Contextualizing Results

IPN Summer School: Advanced Analytics for Neuroscience

July 2, 2021

Justine Hansen

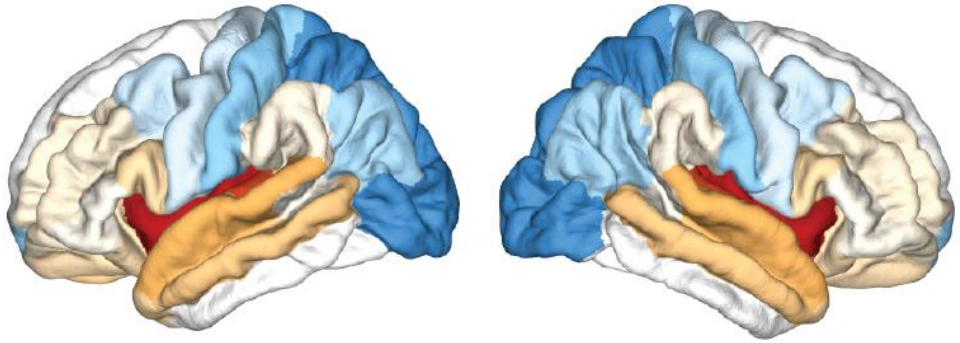
Network Neuroscience Lab

@ JustineYHansen

github.com/netneurolab/ipn-summer-school

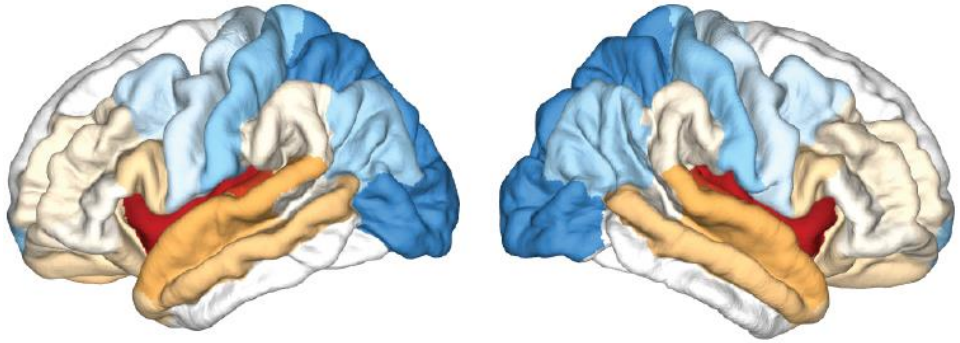
Contextualize?

brain map



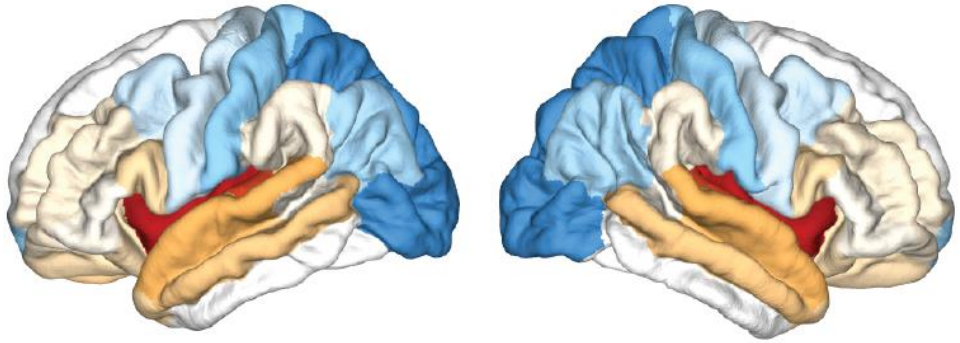
Contextualize?

brain map of fMRI task activations



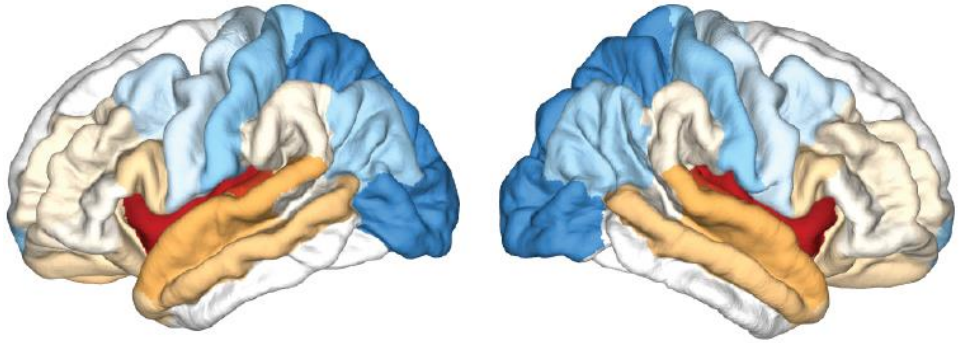
Contextualize?

brain map of neurotransmitter receptor densities



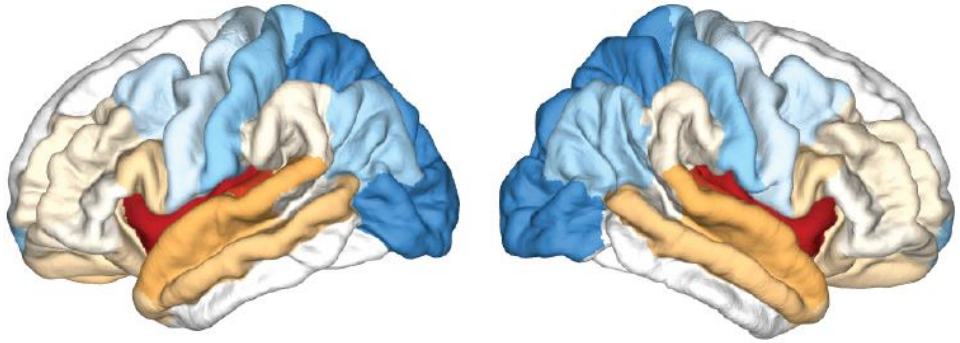
Contextualize?

brain map of principal component scores



Contextualize?

brain map of disease atrophy



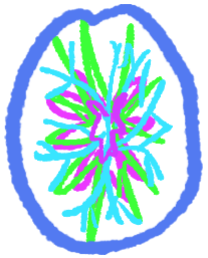
Contextualize?

gene transcription

receptors

synapses

cell types



structure

function

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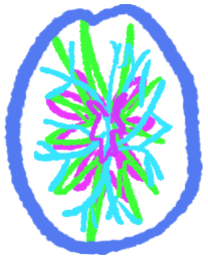

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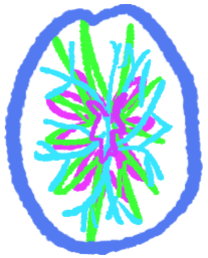

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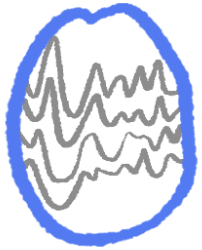
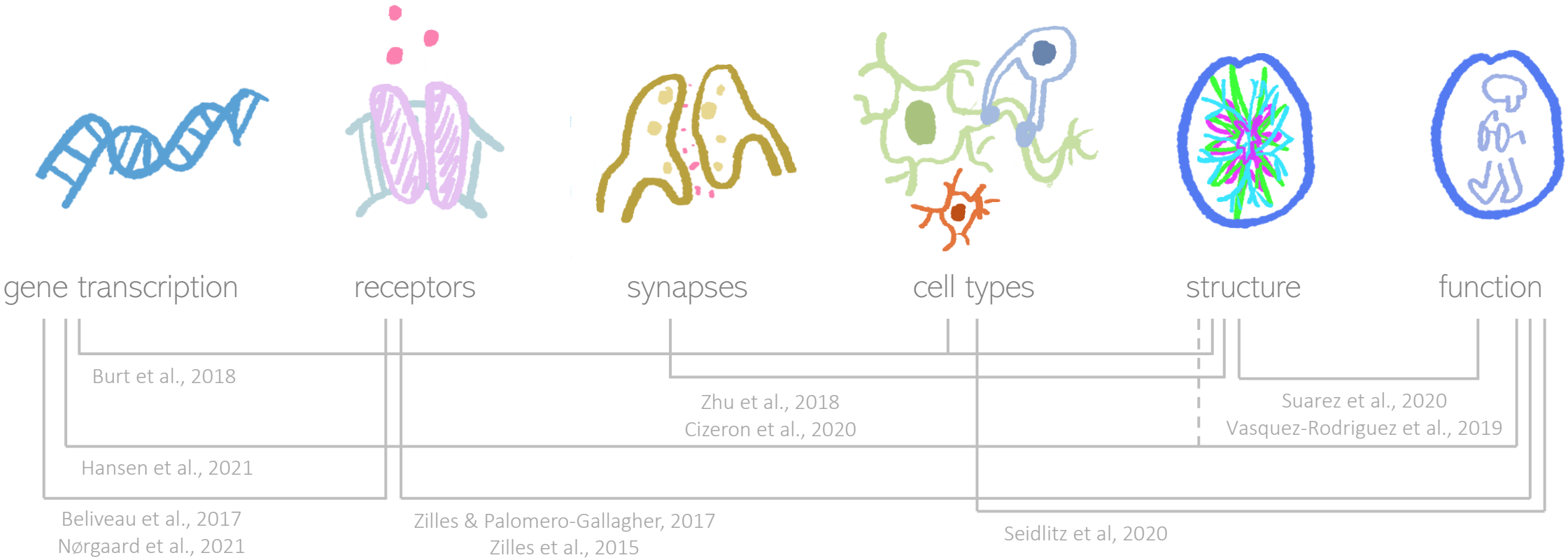
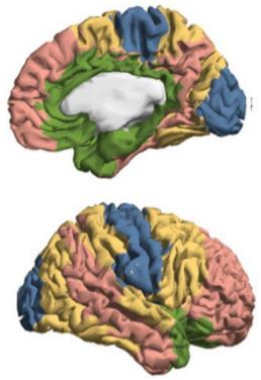


function

Contextualize?



Contextualize?



