

In Silico Discovery of Hemolytic Peptides Through a Novel Approach Based on Network Science and Similarity Searching Methods

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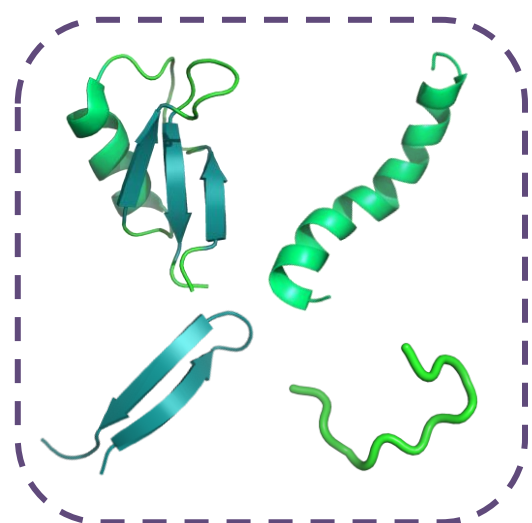
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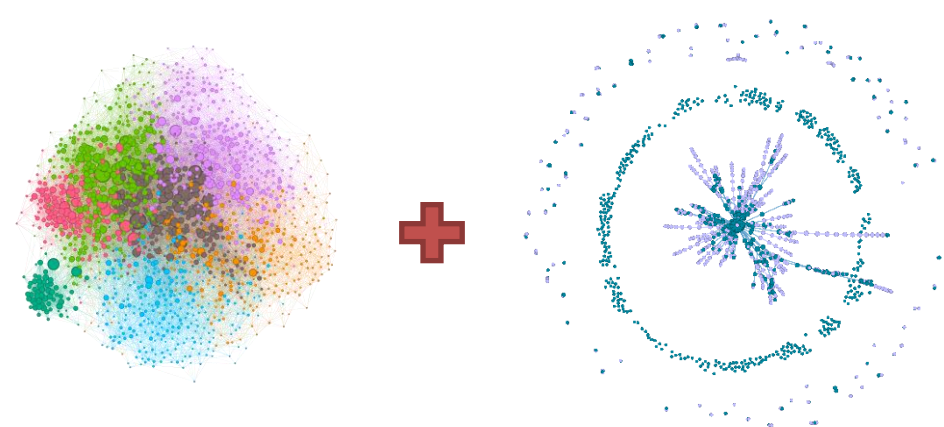
INTRODUCTION & AIM

- Thousands of potential therapeutic peptides
- Only 60 available on the market!



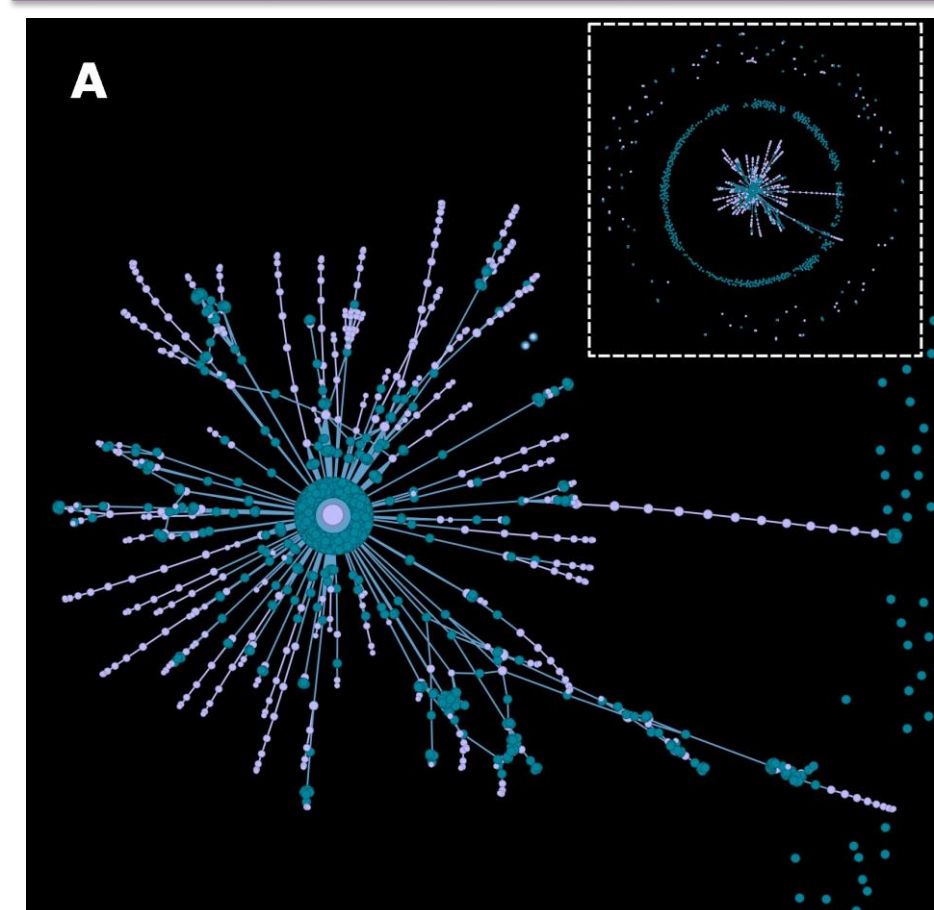
- Antibacterial
 - Anticancer
 - Antiviral
 - Tumor-homing
 - Antiparasitic
- Hemolytic (Toxic)**

