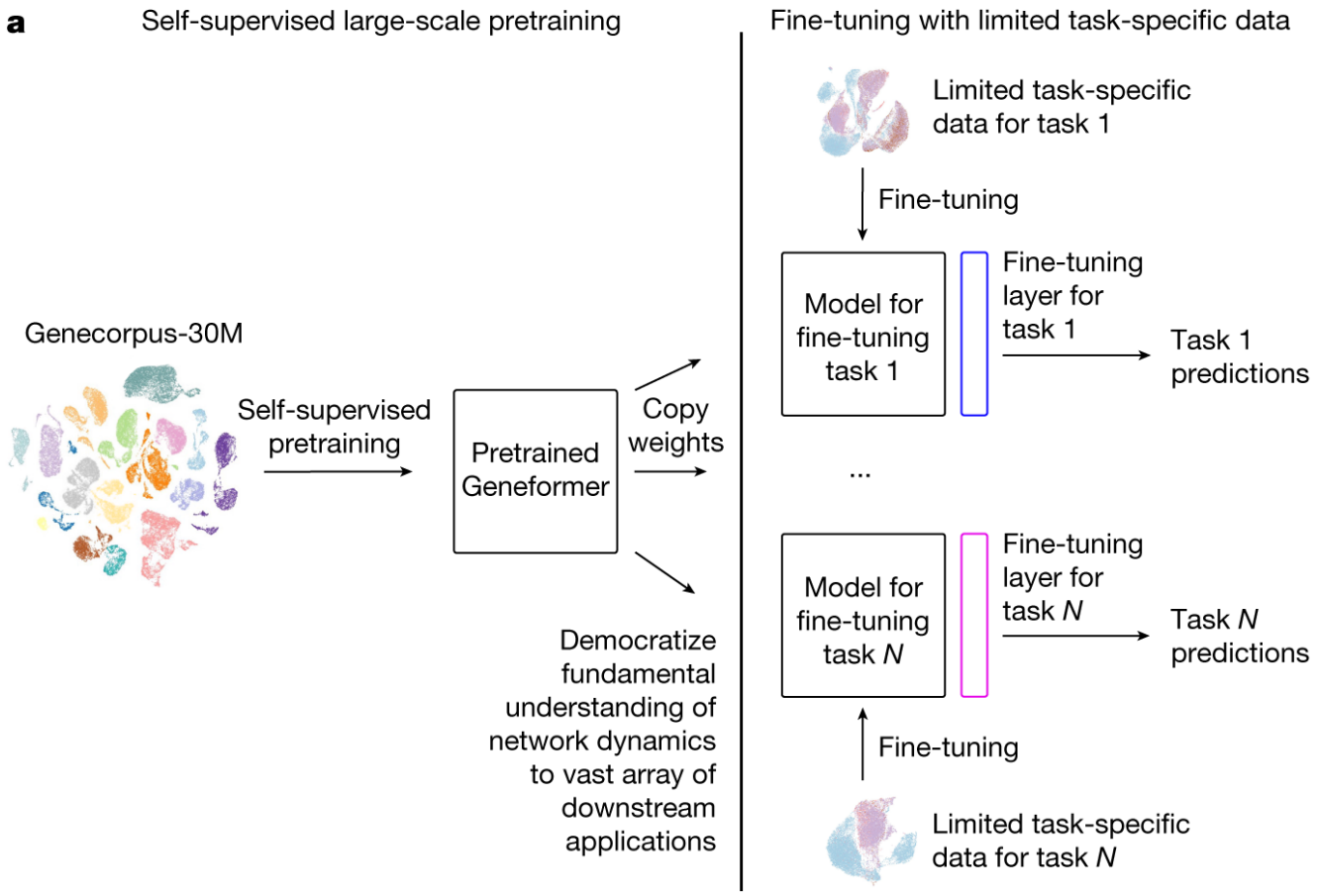
- Problem
- Solution
- Application

Predicting structure attributes from info amino acid sequence



Jumper, Nature 2021

Predicting cell or gene attributes from expression



Theodoris, Nature 2023

Problem

Use only expression or sequence data but do not incorporate text – the extensive literature knowledge?

- Problem
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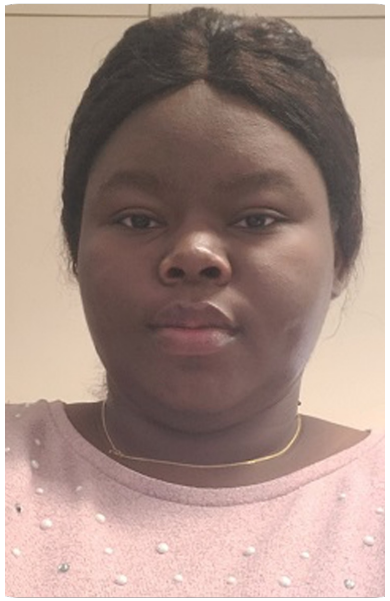
Ala Jaraweh

