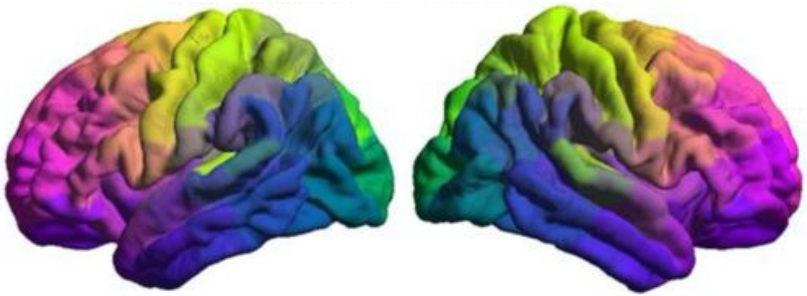
GRADIENTS OF BRAIN ORGANIZATION: *WHAT, WHY, HOW?*



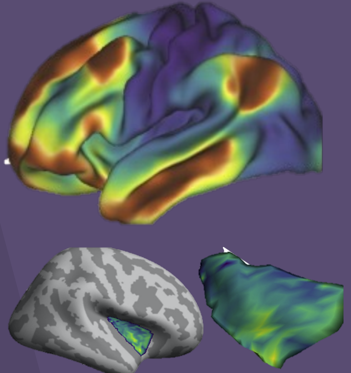
Penn LINC Lab Meeting 9.21.20

GRADIENTS: *WHAT*?

An axis of continuous feature variation across areas of the brain

- Can be examined across the cortex or within one structure
- Can be computed at the level of vertices, voxels, or regions
- Can be derived from one metric or multivariate feature matrix

Gradients help us quantify and visualize inter-area feature similarity and divergence across the brain



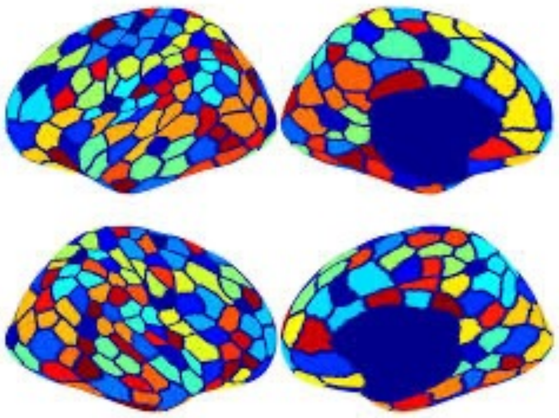
GRADIENTS:

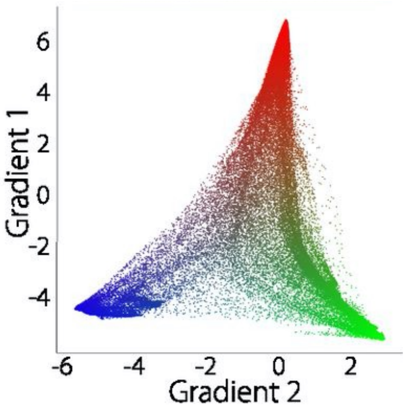
WHAT?

DISCRETE

↓

SPECTRUM





GRADIENTS: *WHAT?*

DISCRETE

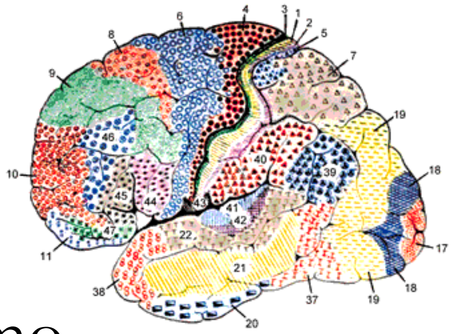
↓

SPECTRUM

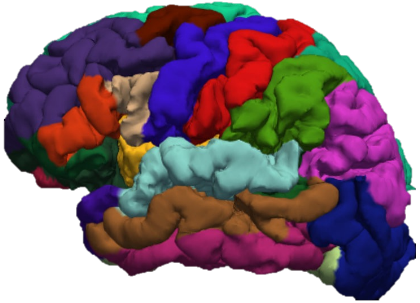
GRADIENTS:

WHY?