Paquola et al., 2019

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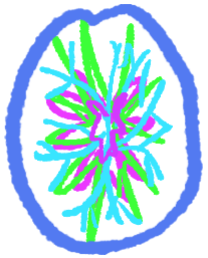

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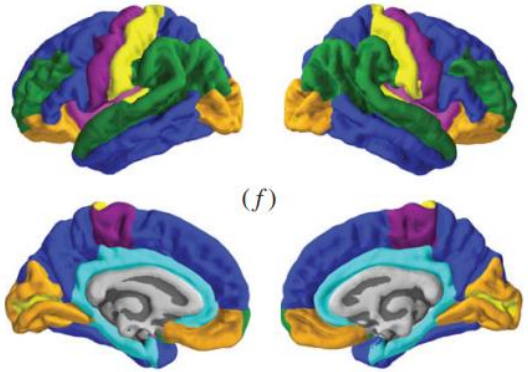
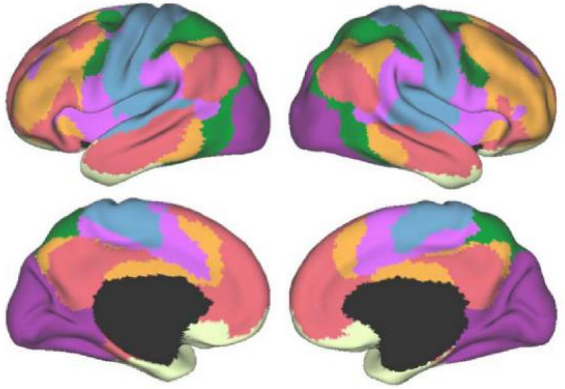
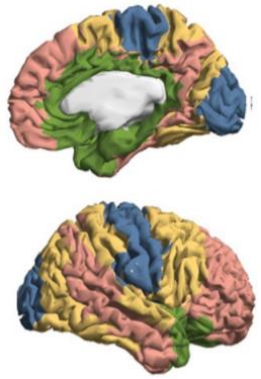


Vertes et al., 2016



Yeo & Krienen et al., 2011

Contextualize?



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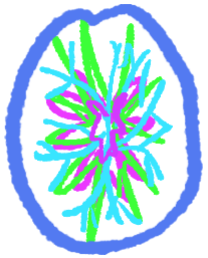

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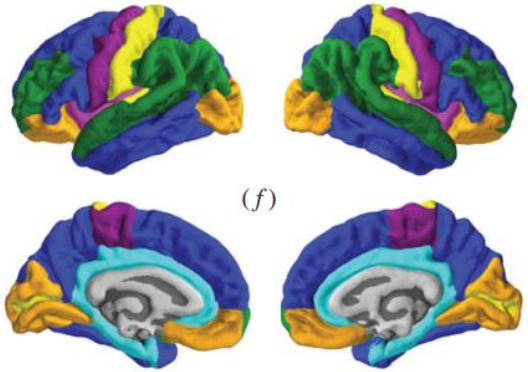

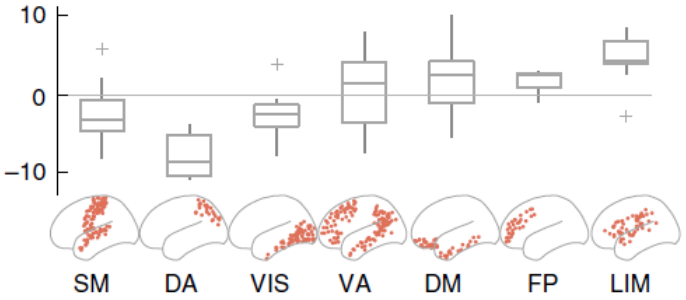

Vertes et al., 2016

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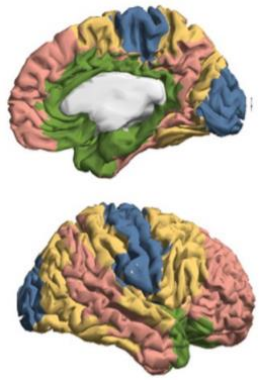

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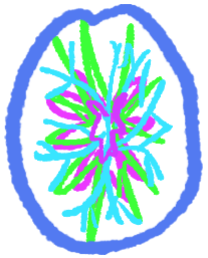

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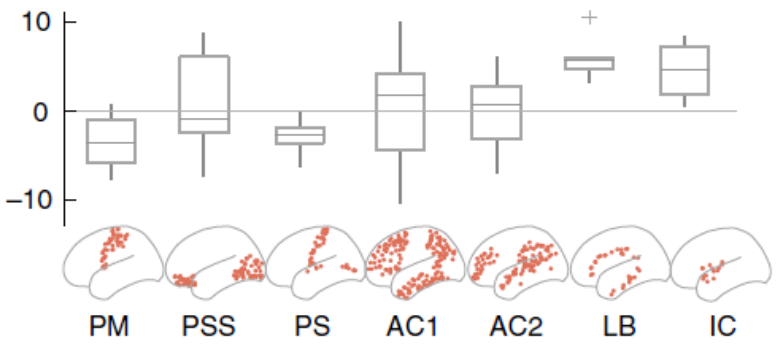

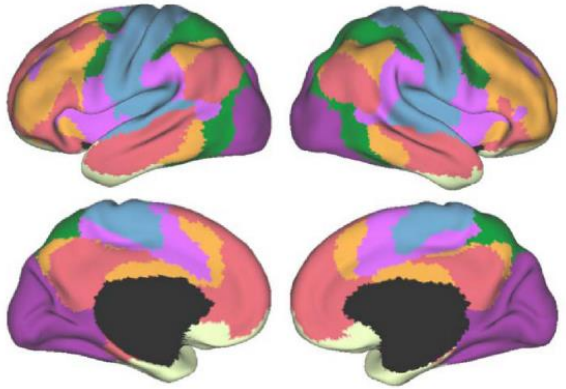

Yeo & Krienen et al., 2011

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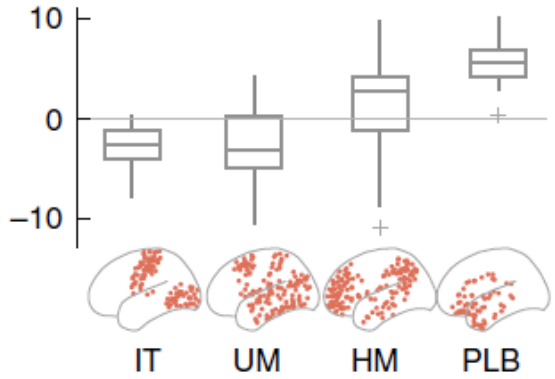

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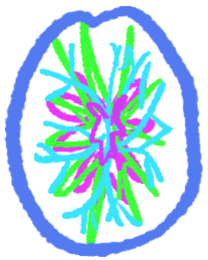

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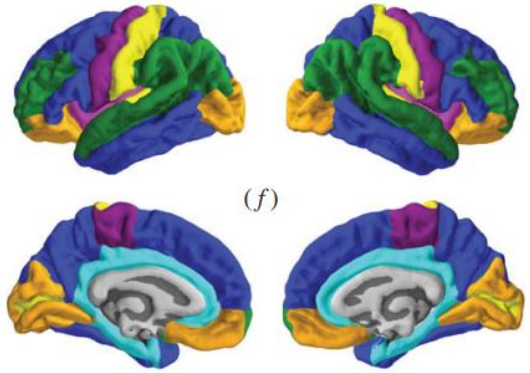
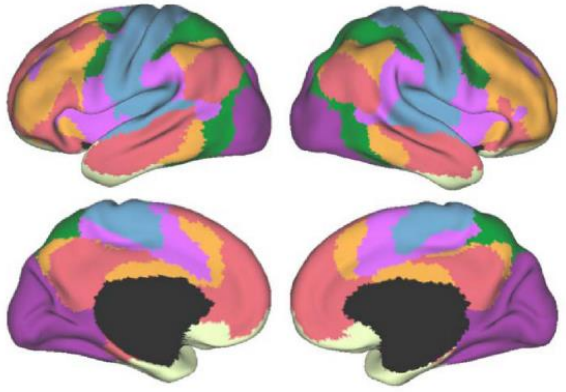


Vertes et al., 2016



Yeo & Krienen et al., 2011

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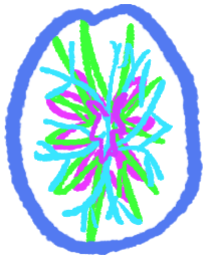

structure

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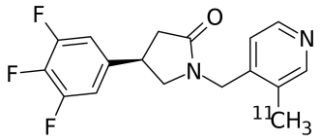
ALLEN INSTITUTE

JuSpace



CONNECTOME COORDINATION FACILITY

ENIGMA

BRAINSPAN
ATLAS OF THE DEVELOPING HUMAN BRAIN

neurosynth.org

abagen

biobank uk
Enabling scientific discoveries that improve human health

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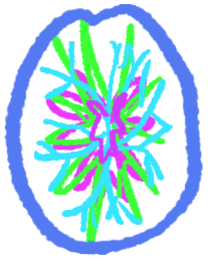

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function

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neurosynth.org

Outline

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1. Whole-brain microarray expression data (AHBA)

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2. Whole-brain cognitive association maps (Neurosynth)

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1. Whole-brain microarray expression data (AHBA)