Oladimeji Macaulay

David Arredondo

Luis Tofoya

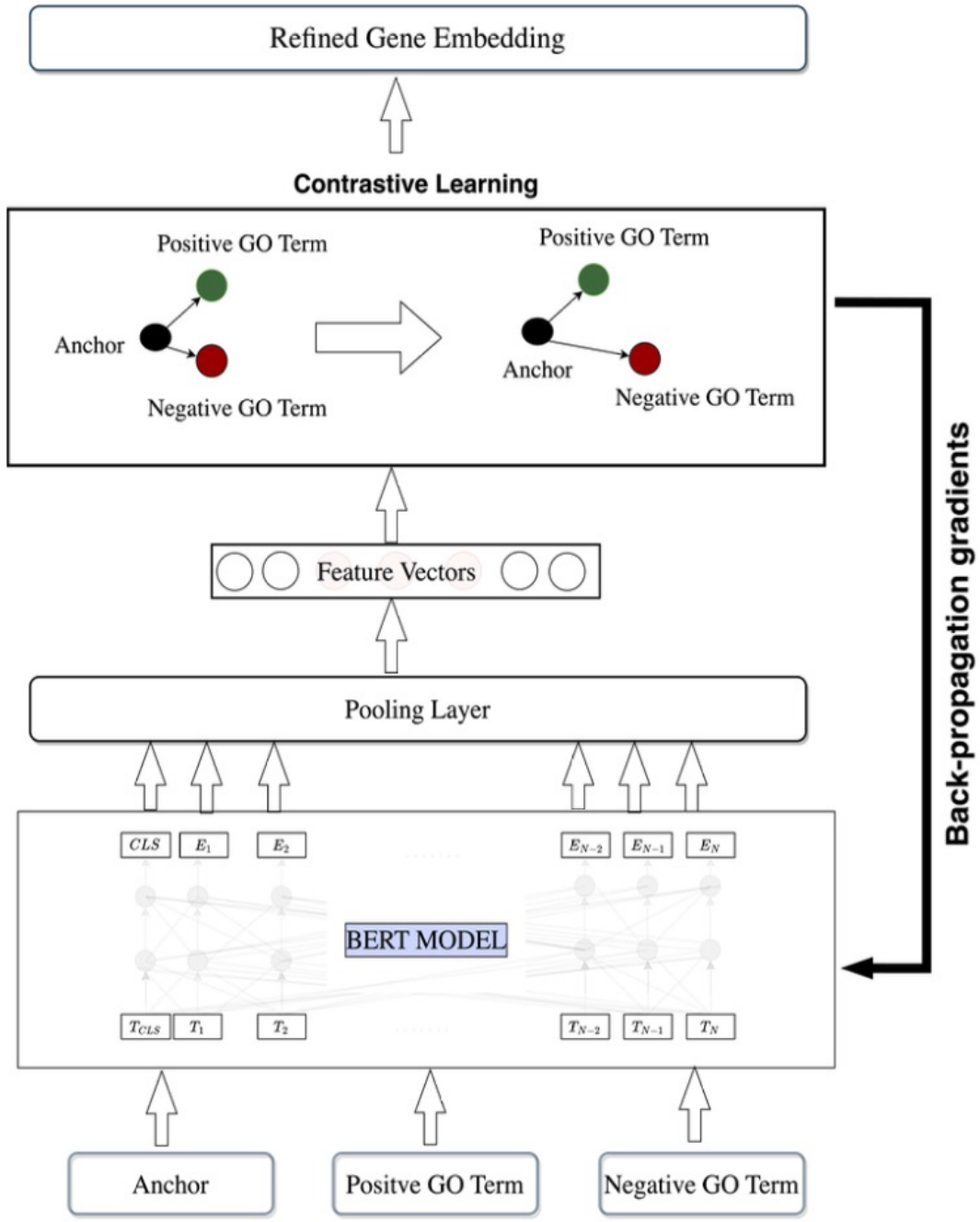


Funmi Oyebamiji

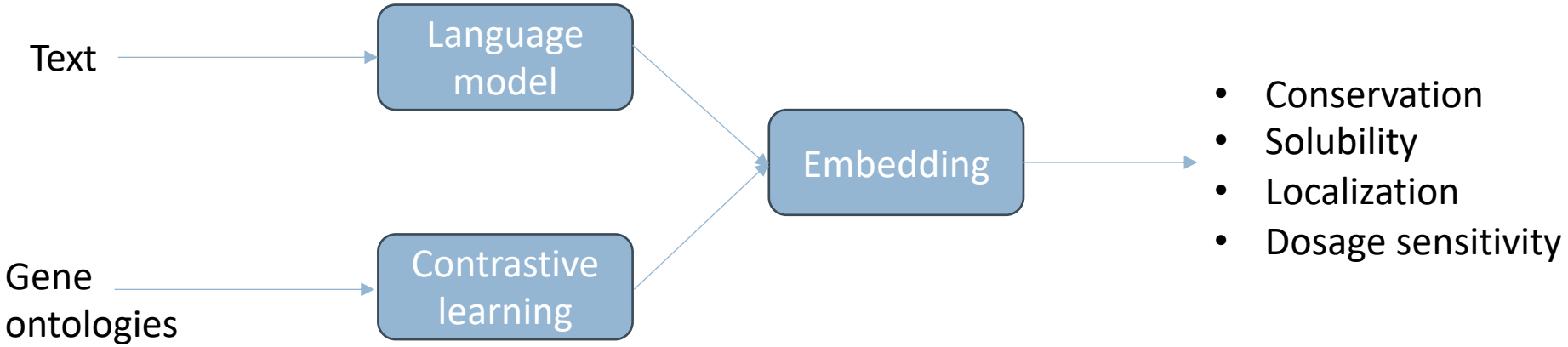
Kushal Virupakshappa

Infer gene attributes using text

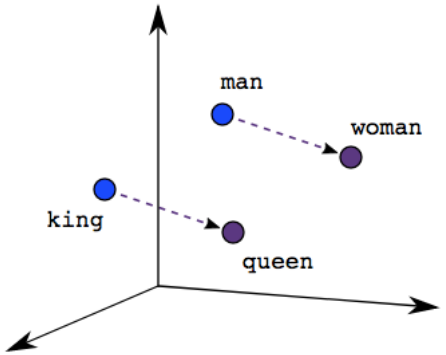
GeneLLM: A novel framework for deriving insights from text and ontologies



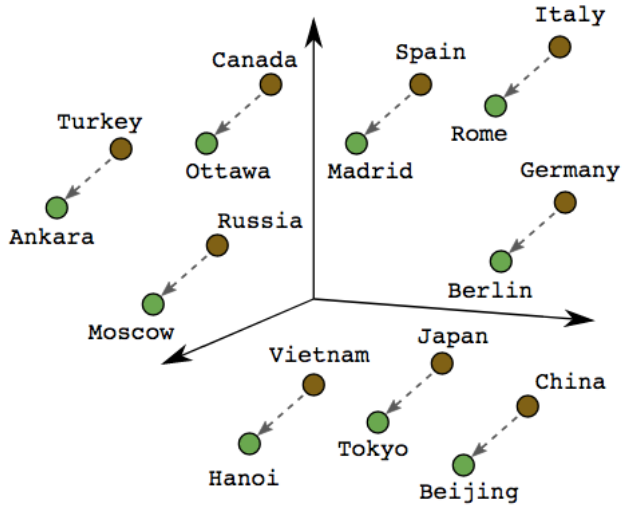
GeneLLM: A novel framework for deriving insights from text and ontologies