Vogt
Brodmann
Von Economo



FreeSurfer
Schaefer
Atlases *etc.*



Bailey and von Bonin (1951):

Drawing of sharp areal boundaries is a fundamental defect of most maps

Elkhonon Goldberg (1989):

Gradiental approach to neocortical functional organization

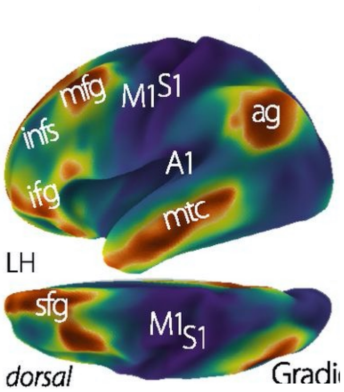
Mesulam (1998):

From sensation to cognition

Daniel Margulies,
Boris Bernhardt

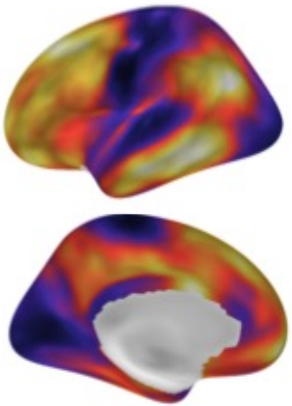
GRADIENTS: *WHY*?

FC Strength



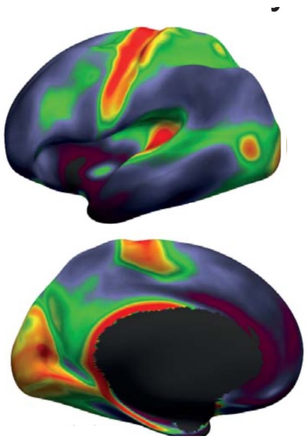
Margulies et al. 2016

FC Distance



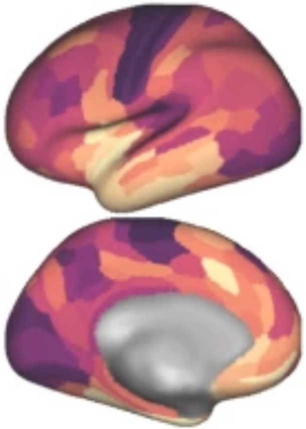
Oligschläger et al. 2017

T1w/T2w Ratio



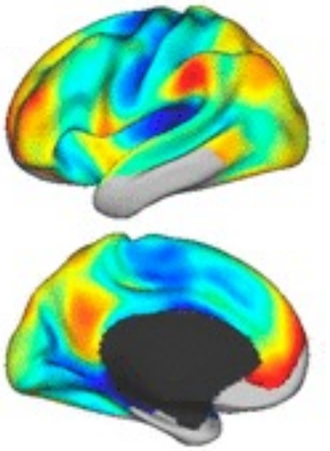
Wang et al. 2019

GRIN2B exp.



