



A Protein-Protein Interactome for an African Cichlid

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1. Motivation

- *Astatotilapia burtoni* is a mouthbrooding African cichlid fish
- Mouthbrooding – a period of roughly 2 weeks where a mother will protect her developing offspring in her mouth, while simultaneously ceasing to eat
- Mouthbrooding is a complex behavioral phenotype that involves an energy reallocation from mother to offspring, which is counterproductive to individual fitness
- Preliminary research has shown that mouthbrooding is associated with dysregulation of neuropeptides related to feeding behavior and parental care

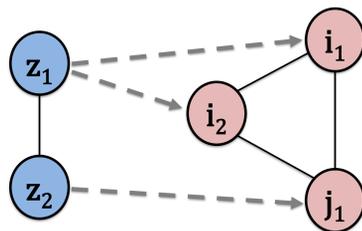


How can we use a systems-level approach to study the molecular substrates of mouthbrooding in a non-model organism?

2. Constructing an Orthologous Interactome

We constructed an orthologous protein-protein interactome for *A. burtoni* from an existing zebrafish (*Danio rerio*) protein-protein interactome using the following rule:

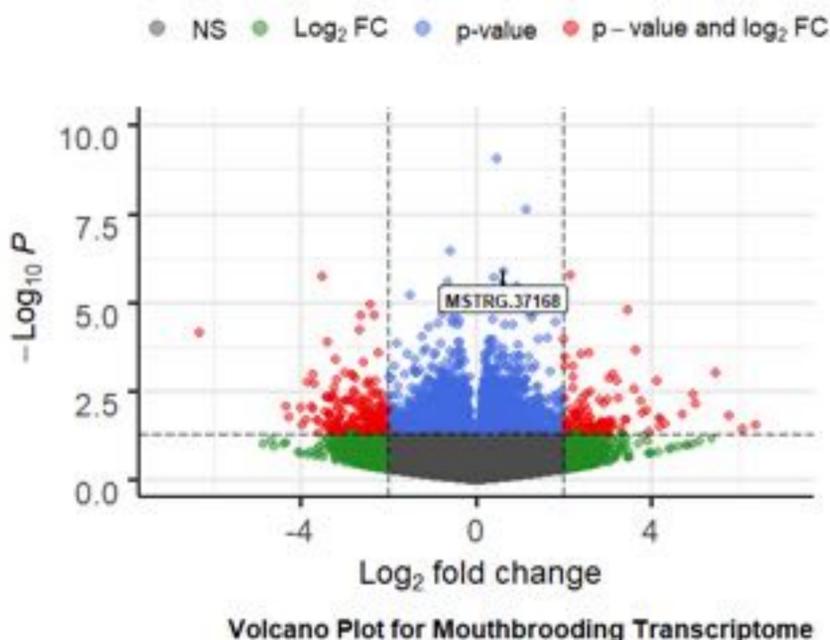
For zebrafish proteins z_1, z_2 that share an interaction (z_1, z_2) , with corresponding *A. burtoni* ortholog sets $T_1 = \{i_1, i_2, \dots, i_k\}$, $T_2 = \{j_1, j_2, \dots, j_l\}$, create a set of interactions between all $t_1 \in T_1$ and all $t_2 \in T_2$.



Orthologs for *A. burtoni* were generated using OrthoFinder. The resulting network was weighted with gene expression data from the brains mouthbrooding fish.

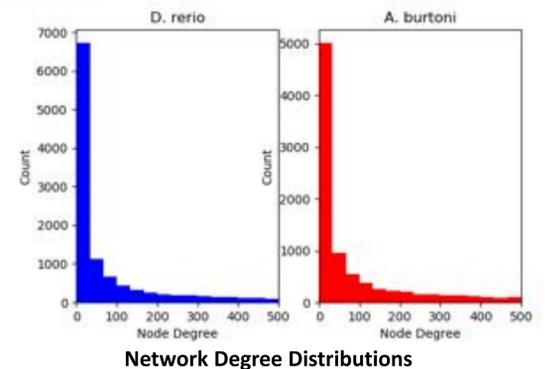
3. Brain Transcriptome Analysis

RNA-seq was performed on the brains of mouthbrooding and non-mouthbrooding fish and analyzed with DESeq2. There were 2,987 differentially expressed transcripts in mouthbrooding fish, 30 of which remained significant when corrected for FDR (Binomial Wald test, $\alpha = 0.05$). Of these transcripts, neurotensin was overexpressed in mouthbrooding fish and was determined to be a candidate gene for mediating this behavior, due to its involvement in both feeding and parental care (MSTRG.37168).

