

## Summary

We tested the idea that the “wiring diagram” of the adult brain has a relationship with regional gene expression. We were inspired by similar work carried out by groups examining the nematode worm *C. elegans*. By using large-scale databases of brain connectivity and gene expression in rodents, we found that many genes involved in the development of the brain show correlations with anatomical connectivity patterns. Some of the genes we found have been implicated in disorders such as autism, which is suspected to affect brain wiring. While the biological causes of the patterns we found are not yet known, we believe they provide new insight into the patterns of gene expression in the brain and will spur further study of this problem.

## Methods and Data

### Gene expression data

- From the Allen Mouse Brain Atlas (Lien et al.)
- Male 56 day old C57BL/6J mouse brain
- Smoothed average expression values from 142 regions
- Non-overlapping region volumes
- Non-expressing genes removed

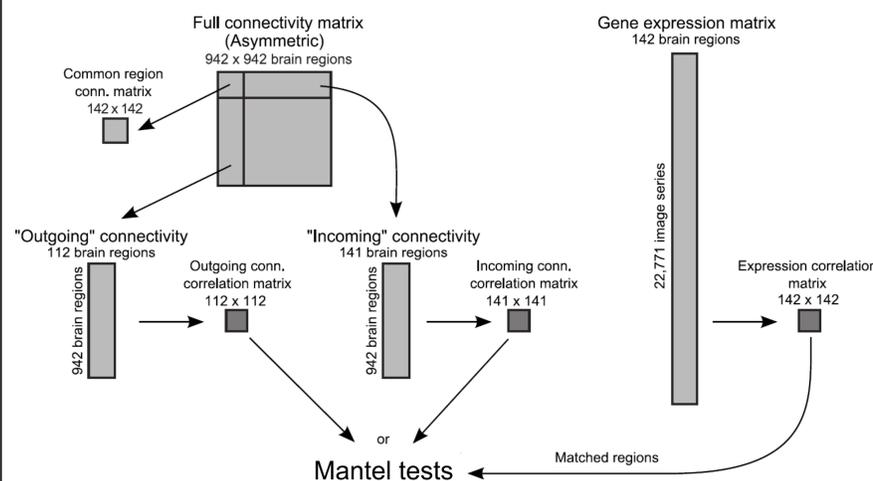
### Neuroanatomical connectivity data

- Brain Architecture Management System (Bota et al.)
- Curated tract tracing studies in Rat
- Connections propagated up to parent regions
- Binary representation of connectivity

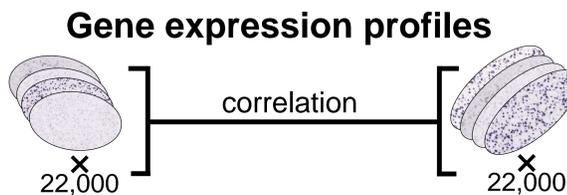
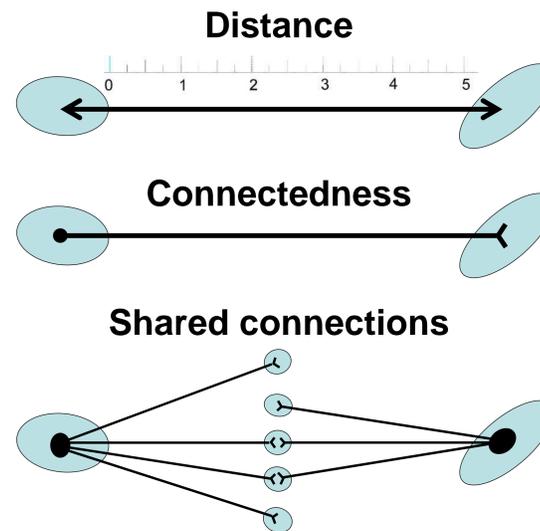
### Statistical tests

- Mantel test (correlation of region to region comparisons)
- Significance determined from empirical null distribution
- Greedy backward elimination algorithm for gene ranking