Learning relationships between objects with **Embedding**



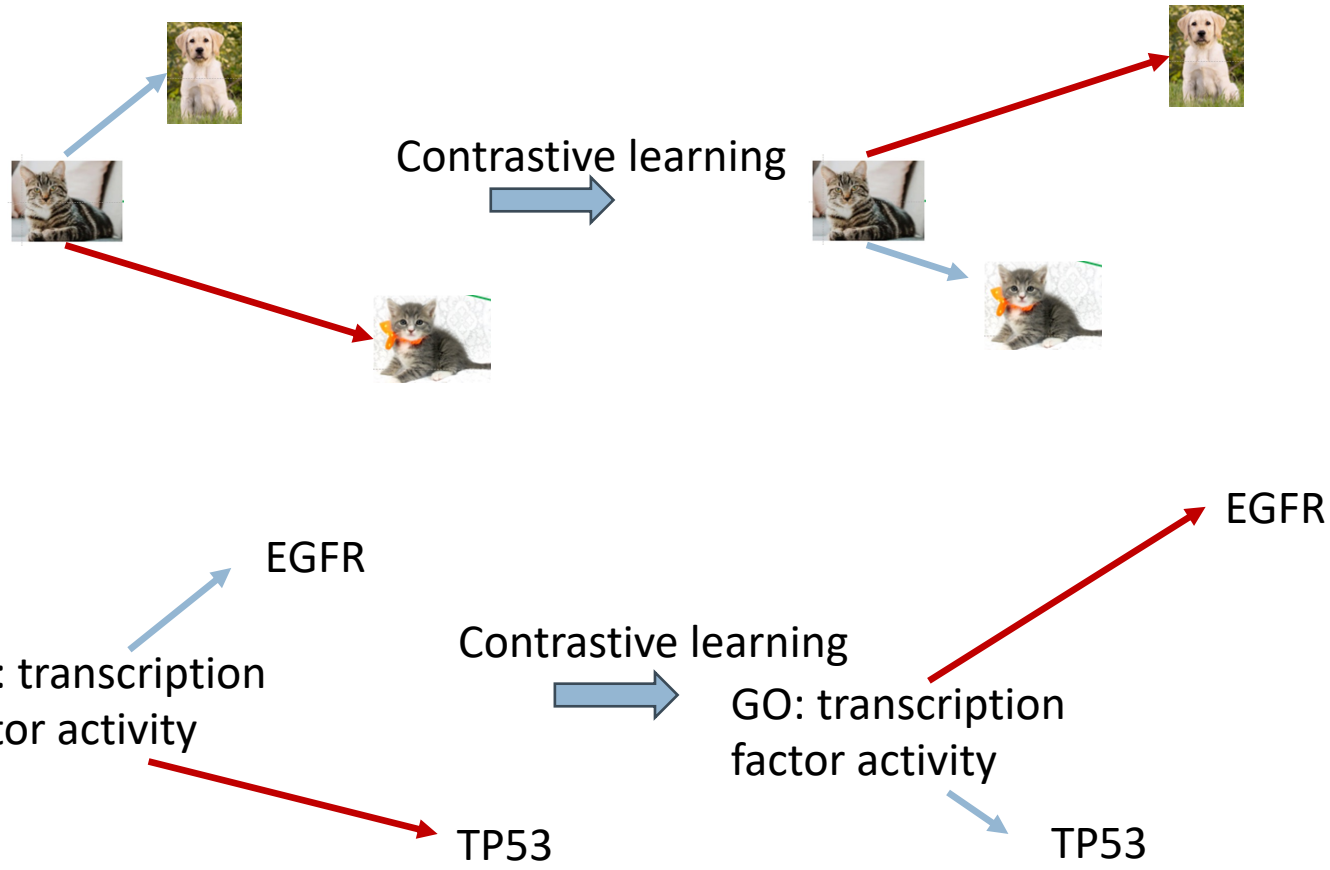
Male-Female



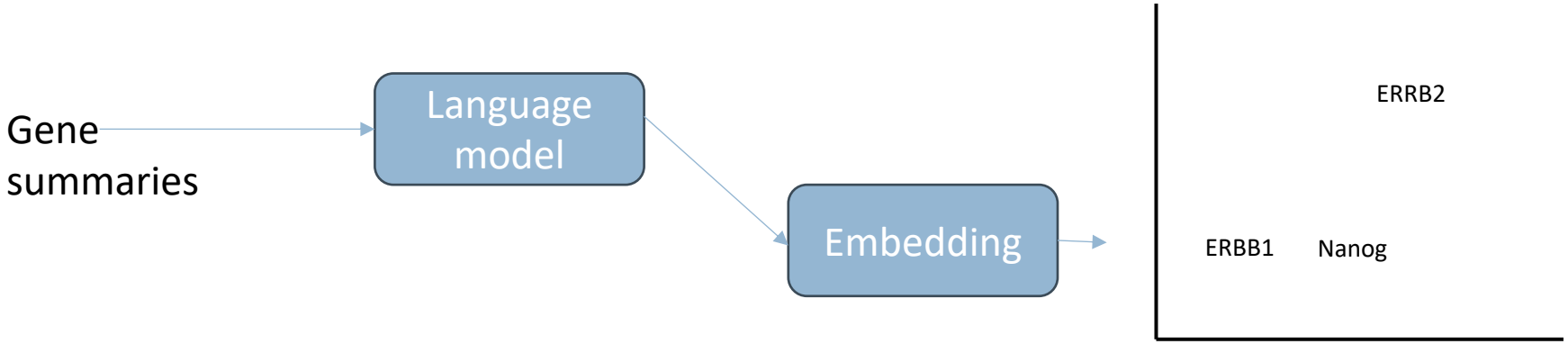
Country-Capital

Closer points are more similar

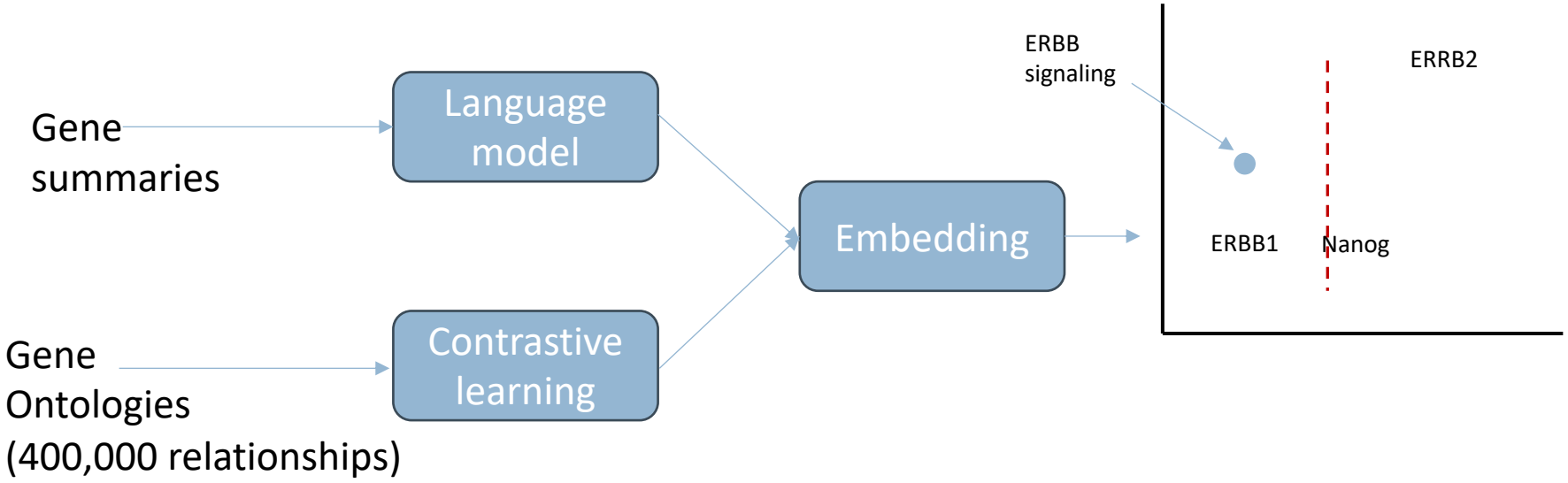
Contrasting similar and dissimilar Ontology-Gene relationships