2. Whole-brain cognitive association maps (Neurosynth)

3. Comparing spatial brain maps: the spin test

The Allen Human Brain Atlas

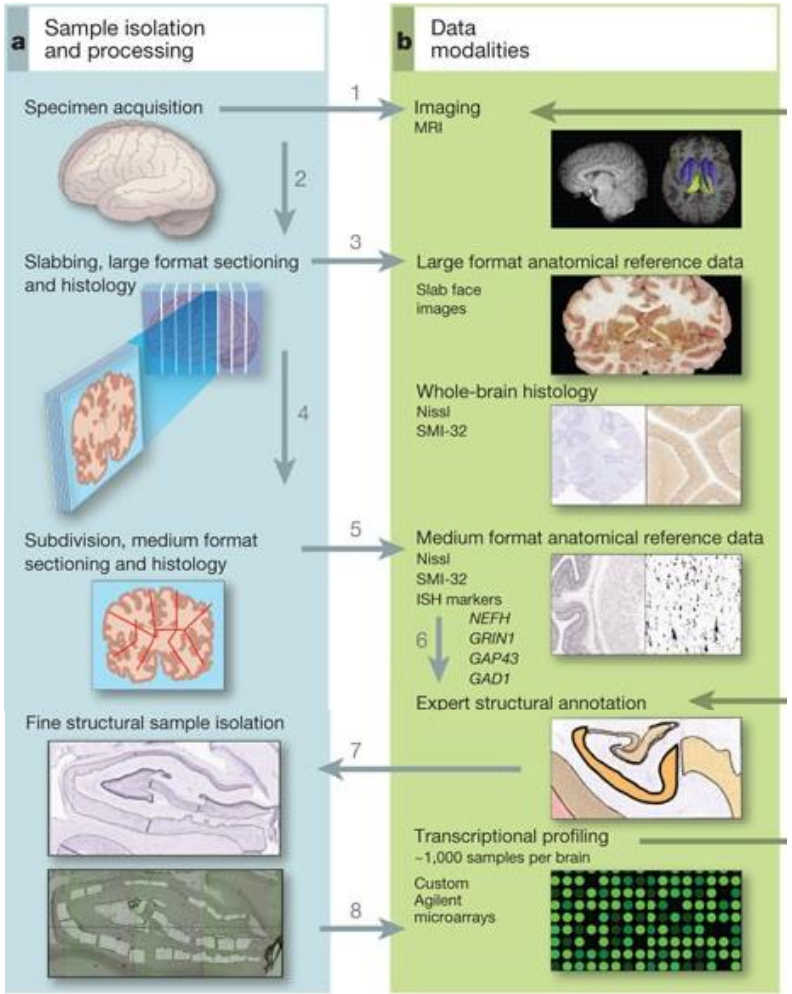
ARTICLE

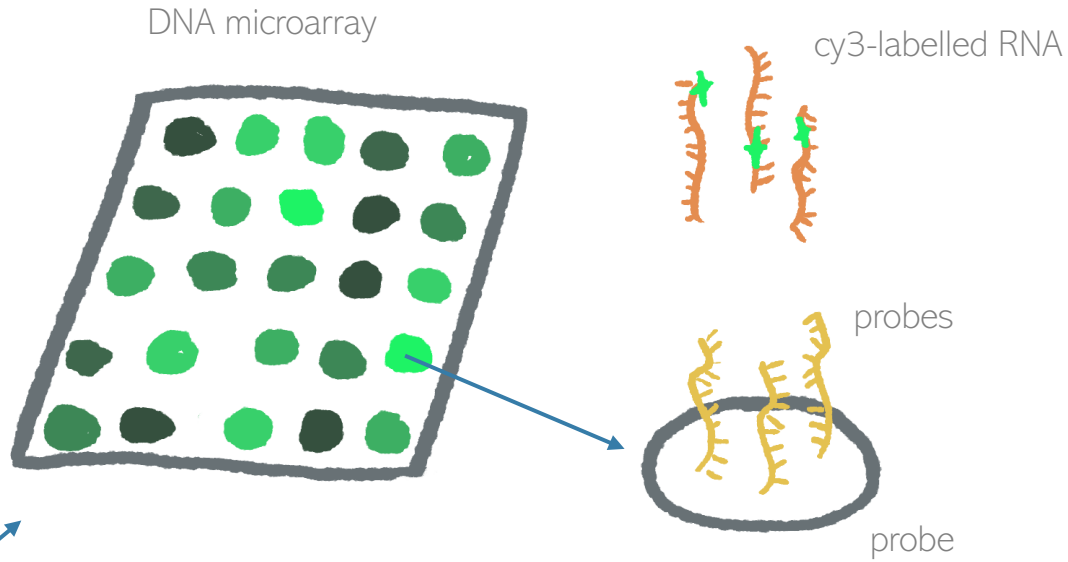
doi:10.1038/nature11405

An anatomically comprehensive atlas of the adult human brain transcriptome

Michael J. Hawrylycz[1]*, Ed S. Lein[1]*, Angela L. Guillozet-Bongaarts[1], Elaine H. Shen[1], Lydia Ng[1], Jeremy A. Miller[1], Louie N. van de Lagemaat[2], Kimberly A. Smith[1], Amanda Ebbert[1], Zackery L. Riley[1], Chris Abajian[1], Christian F. Beckmann[3], Amy Bernard[1], Darren Bertagnolli[1], Andrew F. Boe[1], Preston M. Cartagena[4], M. Mallar Chakravarty[1,5], Mike Chapin[1], Jimmy Chong[1], Rachel A. Dalley[1], Barry David Daly[6], Chinh Dang[1], Suvro Datta[1], Nick Dee[1], Tim A. Dolbeare[1], Vance Faber[1], David Feng[1], David R. Fowler[7], Jeff Goldy[1], Benjamin W. Gregor[1], Zeb Haradon[1], David R. Haynor[8], John G. Hohmann[1], Steve Horvath[9], Robert E. Howard[1], Andreas Jeromin[10], Jayson M. Jochim[1], Marty Kinnunen[1], Christopher Lau[1], Evan T. Lazarz[1], Changkyu Lee[1], Tracy A. Lemon[1], Ling Li[11], Yang Li[1], John A. Morris[1], Caroline C. Overly[1], Patrick D. Parker[1], Sheana E. Parry[1], Melissa Reding[1], Joshua J. Royall[1], Jay Schulkin[12], Pedro Adolfo Sequeira[13], Clifford R. Slaughterbeck[1], Simon C. Smith[14], Andy J. Sodt[1], Susan M. Sunkin[1], Beryl E. Swanson[1], Marquis P. Vawter[13], Derric Williams[1], Paul Wohnoutka[1], H. Ronald Zielke[15], Daniel H. Geschwind[16], Patrick R. Hof[17], Stephen M. Smith[18], Christof Koch[1,19], Seth G. N. Grant[2] & Allan R. Jones[1]

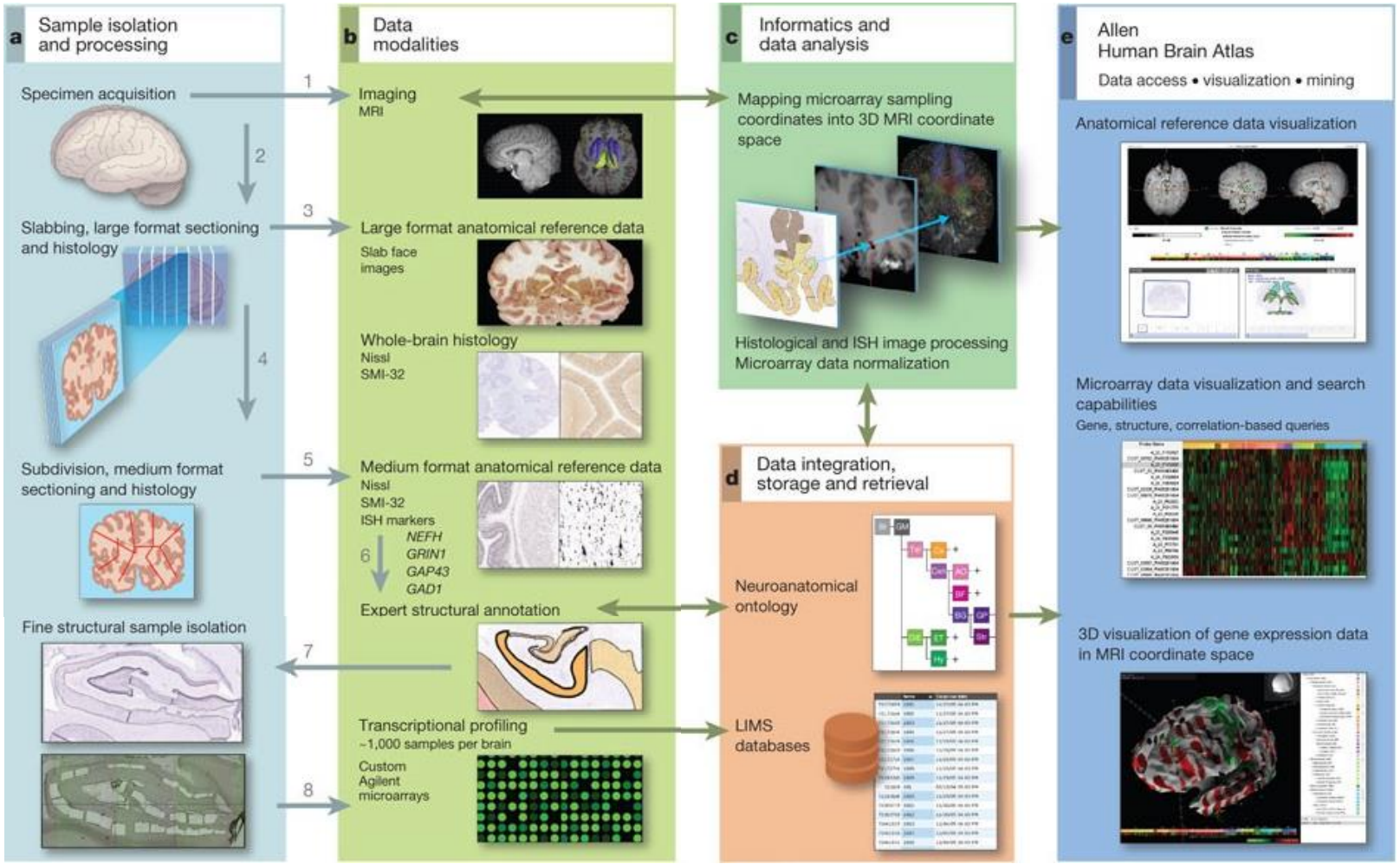
The Allen Human Brain Atlas: data collection