AIM:
Better understanding of hemolytic peptides

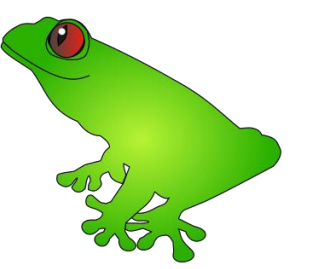


- Origin, function, dataset and target metadata information
- Chemical space exploration
- Motif Discovery
- Model Classifier

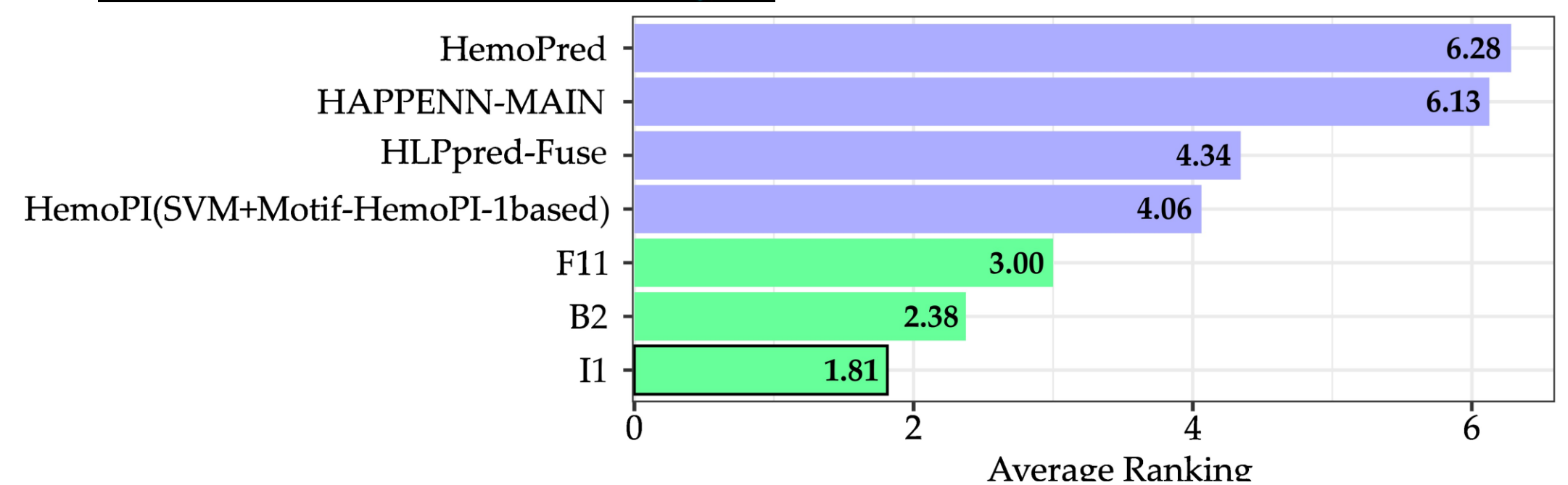
RESULTS & DISCUSSION



- 52.8% synthetic peptides
- Class Amphibia
- 94.5% both hemolytic and antimicrobial
- Evaluated against human pathogens

