Computational analysis in whole brain of *C. elegans* uncovers inherent hyperbolic geometry and aids in discovery of neural receptive fields

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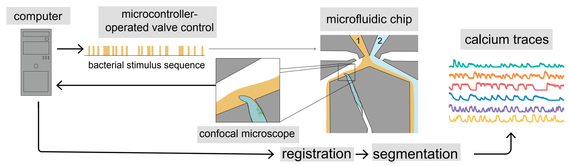
Introduction

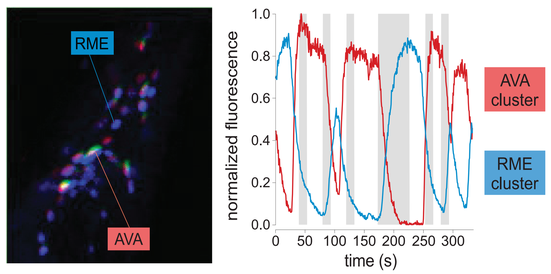
We examined recorded whole-brain activity of Caenorhabditis elegans (*C. elegans*) experiencing bacterial food stimuli and modeled how sensory inputs affect sensory and motor neurons in a network state dependent manner. We classified active neurons into six functional clusters: two sensory neuron clusters (ON, OFF), and four motor/command neuron clusters (AVA, RME, SMDD, SMDV). We proceeded to analyze our multi-dimensional calcium trace data without losing the distance measures between points using a hyperbolic embedding technique, Hyperbolic Multidimensional Scaling (HMDS). The relationship between stimulus and neuronal output, the receptive field, for each category of neuron was analyzed using Maximum Noise Entropy (MNE). In short, we aim to use computational methods inspired by techniques in non-Euclidean geometry and Information heory to analyze *c. elegans* whole brain calcium imaging data in an attempt to uncover potential network states and their dynamics.

C. elegans whole brain imaging

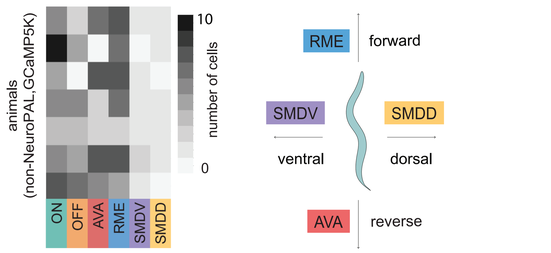


Adult animals were washed, treated with a paralytic and loaded into in a microfluidic device that trapped the worm body while exposing only the nose to patterns of fluctuating bacteria and M9 buffer liquid flows flows. Changes in fluorescence were observed using Zeiss Airyscan 880, at 2 volumes per second in z plane.

Sensory and Motor Neuron Classification

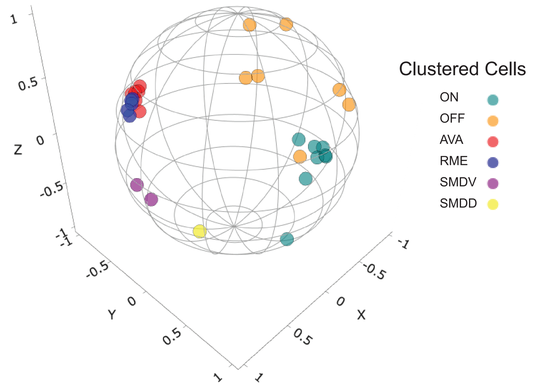


Fluorescence imaging of genetically-encoded nuclear-localized calcium indicator (GCaMP5K) was compared to a Neuropal strain to confirm cell identity associated with activity patterns found in the primary strain.