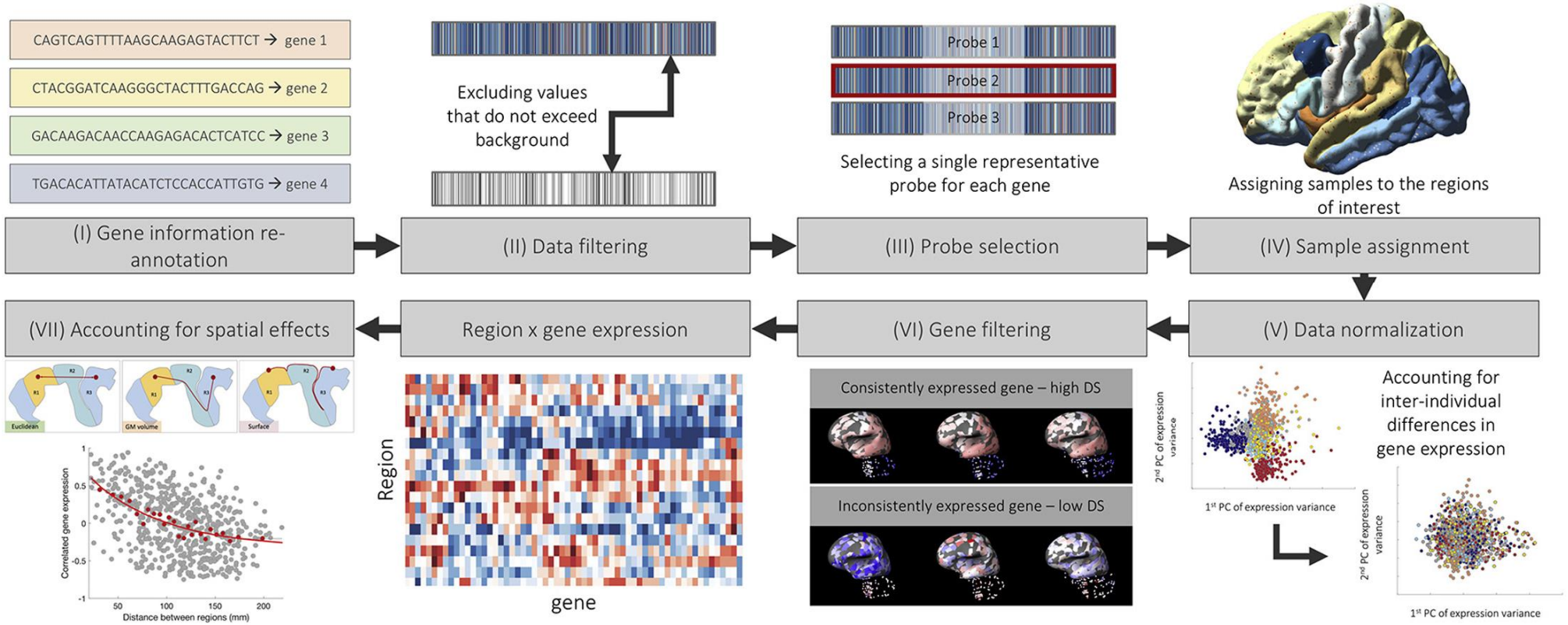
Hawrylycz et al., 2012

The Allen Human Brain Atlas: data collection



Hawrylycz et al., 2012

The Allen Human Brain Atlas: processing



Arnatkevičiūtė et al., 2019

The Allen Human Brain Atlas: processing

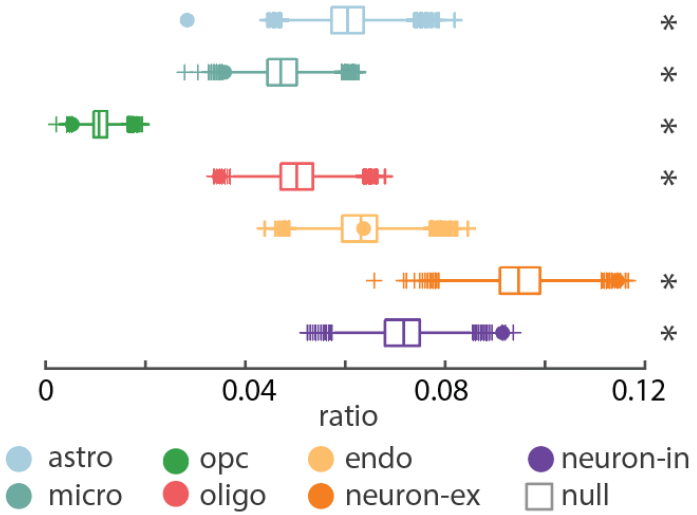
Option	*Choices*	*Description*
Volumetric or surface atlas	2/n	Whether to use a volumetric or surface representation of the atlas
Individualized or group atlas	0/2	Whether to use individualized donor-specific atlases or a group-level atlas
Use non-linear MNI coordinates	2/2	Whether to use updated MNI coordinates provided by `alleninf` package
Mirror samples across L/R hemisphere	3/4	Whether to mirror (i.e., duplicate) samples across hemisphere boundary
Update probe-to-gene annotations	2/2	Whether to update probe annotations based on Arnatkevičiūtė et al. (2019)
Intensity-based filtering threshold	3/n	Threshold for intensity-based filtering of probes
Inter-areal similarity threshold	0/n	Threshold for removing samples with low inter-areal correspondence
Probe selection method	6/8	Method by which to select which probe(s) should represent a given gene
Donor-specific probe selection	3/3	How specified probe selection should integrate data from different donors
Missing data method	2/3	How to handle when brain regions are not assigned expression data
Sample-to-region matching tolerance	3/n	Distance tolerance for matching tissue samples to atlas brain regions
Sample normalization method	3/10	Method for normalizing tissue samples (across genes)
Gene normalization method	3/10	Method for normalizing genes (across tissue samples)
Normalize only matched samples	2/2	Whether to perform gene normalization for all versus matched samples
Normalizing discrete structures	2/2	Whether to perform gene normalization within structural classes
Sample-to-region combination method	2/2	Whether to aggregate tissue samples in regions within or across donors
Sample-to-region combination metric	2/2	Metric for aggregating tissue samples into atlas brain regions

Markello et al, 2021

To the rescue: abagen

Markello et al, 2021

Cell type deconvolution



ARTICLE

https://doi.org/10.1038/s41467-020-17051-5 OPEN

Transcriptomic and cellular decoding of regional brain vulnerability to neurogenetic disorders

Jakob Seidlitz[1,2✉], Ajay Nadig[1], Siyuan Liu[1], Richard A. I. Bethlehem[2], Petra E. Vértes[2,3,4], Sarah E. Morgan[2], František Váša[2], Rafael Romero-Garcia[2], François M. Lalonde[1], Liv S. Clasen[1], Jonathan D. Blumenthal[1], Casey Paquola[5], Boris Bernhardt[5], Konrad Wagstyl[2,6], Damon Polioudakis[7], Luis de la Torre-Ubieta[7,8], Daniel H. Geschwind[7,9], Joan C. Han[10,11,12], Nancy R. Lee[13], Declan G. Murphy[14], Edward T. Bullmore[2,15] & Armin Raznahan[1✉]

github.com/jms290/PolySyn_MSNs

github.com/netneurolab/hansen_genescognition

Gene Set Enrichment Analysis

To be discussed later

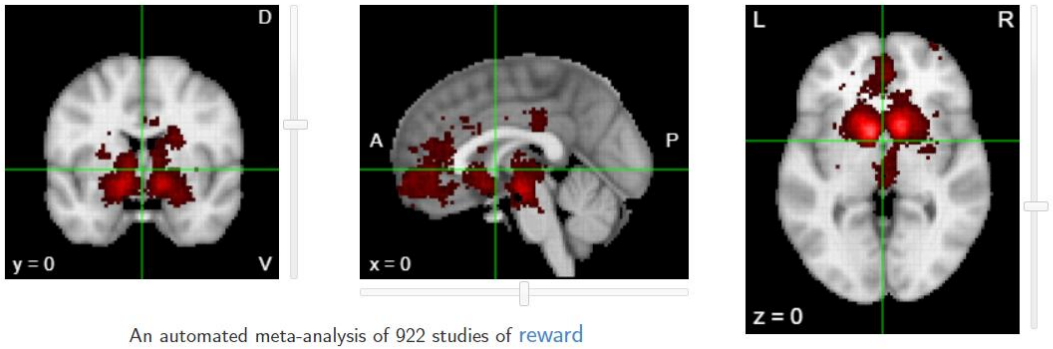
Neurosynth

Neurosynth.org Home Meta-analyses Studies Locations Genes Decoder Code FAQs

neurosynth.org

Neurosynth is a platform for large-scale, automated synthesis of functional magnetic resonance imaging (fMRI) data.

It takes thousands of published articles reporting the results of fMRI studies, chews on them for a bit, and then spits out images that look like this:



An automated meta-analysis of 922 studies of reward

ARTICLES

Large-scale automated synthesis of human functional neuroimaging data

Tal Yarkoni[1], Russell A Poldrack[2–4], Thomas E Nichols[5,6], David C Van Essen[7] & Tor D Wager[1]