GeneLLM: framework to extract insights from text and ontologies



GeneLLM: framework to extract insights from text and ontologies



- Problem
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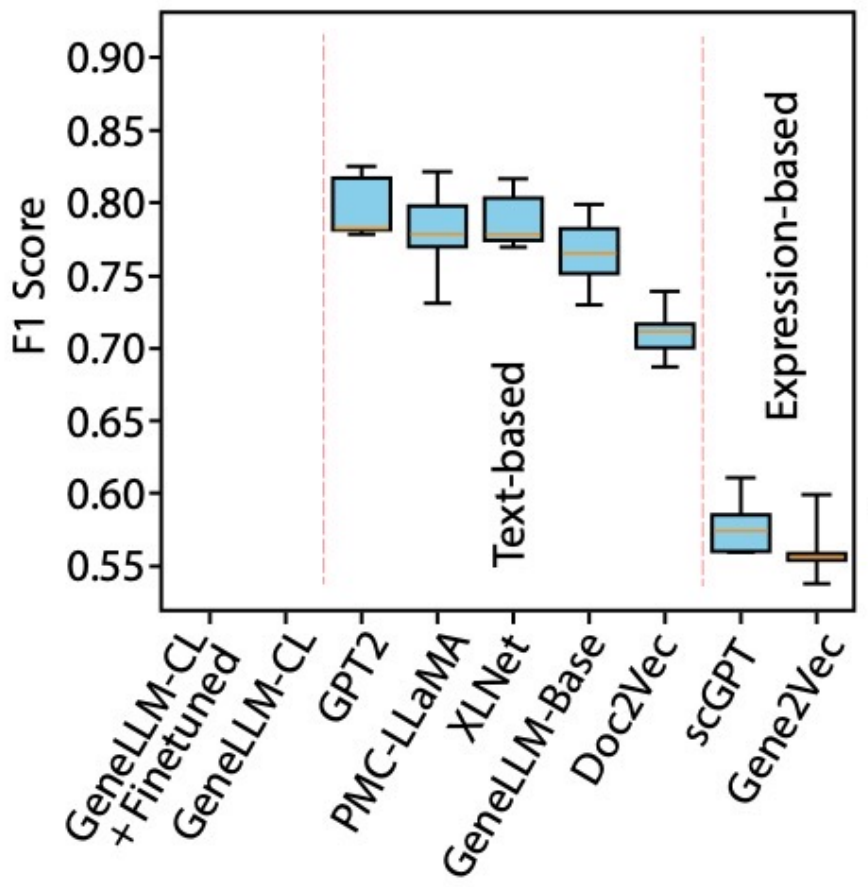
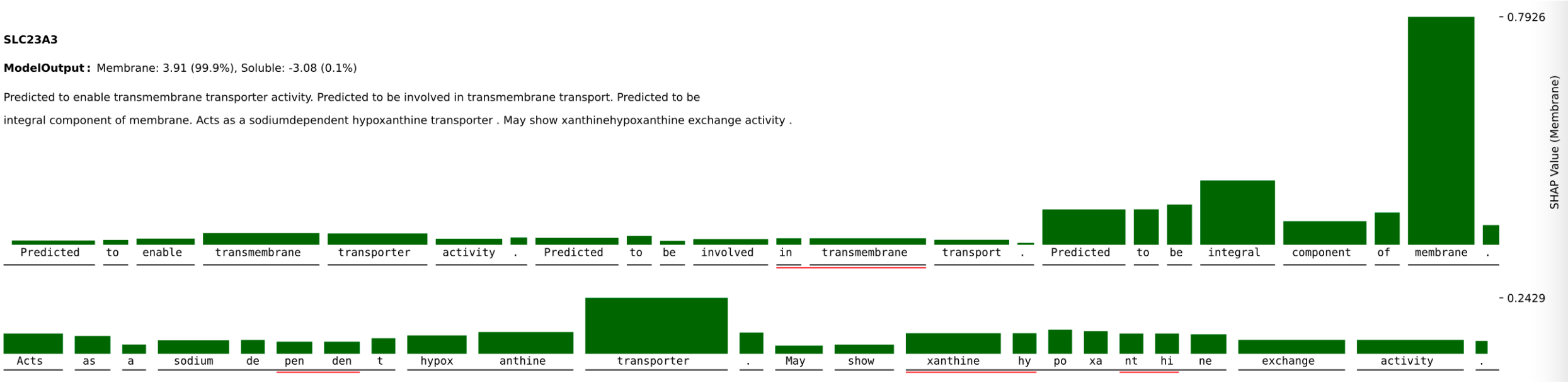
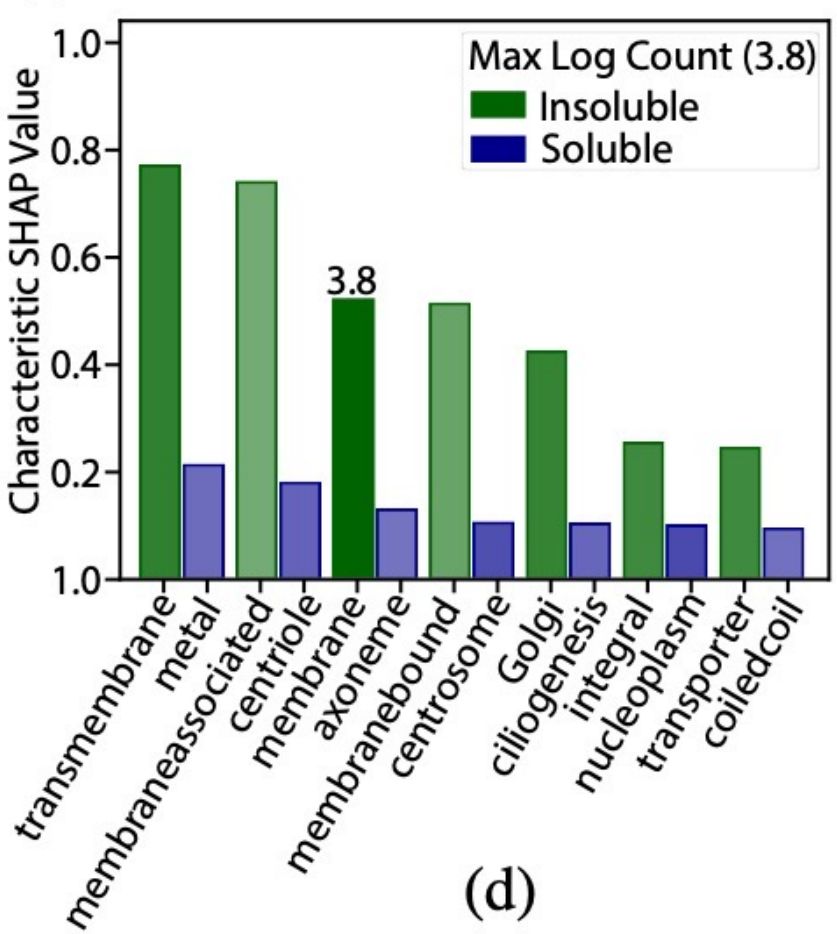
Text is more effective for protein solubility prediction



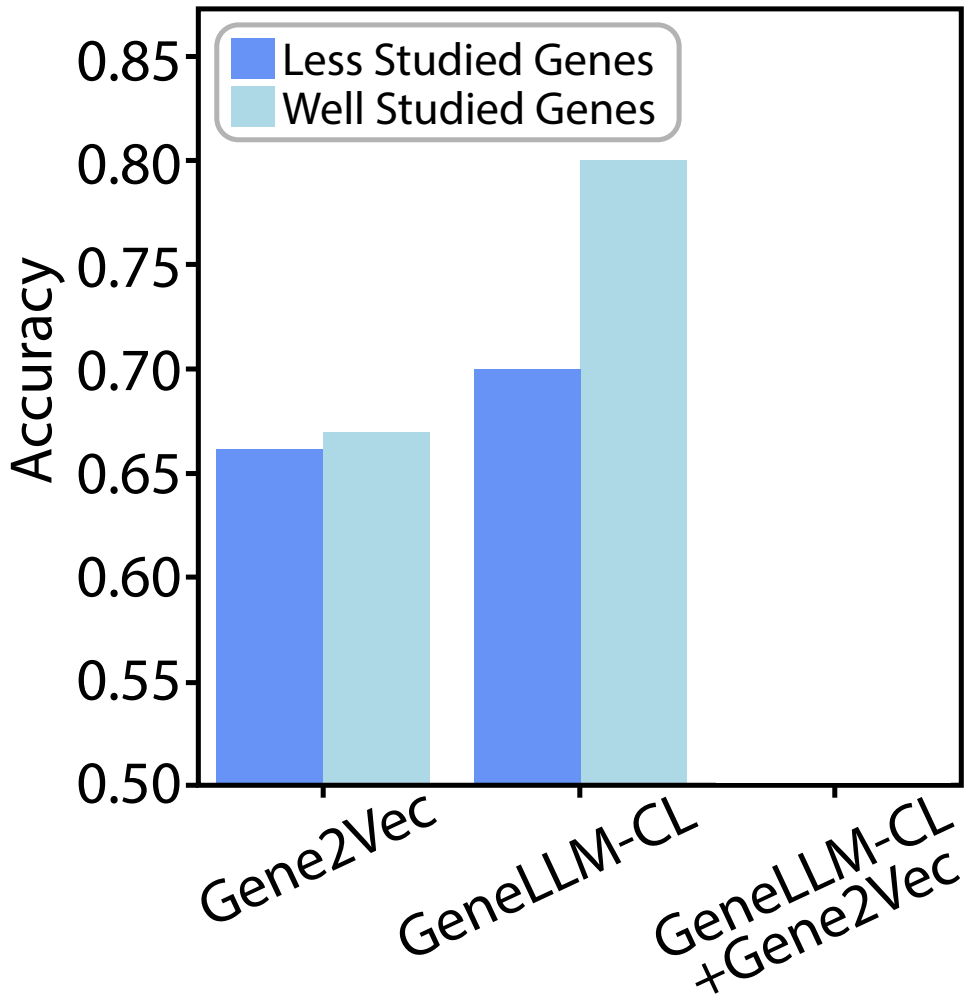
Membrane important word for predicting solubility: Interpreting Predictions with SHAP