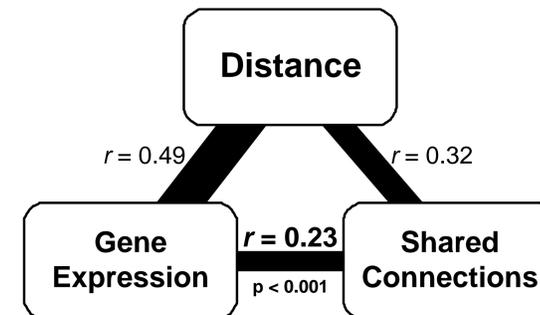
### Workflow



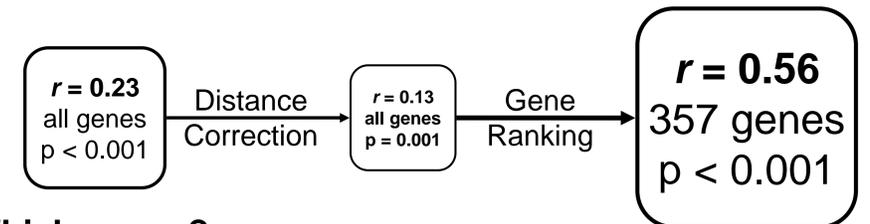
## How to compare two brain regions?



### Are these measures correlated?



## There is a statistical relationship between gene expression and connectivity.



### Which genes?

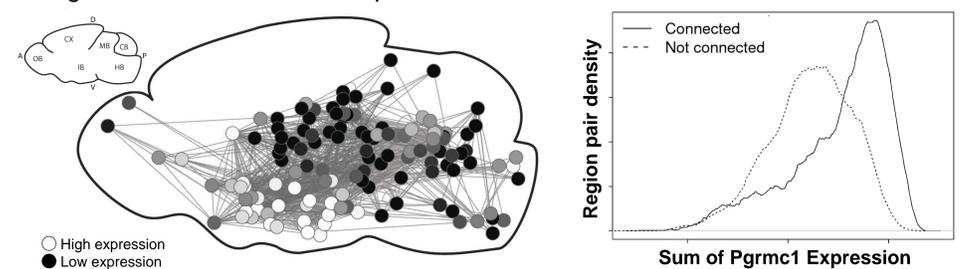
- Neurodevelopmental genes: L1Cam, Cntfr, Citron, Lhx2 ...
- Heparan sulfate: Glypican 3, Hs3st1, Hs6st1, Hs6st2 ...
- Semaphorins and receptors: Sema3a, Sema6a, Nrp1&2 ...
- Autism candidates: Reelin, Cadps2, En2, Dpp6, Btg3 ...

### Which regions?

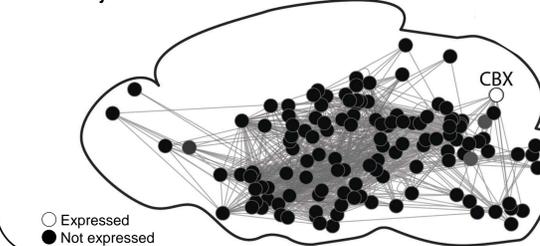
- Interbrain and basal forebrain show the strongest signal

### Examples

#### Progesterone Membrane Component 1



#### Purkinje Cell Protein 2



#### More information at:



<http://goo.gl/3392K>

## Conclusions and Discussion

- Expression patterns of some neurodevelopmental genes carry information on connectivity
- Some of these genes play roles in maintenance or tuning of connectivity at finer scales
- Extracted patterns may be a residue of a developmental process that is no longer active
- The patterns may be functionally relevant with respect to connectivity
- An interesting link between autism candidate genes and connectivity

## References

- Bota M, Dong HW, Swanson LW (2005) Brain architecture management system. *Neuroinformatics* 3: 15-48.  
 Bota M, Swanson LW (2008) BAMS Neuroanatomical Ontology: Design and Implementation. *Front Neuroinformatics* 2: 2.  
 Dong HW (2007) *The Allen Atlas: A Digital Brain Atlas of C57BL/6J Male Mouse*. Hoboken, NJ: Wiley.  
 Lein ES, Hawrylycz MJ, Ao N, Ayres M, Bensinger A, et al. (2007) Genome-wide atlas of gene expression in the adult mouse brain. *Nature* 445: 168-176.

## Acknowledgements

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