Leveraging Graph Neural Networks and Self-Supervised Learning to Generate a Meaningful Chemical Latent Space for Olfactory Tasks

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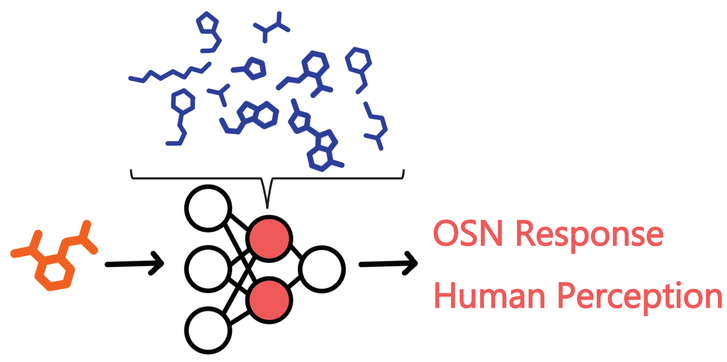
Introduction

• Using odorous molecules to predict human perception or olfactory neuron response is a challenging task.

• Graph neural networks (GNNs) have been shown to perform well analyzing chemical odors to solve complicated olfactory tasks[1-3].

• Self-supervised learning (SSL) has been shown to provide an effective means of regularizing models to reduce overfitting on downstream tasks with limited data[4,5].



Datasets

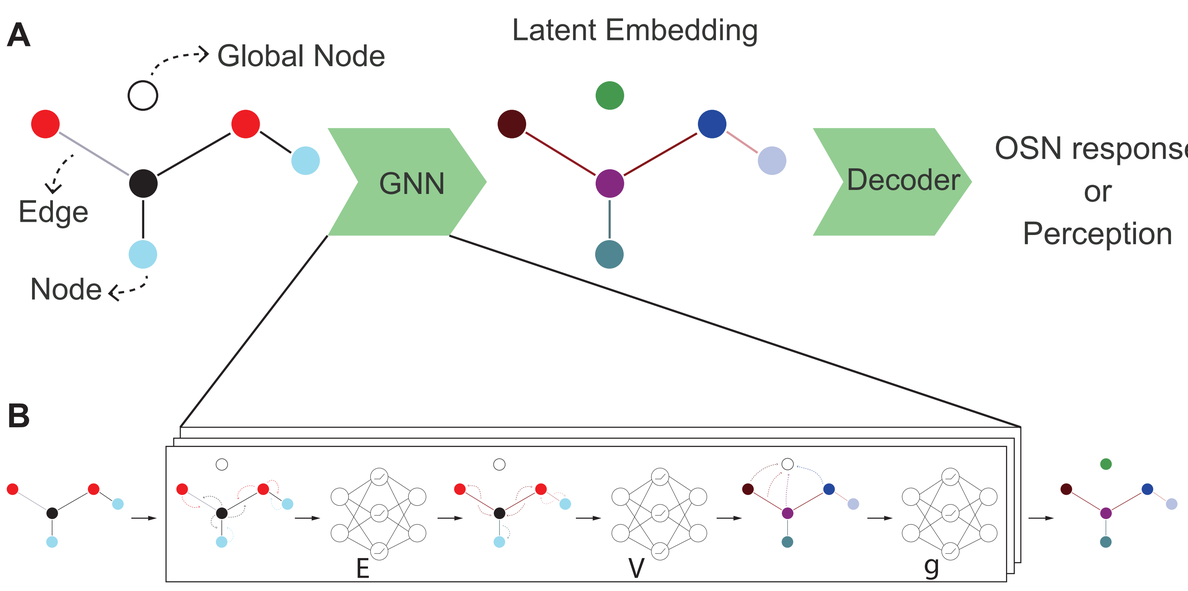
• Zinc15[6] - Close to 1 billion small molecules filtered to 12 million potentially odor like molecules using the “rule of three”[7].

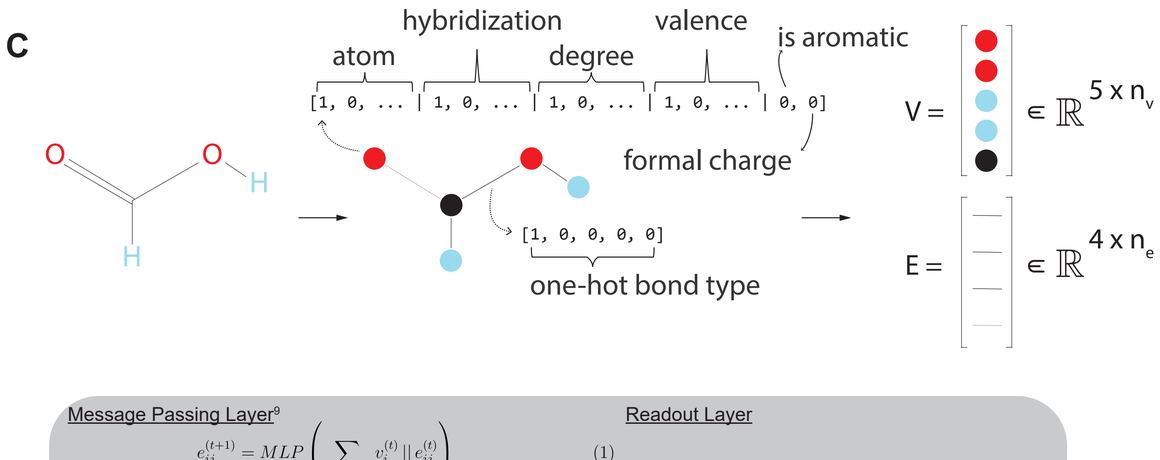
• DoOR[8] - Consensus odorant response profiles for almost every olfactory sensory neuron (OSN) in Drosophila melanogaster.