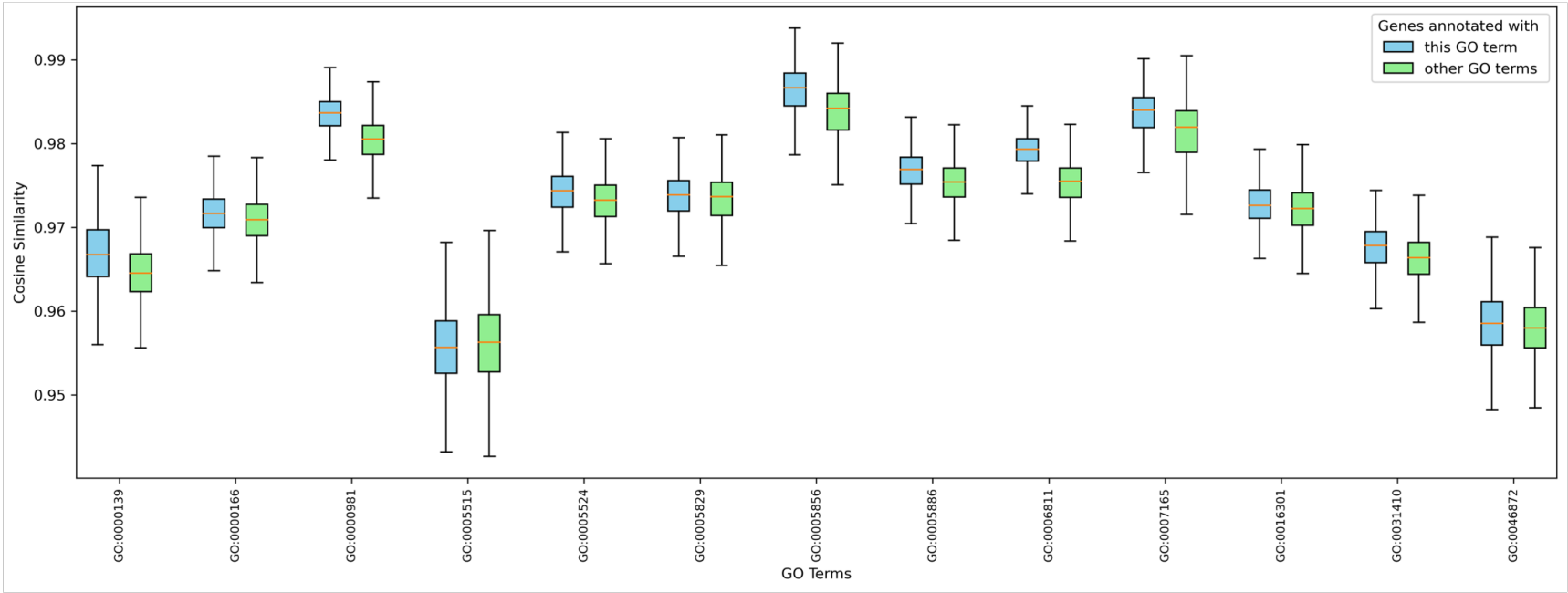
Important word for predicting solubility