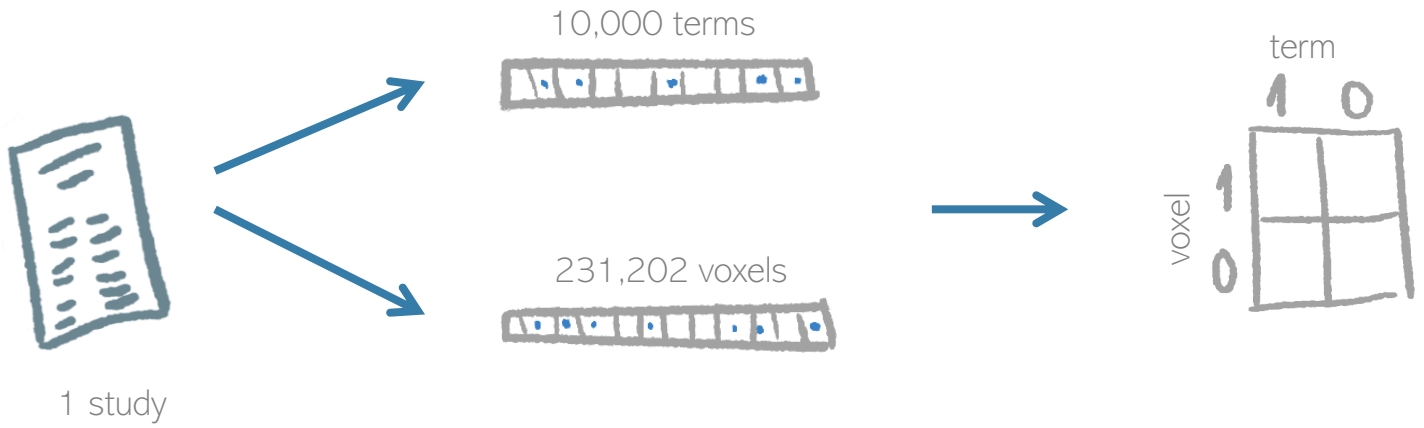
Yarkoni et al., 2011

Neurosynth

15,000+ studies

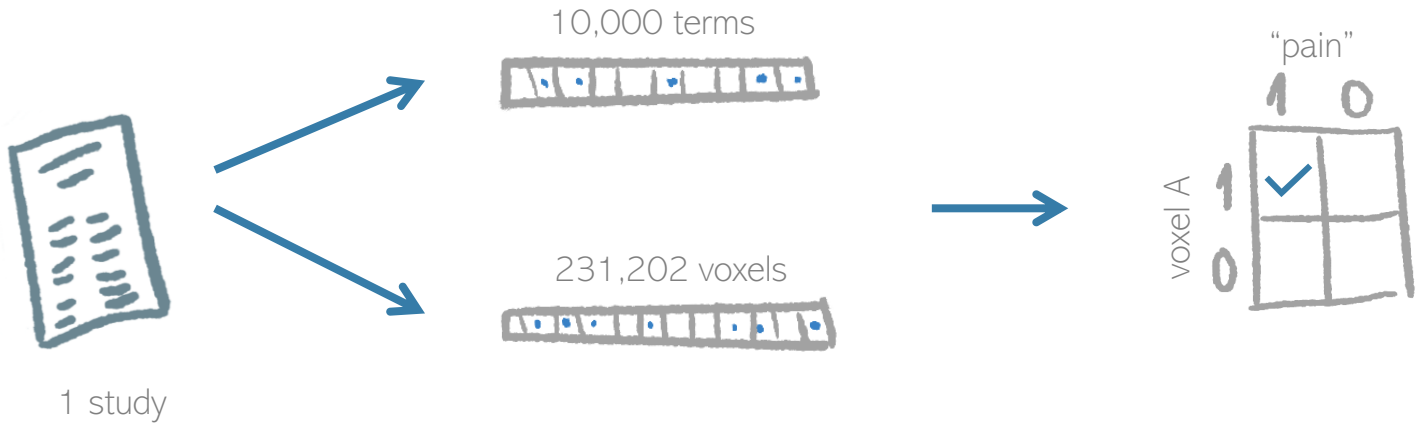
Yarkoni et al., 2011

Neurosynth



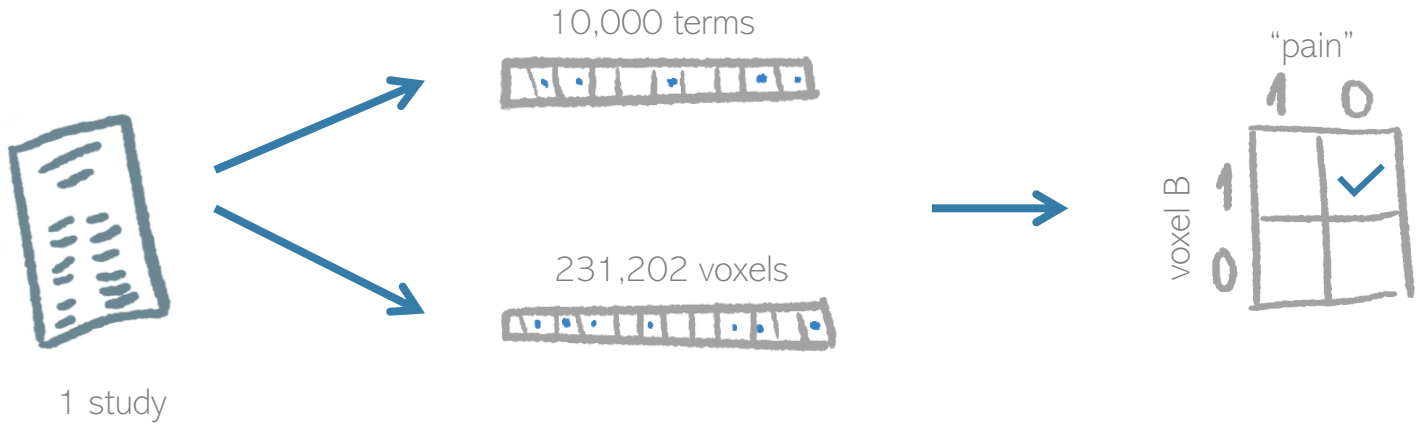
Yarkoni et al., 2011

Neurosynth



Yarkoni et al., 2011

Neurosynth



Yarkoni et al., 2011

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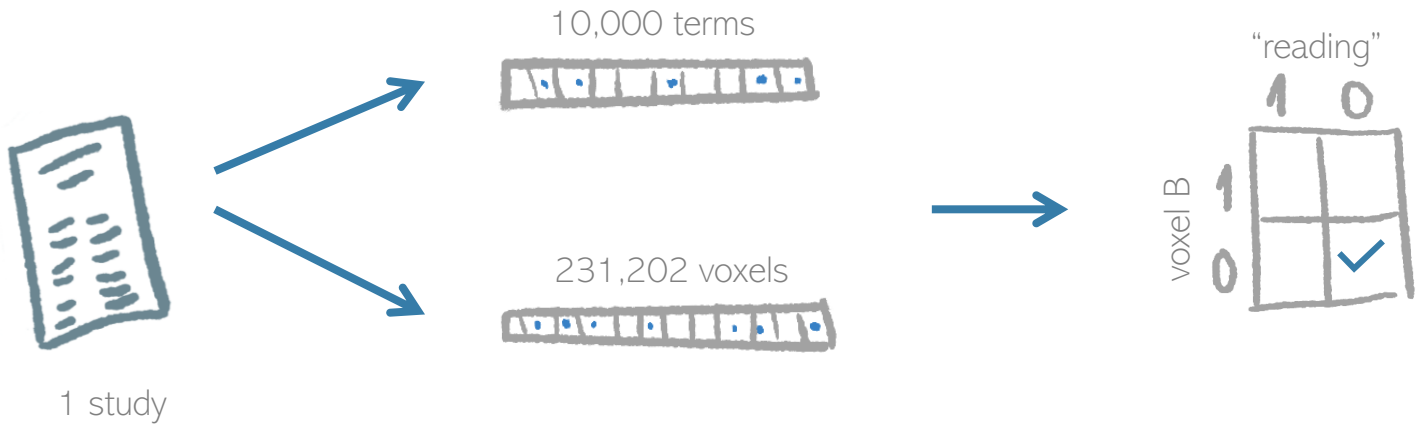
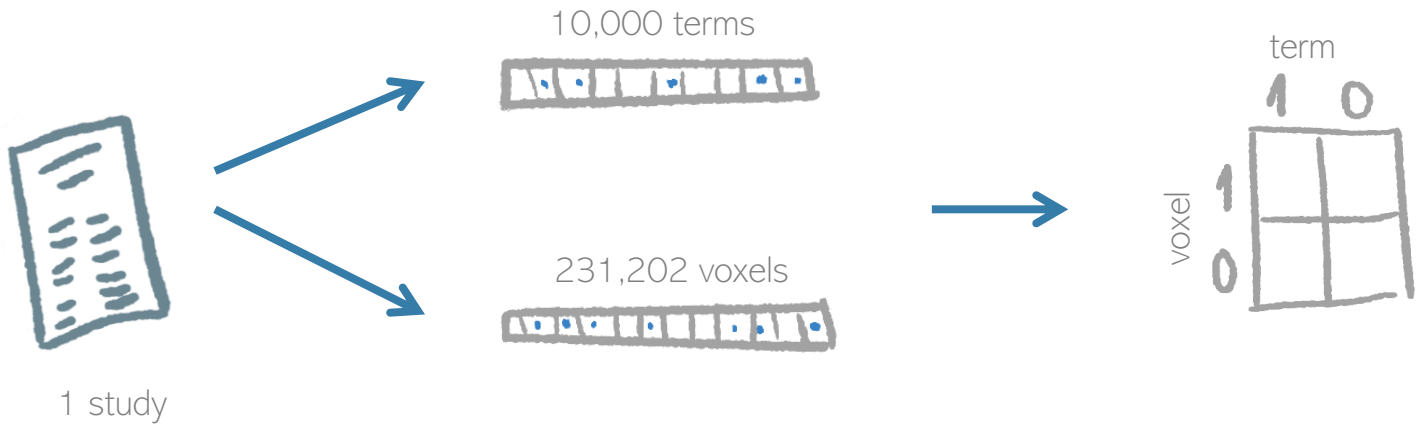


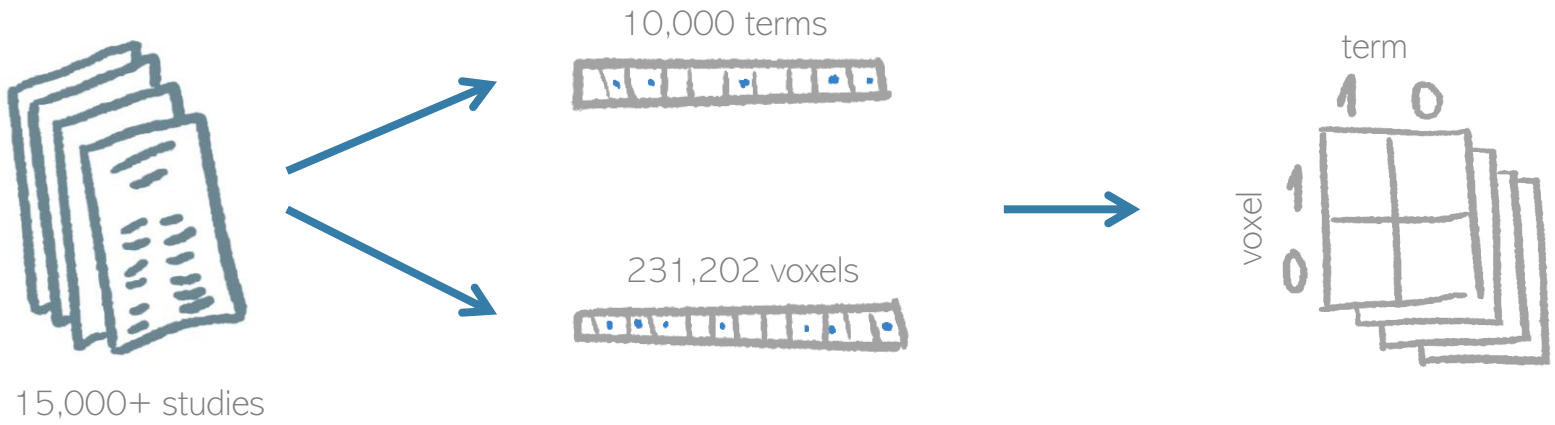
Yarkoni et al., 2011

Neurosynth



Yarkoni et al., 2011

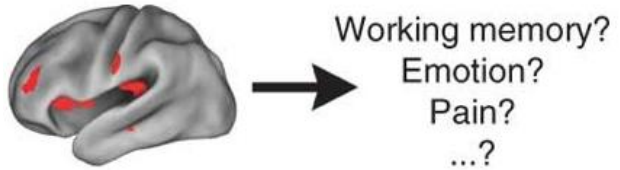
Neurosynth



Map of p-values: is there dependence between voxel activation and presence of term?

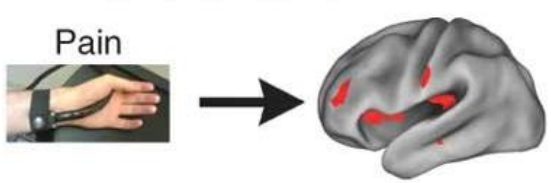
Association test: $P(T = 1 \mid V = 1)$

is voxel activation more consistent across studies that include the term than those that don't?