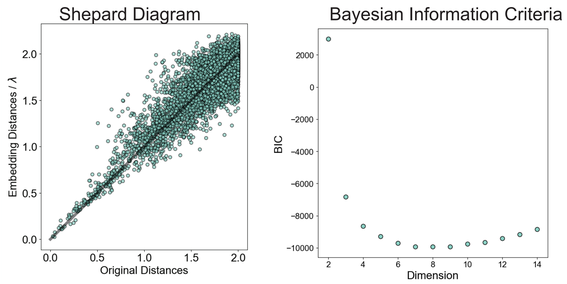


Calcium traces of active neurons could be divided into six functional clusters based on correlated changes in GCaMP fluorescence: two sensory neuron clusters: ON and OFF and four motor/command neuron clusters: AVA, RME, SMDD, SMDV

Hyperbolic Multi Dimensional Scaling

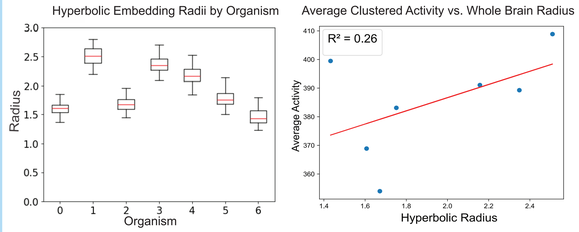


Hyperbolic Embedding Distances and System Dimensionality



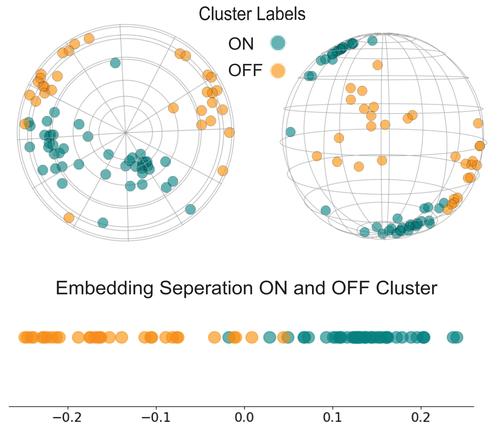
Embedding distances scale linearly with lamda paprameter in HMDS analysis, which shows that the whole brain exhibits a hyperbolic geometry.

Calcium Activity Increases with Hyperbolic Radius



Average activity level of all categorized cells in each organism was determined to be positively correlated with increasing hyperbolic embedding radius.

Hyperbolic Embedding Tangent Space Analysis



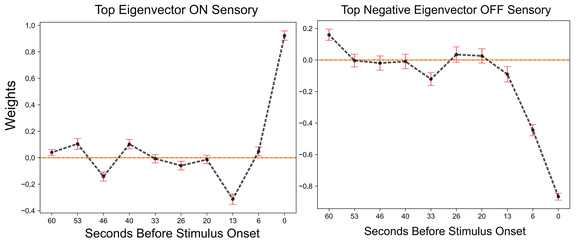
Using hyperbolic embedding coordinates of opposing neuronal clusters, a single axis was determined to effectively seperate each pair of clusters: ON/OFF, AVA/RME, and SMDV/SMDD.

Determining Neuronal Receptive Fields with Maximum Noise Entropy

$$P(y=1 \mid \mathbf{s}) = \frac{1}{1+e^{-z(\mathbf{s})}}, \quad z(\mathbf{s}) = a + \mathbf{h}^\top \mathbf{s} + \mathbf{s}^\top \mathbf{J} \mathbf{s}$$

Probability of a binary response of a neuron to a stimulus vector is modeled using a logistic function of a linear combination of inputs in the expanded feature space. where unknown weights a, h, and J are determined by minimizing the negative log-likelihood.

MNE Determines Neuronal Receptive Fields



In sensory neurons, the receptive field corresponds to a stimulus increasing approximately 13 seconds before response onset for ON neurons and decreasing 20 seconds before for OFF neurons. RFs are represented using the top-most eigenvector of the diagonalized J matrix averaged over trials.

Conclusions

- Neuropal image analysis confirms cell identities of clustered calcium traces, allows neural classification into 6 distinct neural types
- HMDS shows *c. elegans* exhibit a hyperbolic geometry, BIC shows average of 8 optimal dimensions persists across all organisms
- Quadratic MNE component in sensory neurons elucidates temporal nature of receptive fields, shows different timescale depending on neural type

References

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