• Leffingwell / Good Scents[1] - About 5,000 odorous molecules labeled based on human perception.

Methods

Mapping molecular graphs to olfactory tasks using GNNs





Message Passing Layer[9]

$$e_{ij}^{(t+1)} = MLP\left(\sum_{i \in N(e_{ij})} v_i^{(t)} \,||\, e_{ij}^{(t)}\right) \quad (1)$$

$$v_i^{(t+1)} = MLP\left(\sum_{j \in N(v_i)} e_{ij}^{(t+1)} \,||\, v_i^{(t)}\right) \quad (2)$$

$$g^{(t+1)} = MLP\left(\sum_i \sum_j e_{ij}^{(t+1)} \,||\, \sum_i v_i^{(t+1)} \,||\, g^{(t)}\right) \quad (3)$$

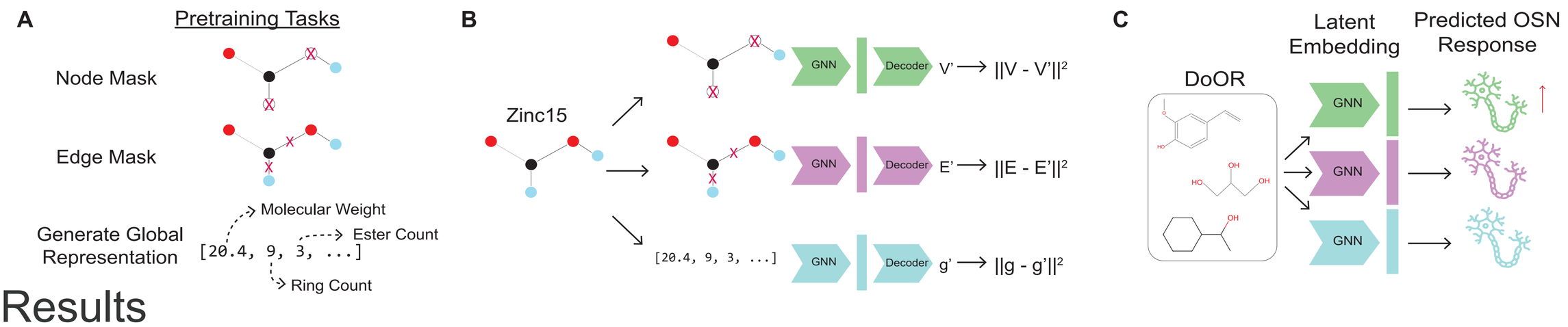
Readout Layer

$$\hat{y}_{global} = DECODER\left(g^{(T)}\right) \quad (4)$$

$$\hat{y}_{node} = DECODER\left(V^{(T)}\right) \quad (5)$$

$$\hat{y}_{edge} = DECODER\left(E^{(T)}\right) \quad (6)$$

Exploring predictive performance with SSL on a large unlabeled set of odors

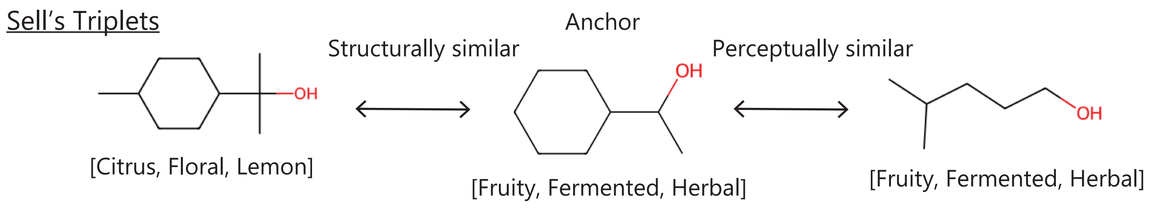


Results

SSL techniques prove effective at enhancing OSN prediction but not human perception prediction

	No Pretrain	Edge Mask	Node Mask	Global	Node Mask + Global
Human Percept (AUROC)	**0.752 [0.012]**	0.635 [0.015]	0.684 [0.011]	0.708 [0.015]	0.724 [0.012]
OSN Prediction (Fraction Correct)	0.307 [0.032]	0.291 [0.049]	0.324 [0.054]	0.362 [0.026]	**0.376 [0.032]**

Latent spaces generated from pre-training exhibit superior performance on adversarial challenges



	No Pretrain	Edge Mask	Node Mask	Global	Node Mask + Global
Fraction Correct	0.249	0.282	**0.294**	0.252	0.154

Discussion / Future Directions

• Inspiration from CNNs and the visual system and maximally excitatory stimulus.

• More complicated pre-training tasks that incorporate domain knowledge of olfaction.

• Expedite deorphanization experiments with online learning.

References

[1] Lee, B. K., et. al. Science (2023). [2] Wei, J. N., et. al. arXiv (2022) [3] Qian, W. W., et. al. eLife (2023) [4] Hu, W. et al. arXiv (2020). [5] Liu, Y. et al. IEEE (2023). [6] T. Sterling and J. J. Irwin, J. Chem. Inf. Model. (2015) [7] E. J. Mayhew et al., Proceedings of the National Academy of Sciences (2022) [8] D. Münch and C. G. Galizia, Sci Rep (2016) [9] Battaglia, P. W., et al. arXiv (2018).

Acknowledgements

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