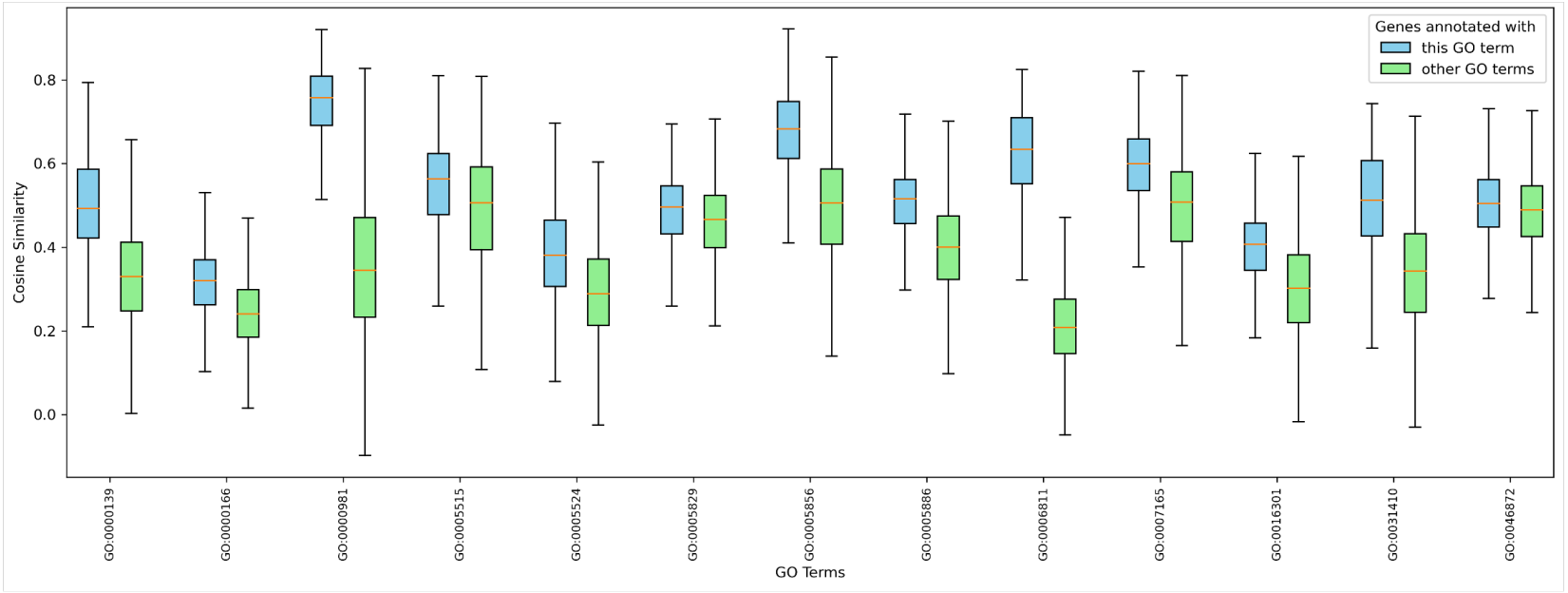


Structured data can mitigate knowledge bias in text

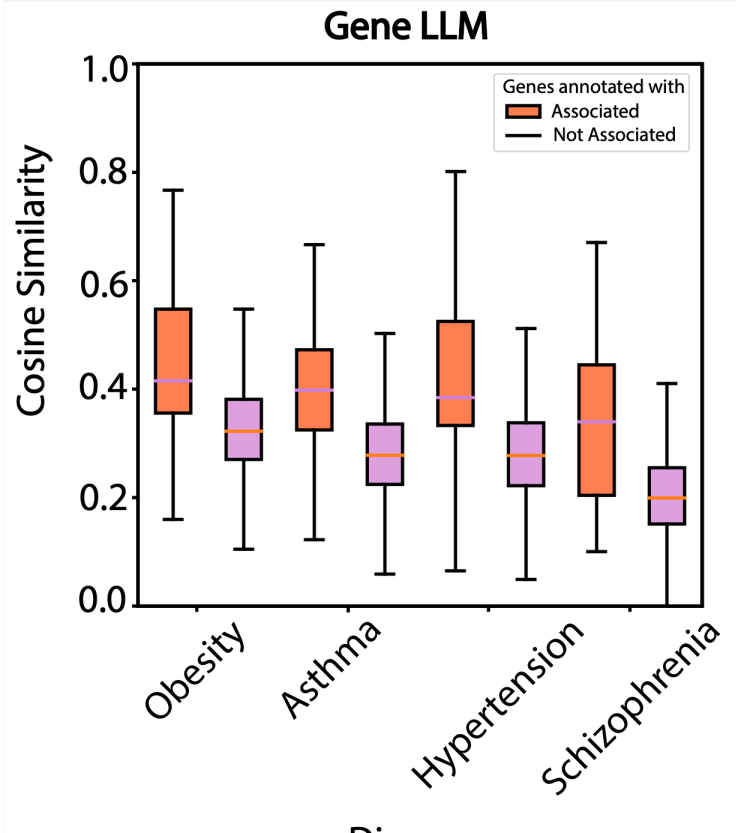


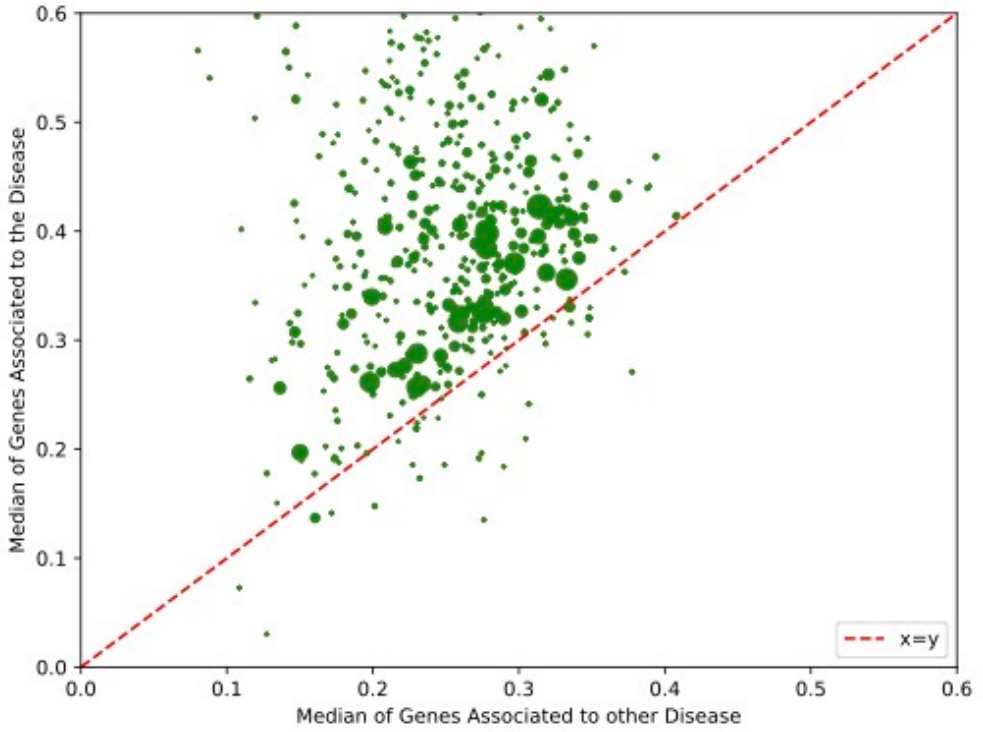
Contrastive learning enables zero-shot learnability