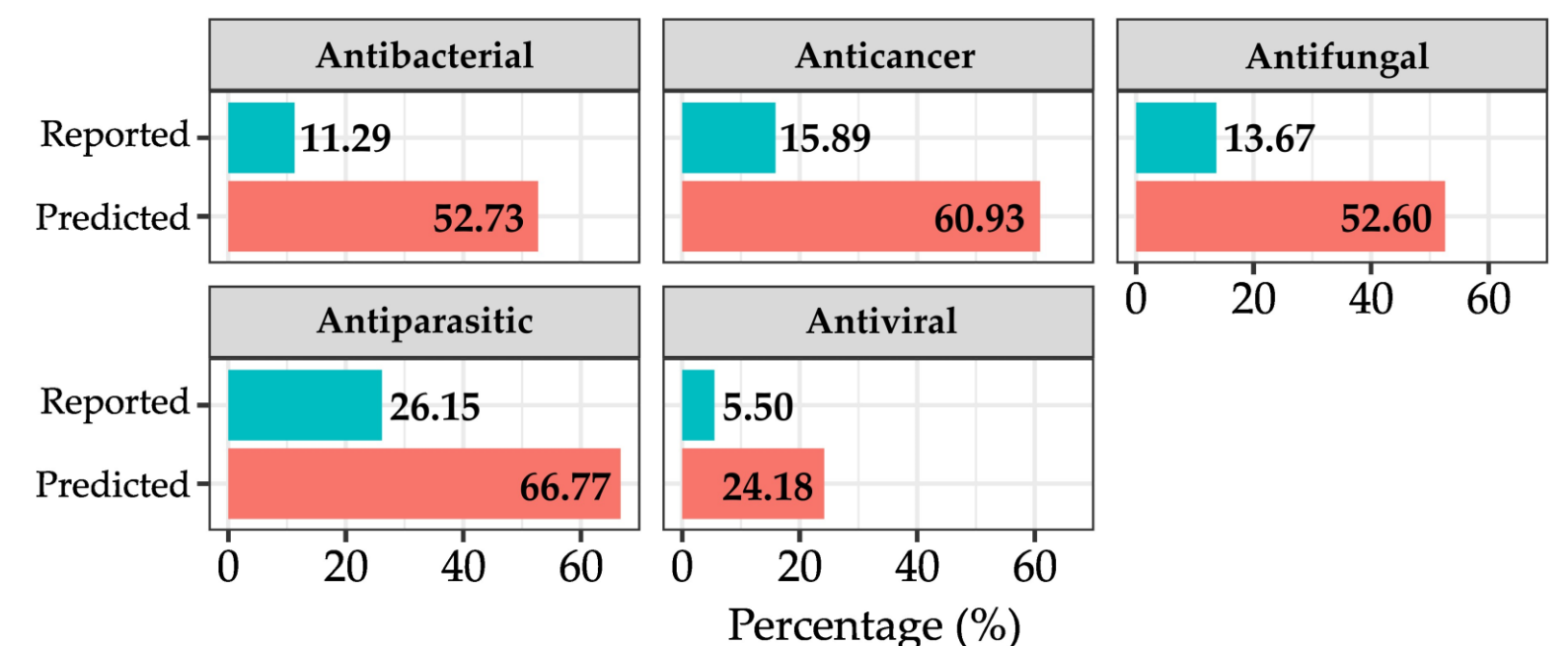


- MQSS models outperformed 10 state-of-the-art ML-based model classifiers



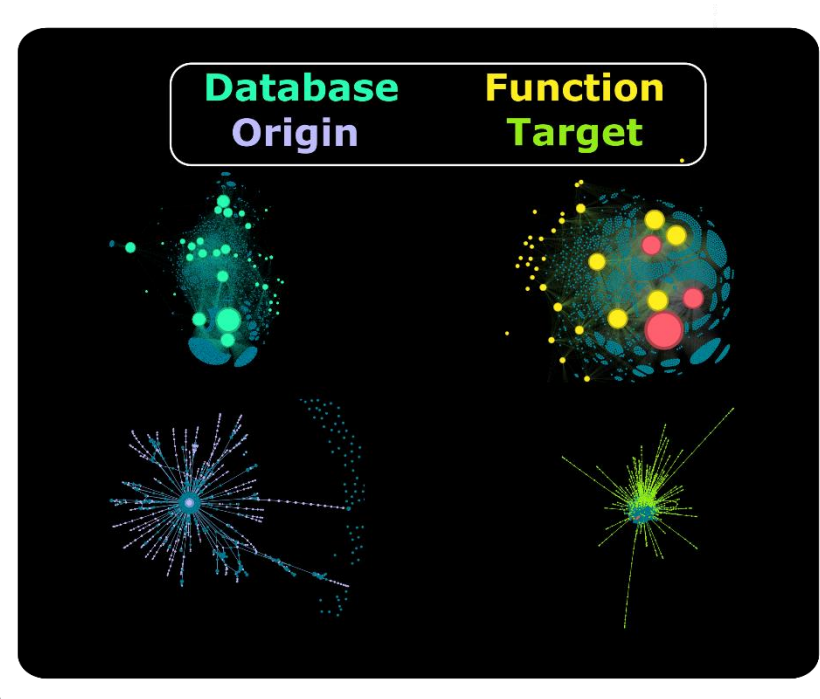
- Prediction: 3.9-fold increase of hemolytic peptides