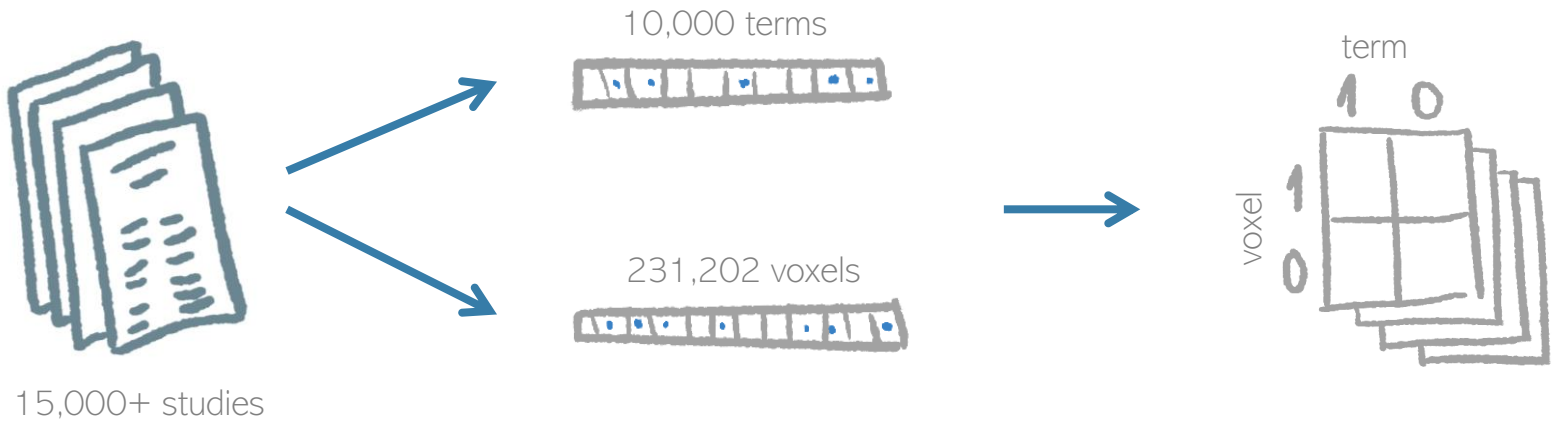
Uniformity test: $P(V = 1 \mid T = 1)$

to what degree does is a voxel consistently activated given term presence?



Yarkoni et al., 2011

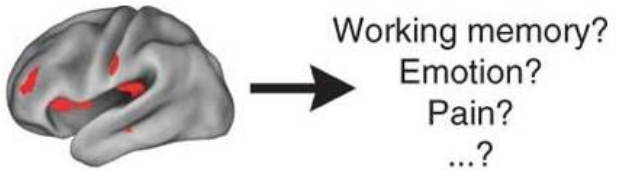
Neurosynth



Map of p-values: is there dependence between voxel activation and presence of term?

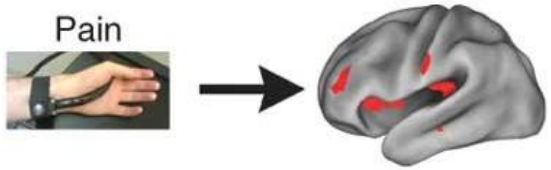
Association test: $P(T = 1 \mid V = 1)$

is voxel activation more consistent across studies that include the term than those that don't?



Uniformity test: $P(V = 1 \mid T = 1)$

to what degree does is a voxel consistently activated given term presence?