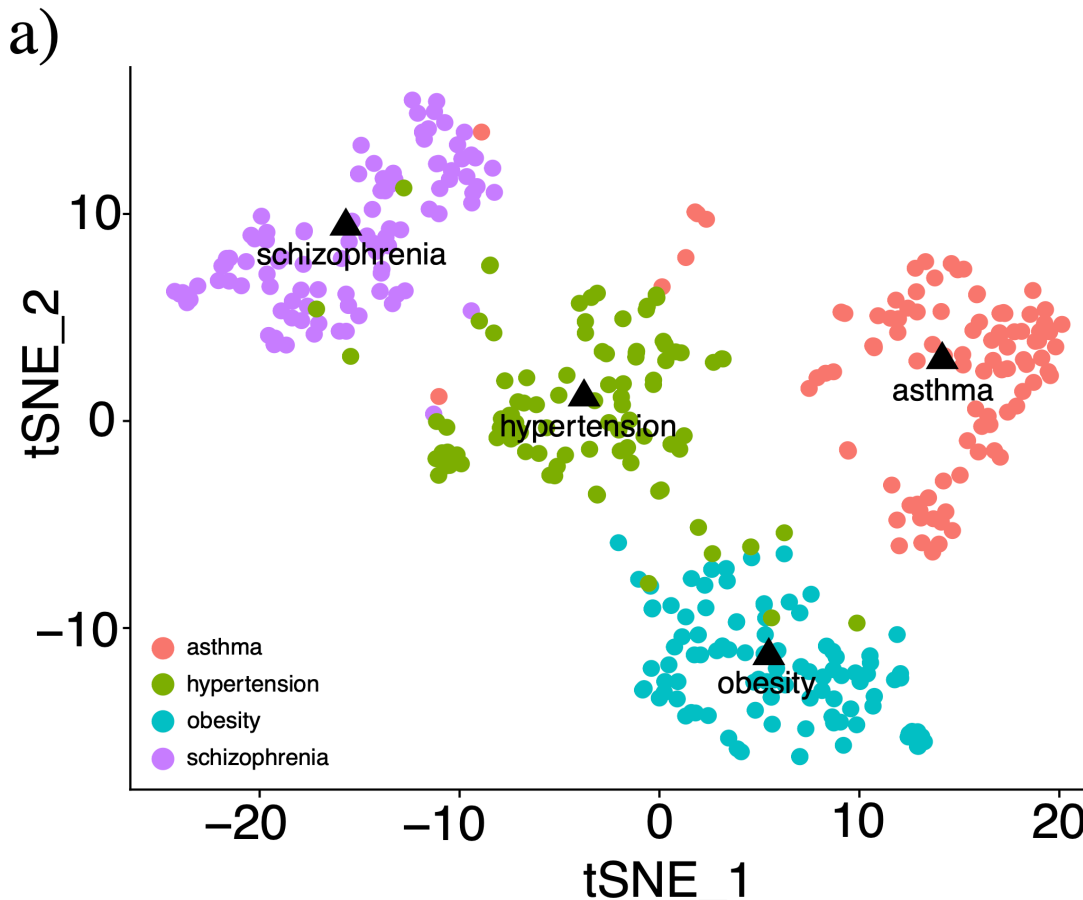


Zero-shot prediction of risk genes

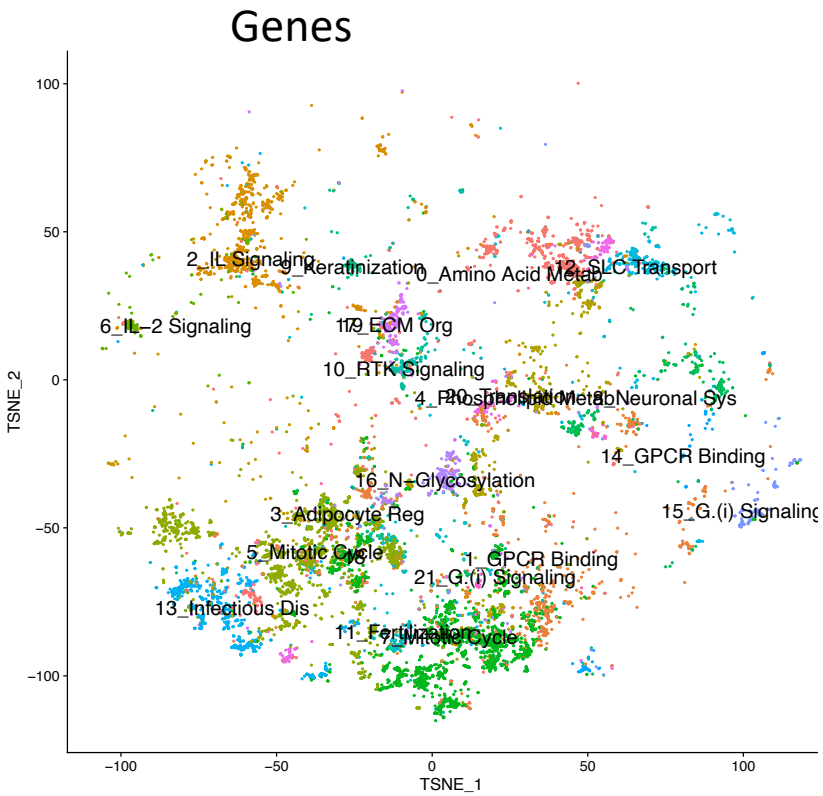


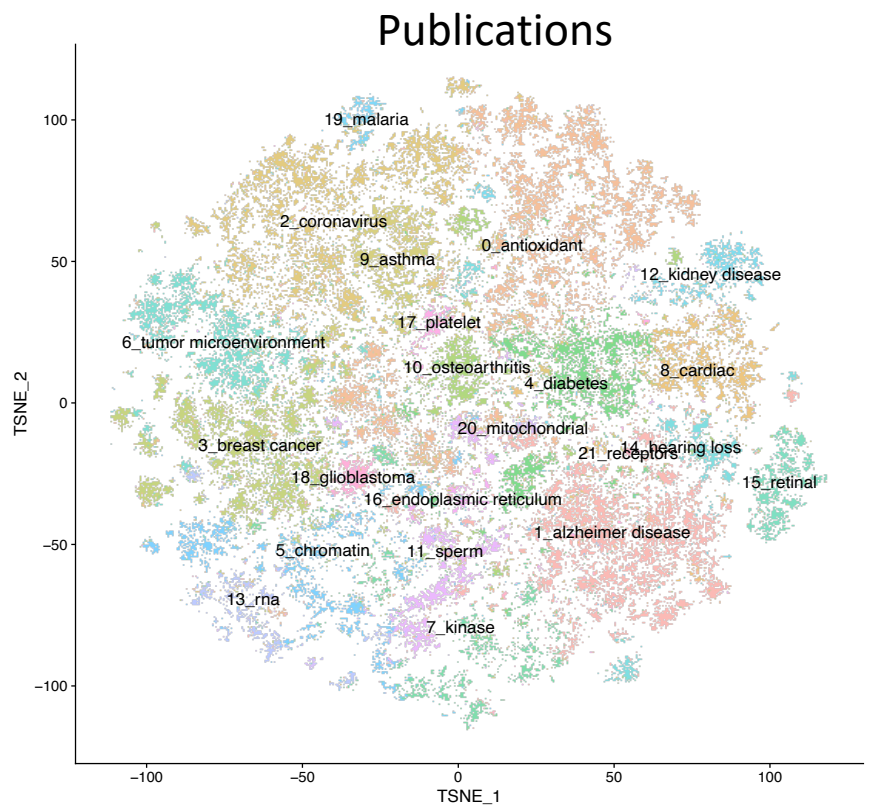


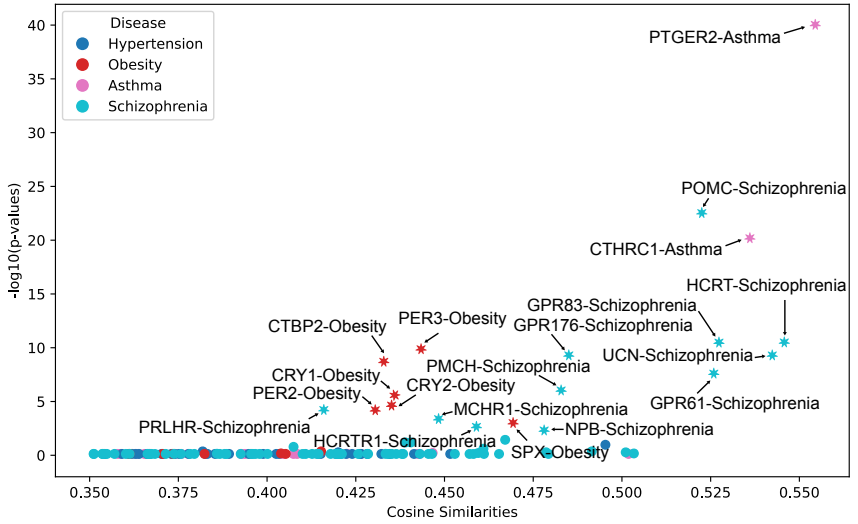
Novel risk genes identification



Can GeneLLM ground disease-gene predictions in scientific literature?