Hemolytic Activity



METHODS

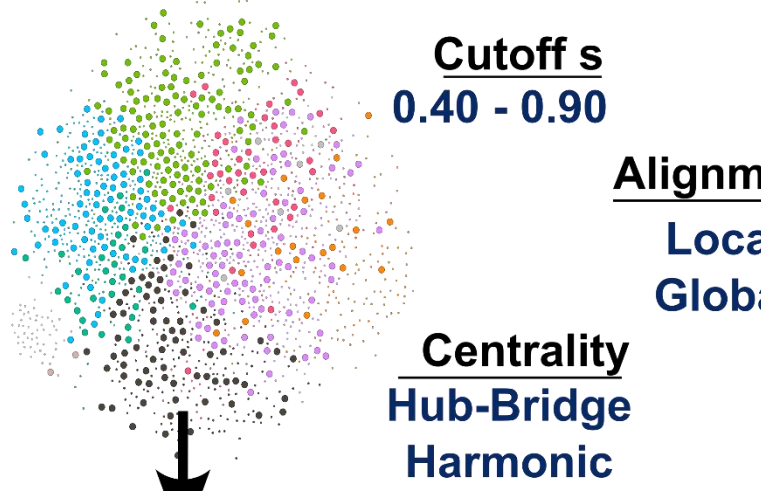
(i) Metadata Networks



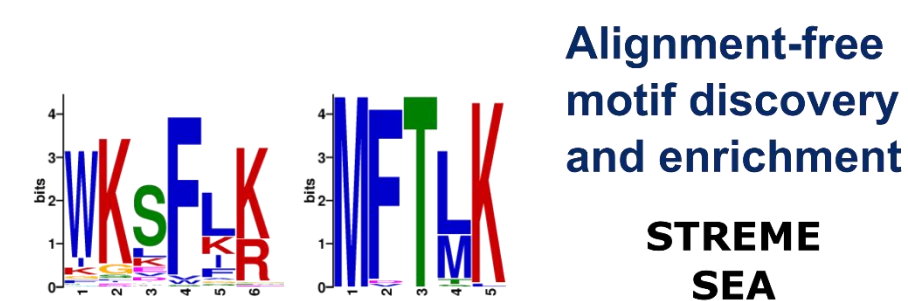
(ii) Half-Space Proximal Networks



(iii) Scaffold Extraction



(iv) Motif Discovery



46 hemolytic motifs

Table 1.

No.	Motif	HemoPI-1			StarPepDB			Big-Hemo		
		ER ^a	E-value	Rank ^b	ER ^a	E-value	Rank ^b	ER ^a	E-value	Rank ^b
1	ALKAIS	3.66	1.92E-09	36	40.10	3.53E-21	35	3.32	8.48E-12	9
2	WKSFJK	19.20	2.80E-40	2	5.06	3.55E-158	1	4.94	6.01E-22	3
3	AKKAL	16.10	7.19E-29	11	3.33	6.66E-101	4	1.55	6.30E-04	24
4	LKKL	12.60	1.44E-31	4	3.62	2.65E-130	2	1.68	1.37E-08	12
5	ISWIK	7.86	5.69E-19	19	6.19	3.45E-59	15	2.51	4.45E-05	22

CONCLUSION

- New approach to explore the chemical space of hemolytic peptides
- Robust model classifiers developed using MQSS method
- Discovery of new motifs associated with hemolytic activity

FUTURE WORK

- Use 3D structure information to develop MQSS models
- Implementation of hemolytic potency models

REFERENCES:

- Castillo-Mendieta, K.; Agüero-Chapin, G.; Marquez, E. A.; Perez-Castillo, Y.; Barigye, S. J.; Pérez-Cárdenas, M.; Pérez-Giménez, F.; Marrero-Ponce, Y. A New Robust Method for Predicting Hemolytic Toxicity from Peptide Sequence. ChemRxiv November 9, 2023. <https://doi.org/10.26434/chemrxiv-2023-1zqzf>.
- Castillo-Mendieta, K.; Agüero-Chapin, G.; Vispo, N. S.; Márquez, E. A.; Perez-Castillo, Y.; Barigye, S. J.; Marrero-Ponce, Y. Peptide Hemolytic Activity Analysis Using Visual Data Mining of Similarity-Based Complex Networks. Preprints March 17, 2023. <https://doi.org/10.20944/preprints202303.0322.v1>