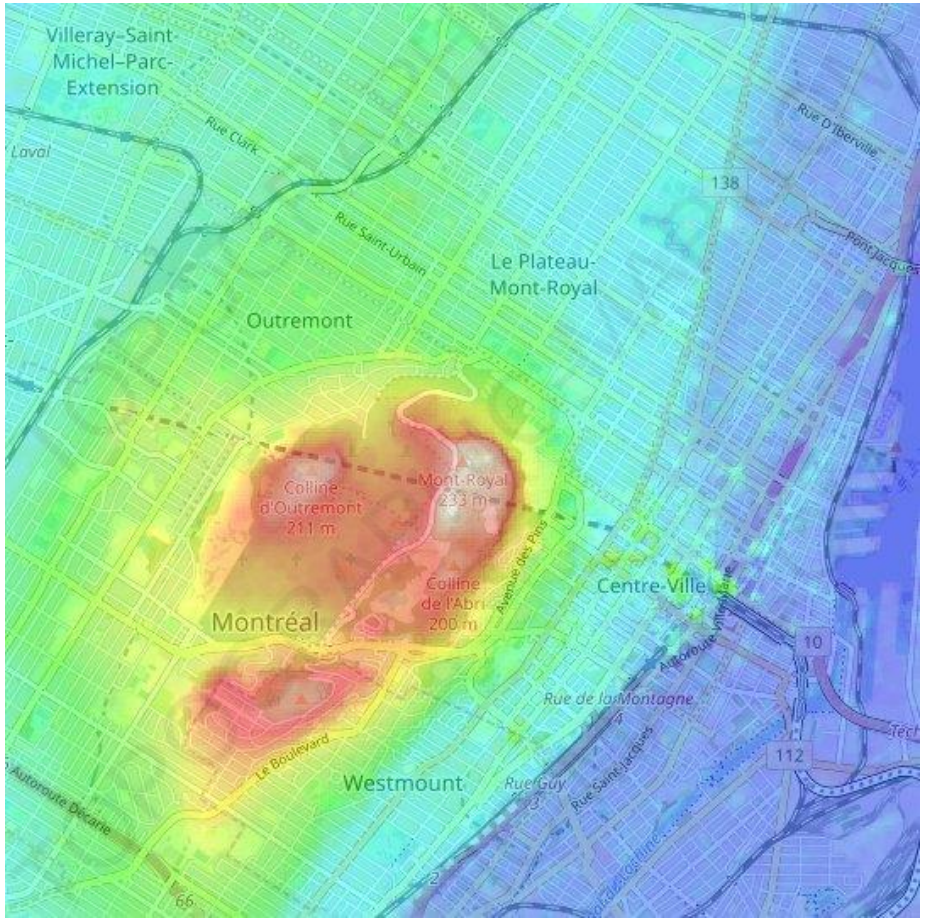


Yarkoni et al., 2011

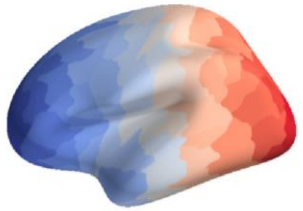
Neurosynth

Yarkoni et al., 2011

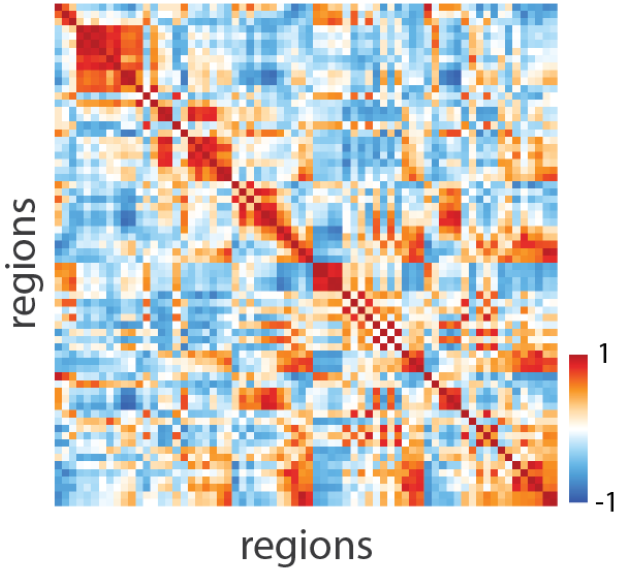
Spatial autocorrelation

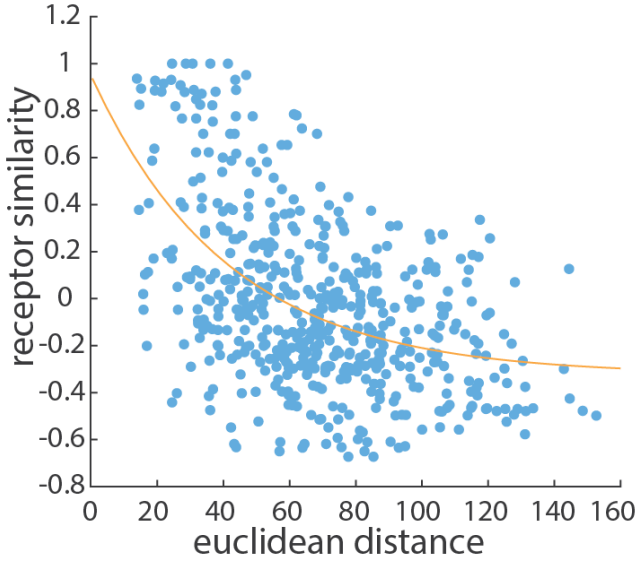


Spatial autocorrelation

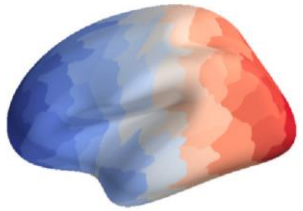


empirical data

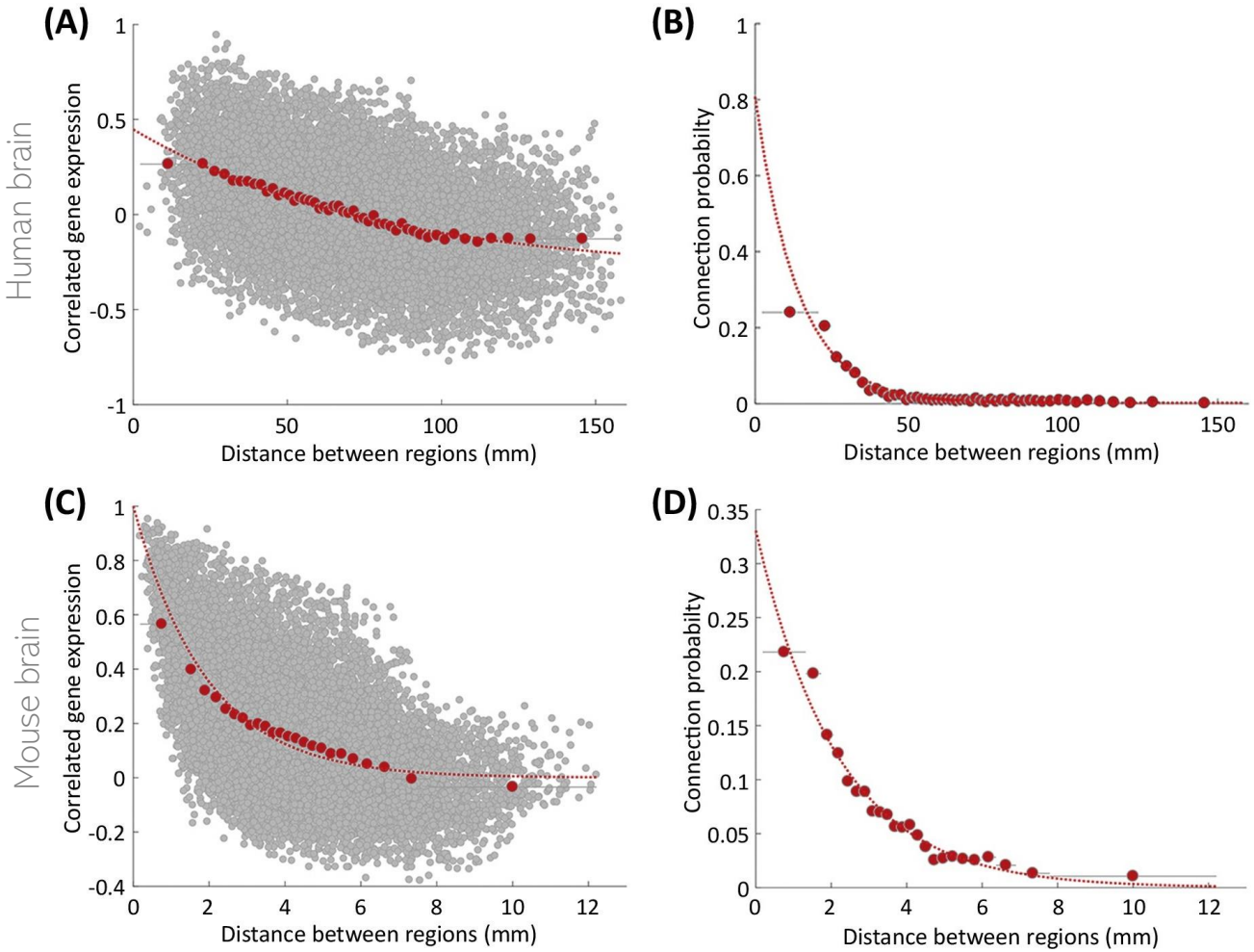




Spatial autocorrelation

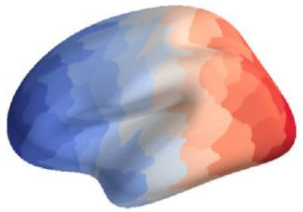


empirical data

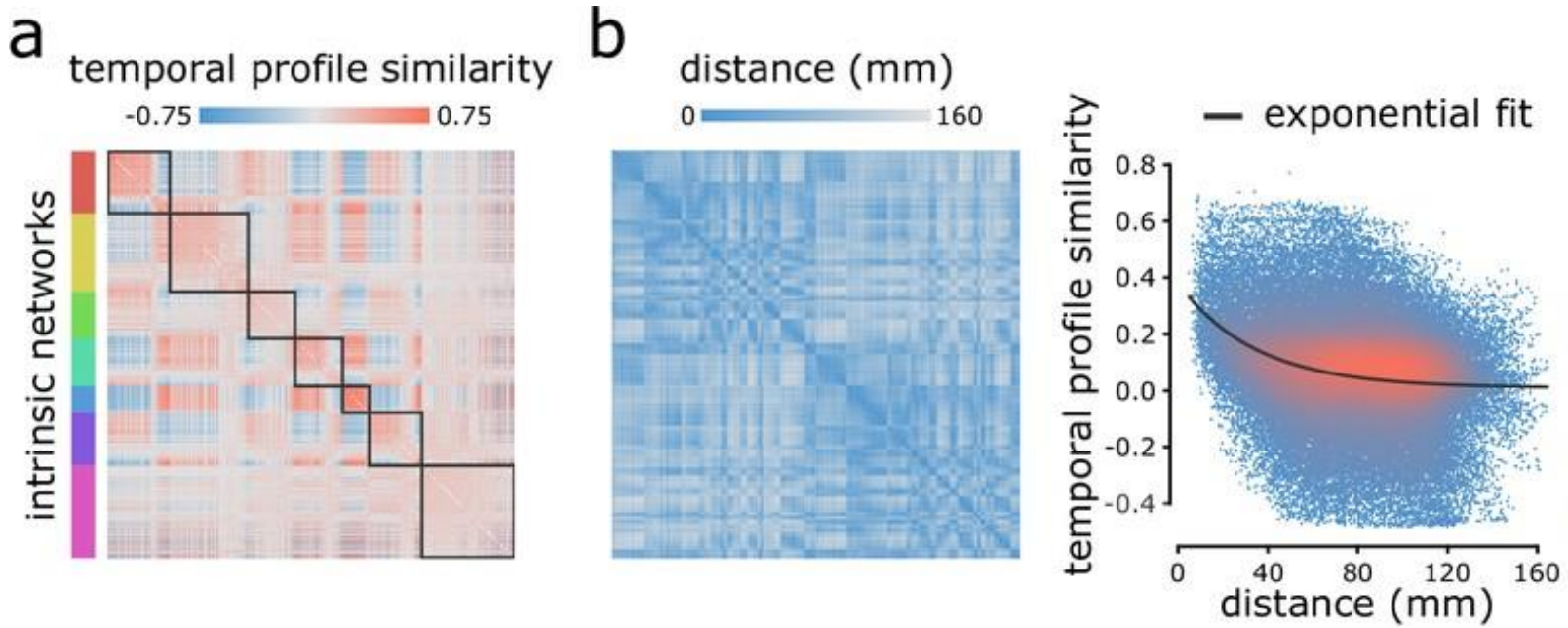


Fornito et al., 2019

Spatial autocorrelation



empirical data



Shafiei et al., 2020

Brain regions are not independent from one another

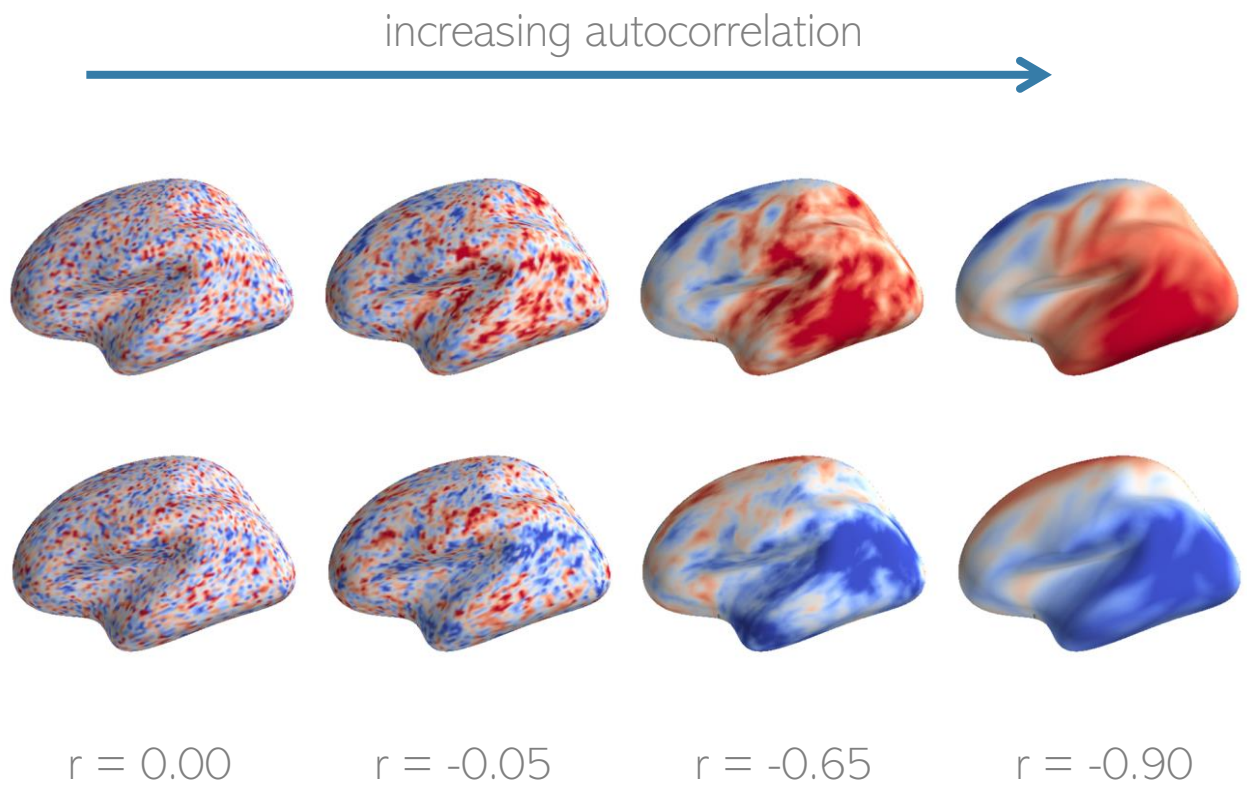
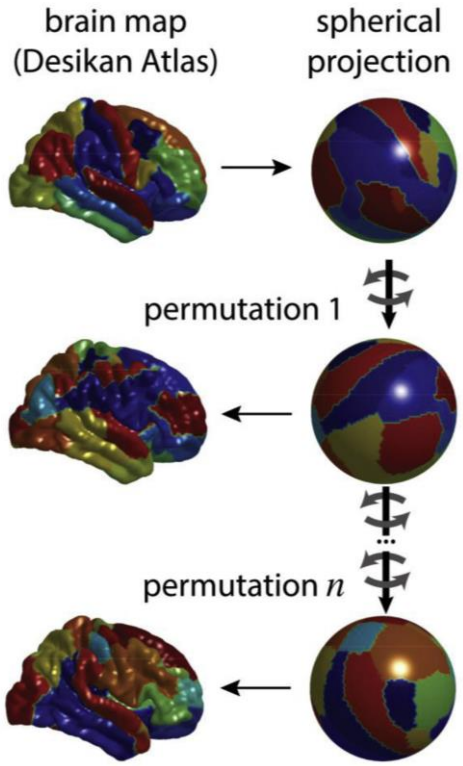
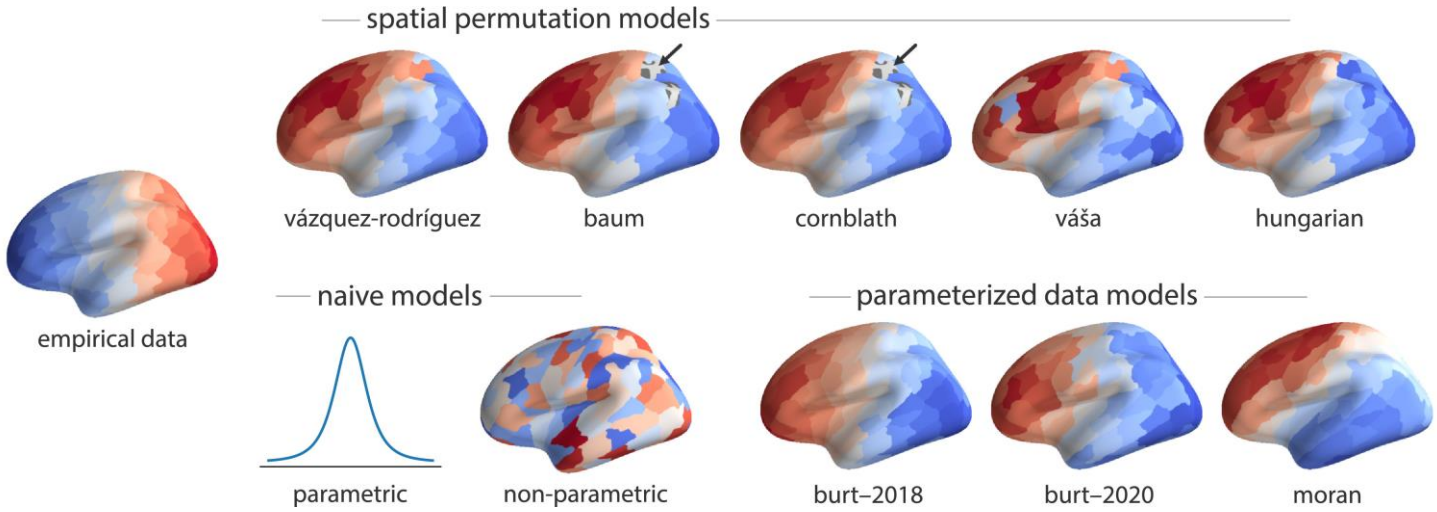