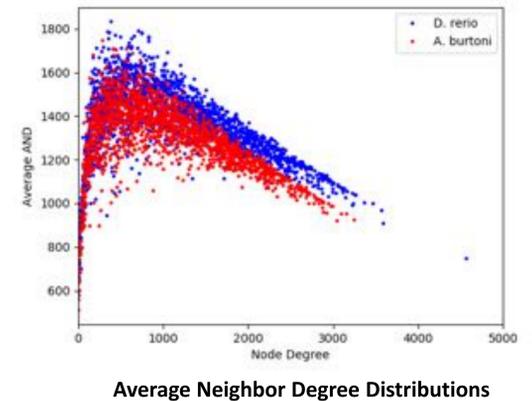
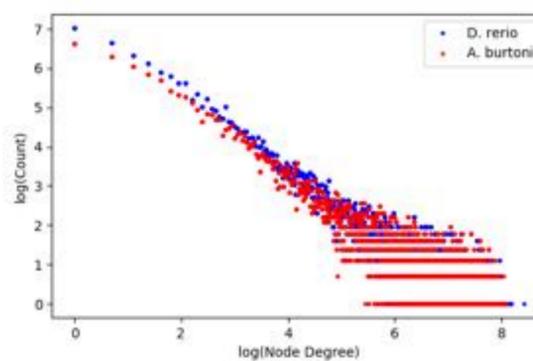


4. A Weighted PPI for *A. burtoni*

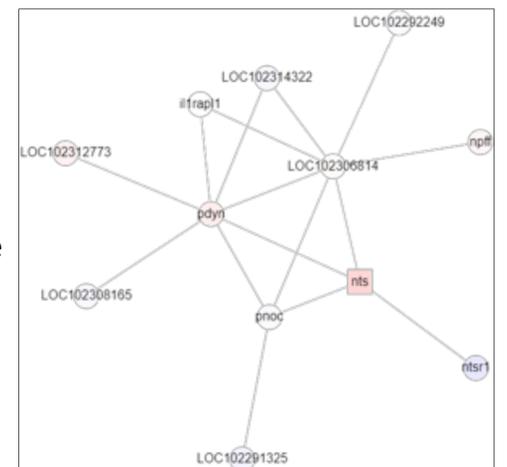
The resulting network had 10,838 proteins and 1,778,361 interactions, with an average node degree of 322 and maintains similar topology to the original zebrafish network. While the *A. burtoni* network has fewer interactions, both networks follow a similar degree distribution.



Furthermore, both networks seem relatively scale-free, since their respective degree distributions mostly follows a power law (left). The same holds true for average neighbor connectivity (right), which tends to decrease with increasing node degree.



As a test case, we focus on the neurotensin (nts) subgraph where red intensity increases with positive expression and blue intensity increases with negative expression (below). Neurotensin shares interactions and has a similar expression profile with other neurotransmitters (e.g. opioid-related peptides) that may also be modulating behavior. While these neighbors' expression levels are not very extreme, the summation of many subtle changes in expression may contribute to the overall modulation of neurotensin expression and/or the mouthbrooding state. Further computational and bench analyses on clusters of differentially expressed genes may reveal a more cohesive picture of the molecular substrates of mouthbrooding. In addition, using brain-region specific RNA-seq libraries to weight the interactome may reveal a clearer picture of how brain regions signal with one another during mouthbrooding.



This project presents a method of bringing PPI approaches to non-model organisms to study complex behavioral phenotypes

5. Acknowledgements

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6. References

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