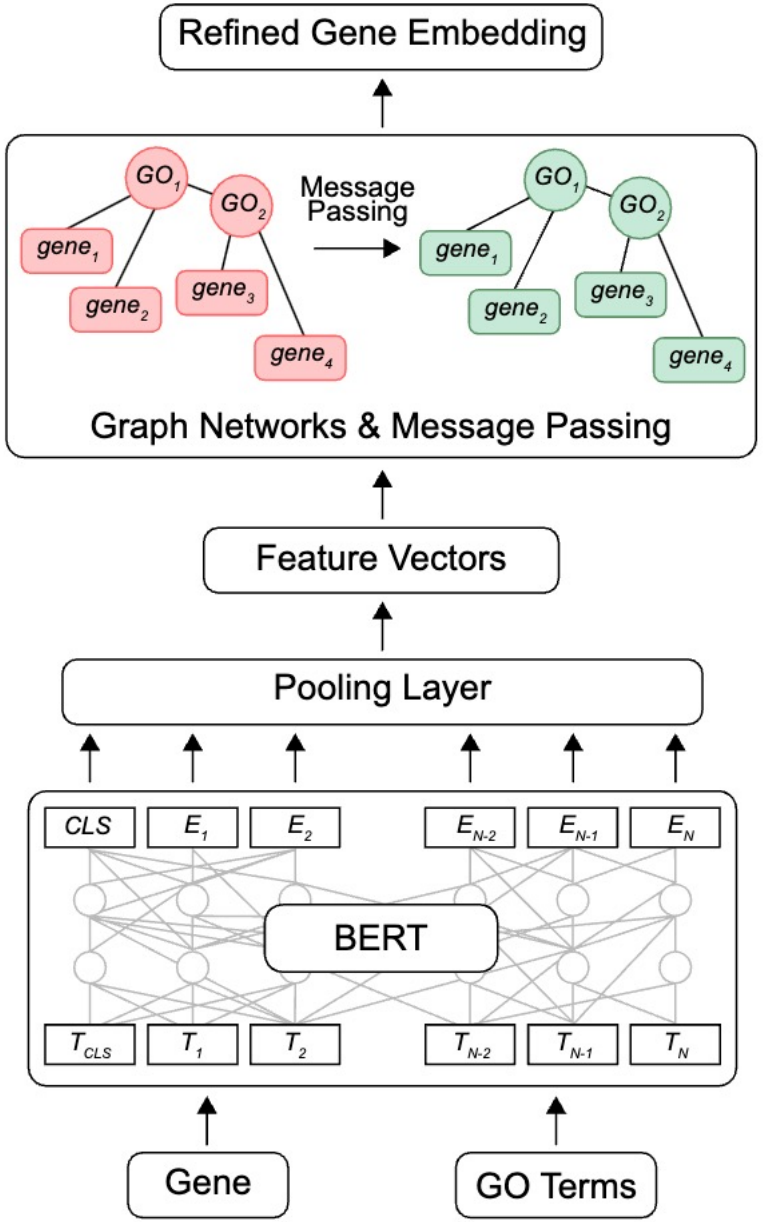
GeneLLM is a foundation model

Model	Dosage Sensitivity	BivalentVs Lys4 Methylated	BivalentVs Non Methylated	Tf range	Tf target type	Solubility	Subcellular localization	Conservation (Pearson Corr.)
Majority Classifier	0.73 ± —	0.58 ± —	0.75 ± —	0.73 ± —	0.41 ± —	0.52 ± —	0.39 ± —	— ± —
GPT2	0.74 ± 0.04	**0.86 ± 0.04**	0.80 ± 0.11	0.71 ± 0.03	0.18 ± 0.02	0.80 ± 0.02	0.77 ± 0.01	0.31 ± 0.02
Doc2Vec	0.74 ± 0.04	0.84 ± 0.06	0.78 ± 0.05	0.66 ± 0.07	0.26 ± 0.01	0.71 ± 0.03	0.69 ± 0.02	0.34 ± 0.01
PMC-LLaMA	0.86 ± 0.05	0.77 ± 0.04	**0.84 ± 0.07**	0.64 ± 0.08	0.08 ± 0.01	0.78 ± 0.03	0.69 ± 0.01	**0.55 ± 0.01**
XLNet	0.74 ± 0.06	0.84 ± 0.06	0.83 ± 0.08	0.69 ± 0.05	0.12 ± 0.01	0.79 ± 0.02	0.76 ± 0.01	0.40 ± 0.01
Gene2Vec	0.84 ± 0.04	0.84 ± 0.06	0.75 ± 0.06	**0.75 ± 0.08**	0.21 ± 0.01	0.56 ± 0.02	0.54 ± 0.02	0.50 ± 0.02
BERT-Base	0.76 ± 0.09	0.83 ± 0.06	0.77 ± 0.10	0.68 ± 0.04	0.17 ± 0.01	0.77 ± 0.02	0.76 ± 0.01	0.43 ± 0.01
GeneLLM	**0.87 ± 0.06**	**0.86 ± 0.09**	0.82 ± 0.08	0.74 ± 0.07	**0.49 ± 0.04**	**0.89 ± 0.01**	**0.83 ± 0.01**	0.53 ± 0.01

Genen outperforms GeneLLM

Model	Dosage Sensitivity	BivalentVs Lys4 Methylated	BivalentVs Non Methylated	Tf range	Tf target type	Solubility	Subcellular localization	Conservation (Pearson Corr.)
GPT2	0.83 ± 0.06	0.91 ± 0.06	0.83 ± 0.09	**0.67 ± 0.13**	0.52 ± 0.04	0.88 ± 0.01	0.91 ± 0.00	0.31 ± 0.02
Doc2Vec	0.78 ± 0.09	0.90 ± 0.08	0.79 ± 0.11	0.47 ± 0.09	0.54 ± 0.04	0.85 ± 0.02	0.85 ± 0.01	0.34 ± 0.01
PMC-LLaMA	**0.89 ± 0.04**	0.87 ± 0.03	**0.90 ± 0.09**	0.52 ± 0.45	0.06 ± 0.01	0.78 ± 0.03	0.83 ± 0.01	**0.55 ± 0.01**
XLNet	0.81 ± 0.08	0.90 ± 0.06	0.81 ± 0.06	0.61 ± 0.08	0.52 ± 0.01	0.86 ± 0.02	0.89 ± 0.01	0.40 ± 0.01
Gene2Vec	0.88 ± 0.04	0.88 ± 0.07	0.75 ± 0.06	0.56 ± 0.12	**0.58 ± 0.01**	0.60 ± 0.02	0.73 ± 0.01	0.50 ± 0.02
BERT-Base	0.85 ± 0.06	0.87 ± 0.05	0.85 ± 0.07	0.49 ± 0.11	0.53 ± 0.02	0.84 ± 0.02	0.90 ± 0.01	0.43 ± 0.01
GeneLLM	**0.89 ± 0.06**	0.87 ± 0.08	0.79 ± 0.10	0.47 ± 0.04	— ± —	0.89 ± 0.01	0.94 ± 0.03	0.53 ± 0.01
GCN	**0.89 ± 0.03**	**0.92 ± 0.01**	**0.90 ± 0.03**	0.59 ± 0.08	0.52 ± 0.03	**0.99 ± 0.02**	**0.95 ± 0.00**	**0.55 ± 0.01**

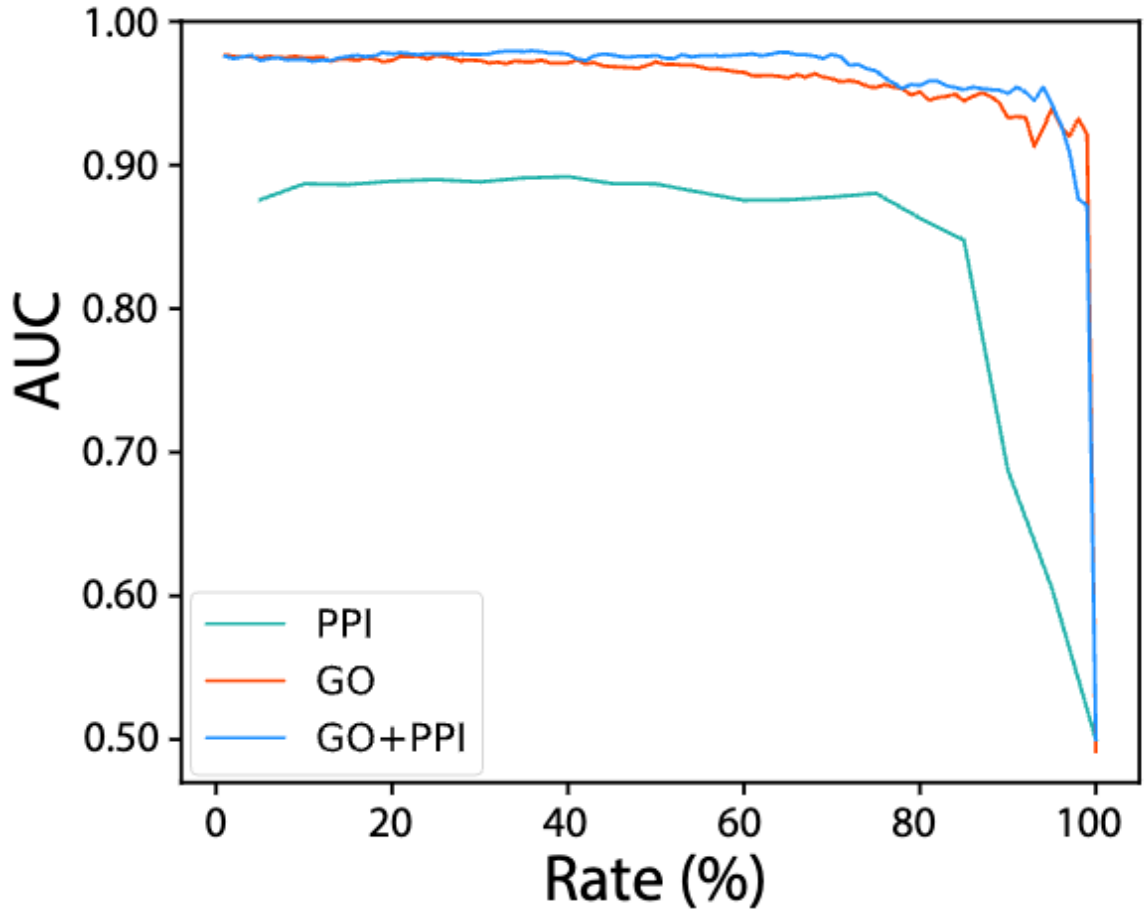
GNN are more effective in leveraging relational data



Yue Hu

Yanfu Zhang

Information propagation infers gene information with 75% data hidden



GeneLLM website
litgene.tumorai.org

Summary

- Text data complements structured data complements and could mitigate knowledge bias
- Increasing interpretability and mitigating bias of AI models enhance their utility
- Scientific literature could be leveraged to increase AI reliability

Acknowledgements

TUMOR AI
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Michael Servilla

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