figure credit: Ross Markello

To the rescue: “spin-tests”



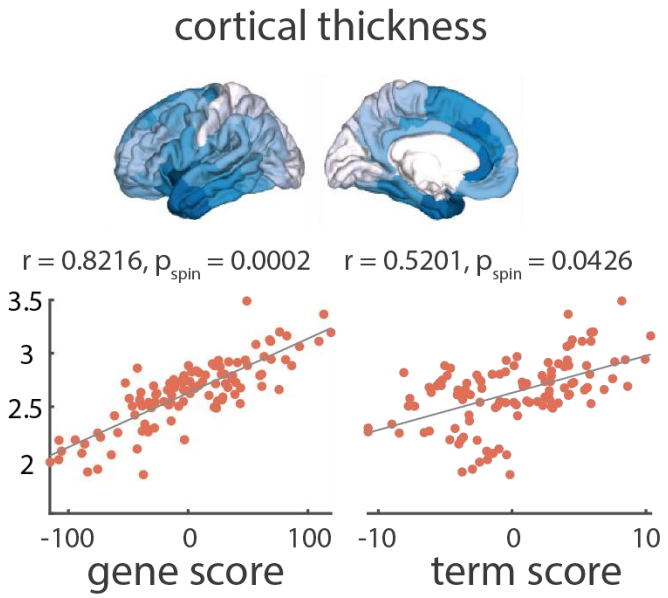
Alexander-Bloch et al., 2018



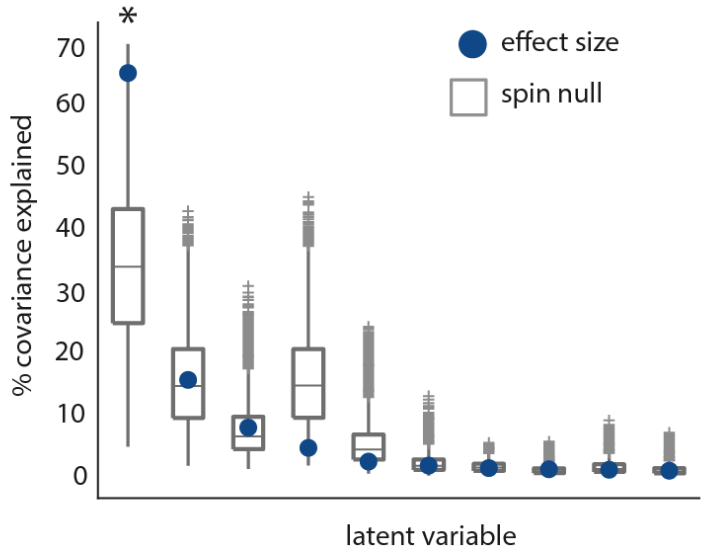
Markello & Misic, 2021

Accounting for spatial autocorrelation in the wild

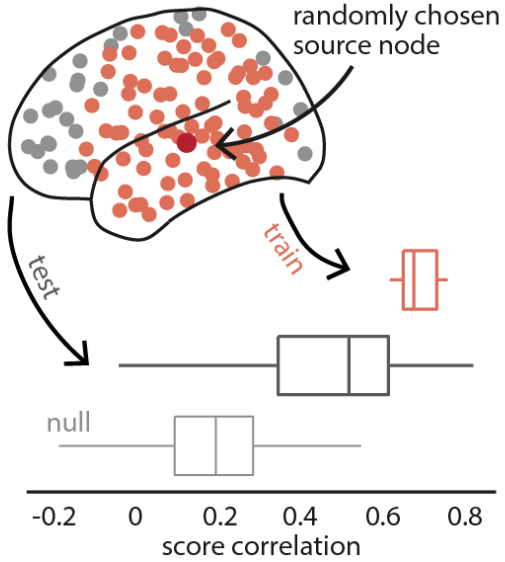
correlations



partial least squares



cross-validation



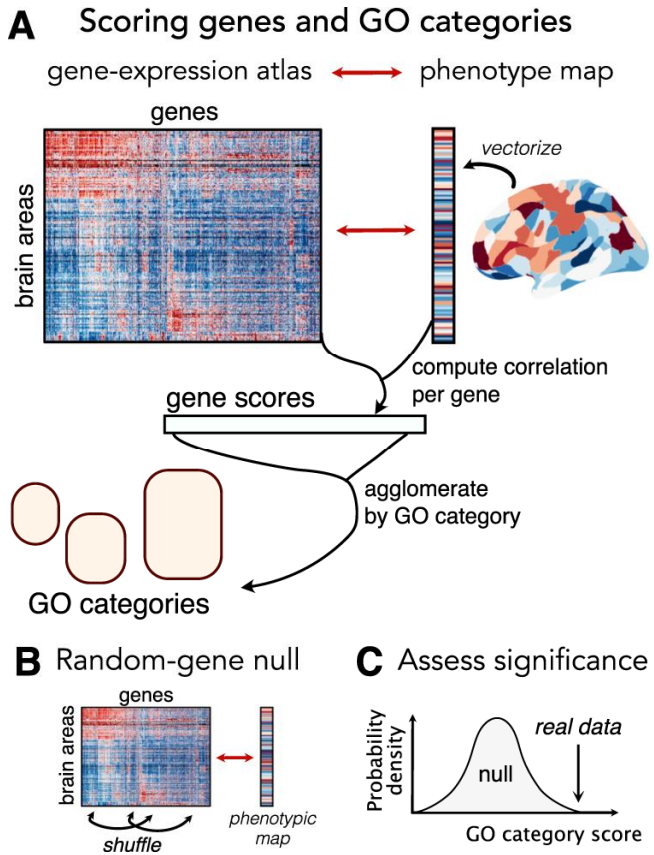
Hansen et al., 2021

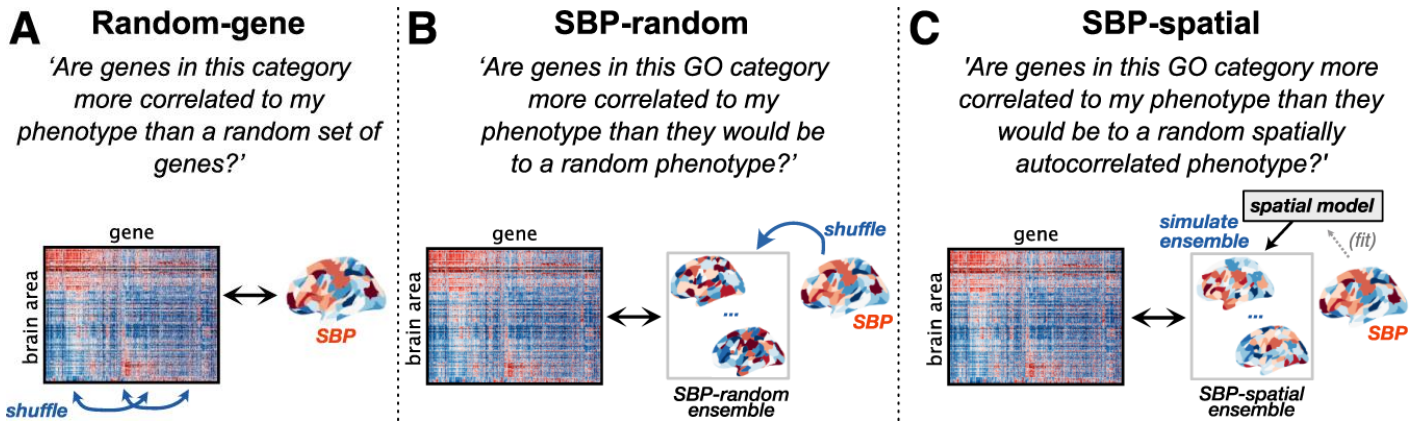
Gene Set Enrichment Analysis

ARTICLE
https://doi.org/10.1038/s41467-021-22862-1 OPEN

Overcoming false-positive gene-category enrichment in the analysis of spatially resolved transcriptomic brain atlas data

Ben D. Fulcher[1,2✉], Aurina Arnatkeviciute[2] & Alex Fornito[2]





github.com/benfulcher/GeneCategoryEnrichmentAnalysis

github.com/netneurolab/hansen_genescognition