Burt et al. 2018

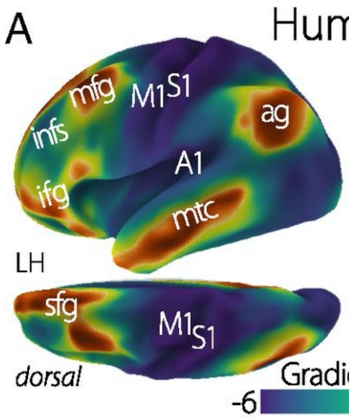
Timescale

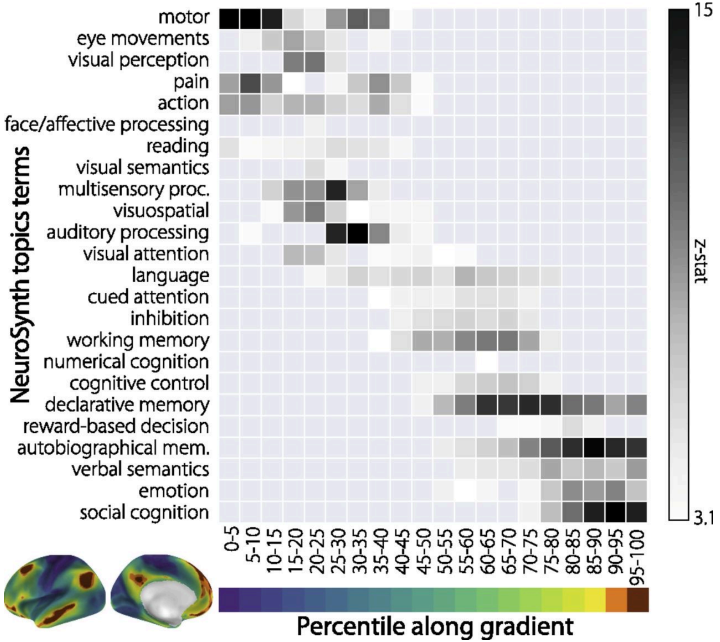


Raut et al. 2020

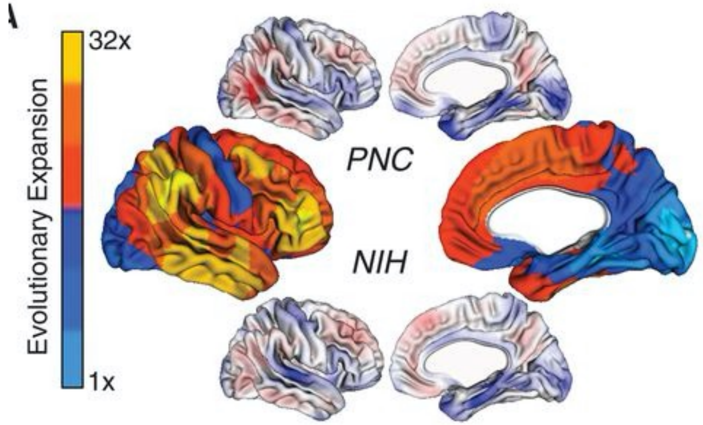
GRADIENTS: *WHY*?

FC Strength





Margulies et al. 2016



Hill et al. 2010
Reardon et al. 2018

Sensory-association gradient: a natural, hierarchical axis of cortical organization with evolutionary origins

A molecular gradient along the longitudinal axis of the human hippocampus informs large-scale behavioral systems

Jacob W. Vogel, Renaud La Joie, Michel J. Grothe, Alexandr Diaz-Papkovich, Andrew Doyle, Etienne Vachon-Presseau, Claude Lepage, Reinder Vos de Wael, Rhalena A. Thomas, Yasser Iturria-Medina, Boris Bernhardt, Gil D. Rabinovici & Alan C. Evans

Nature Communications **11**, Article number: 960 (2020) | Cite this article

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/neuroimage

Dispersion of functional gradients across the adult lifespan

Check for updates

Richard A.I. Bethlehem[a,b,1,*], Casey Paquola[c,1], Jakob Seidlitz[d,e], Lisa Ronan[f], Boris Bernhardt[c], Cam-CAN Consortium[g], Kamen A. Tsvetanov[h,i]

NeuroImage
Open access

10.2
CiteScore

5.902
Impact Factor

Gradients in brain organization

Edited by Daniel Margulies, Boris Bernhardt, Jonathan Smallwood, Shella Keilholz
Last update 11 September 2020

Complementary to mapping discrete regional boundaries, recent years have seen a rise of new methods and applications to study smooth spatial transitions — or gradients — in numerous aspects of brain organization. Already recognized in early post-mortem histological work, r...

GRADIENTS: *WHY*?

- Help identify intrinsic patterns of cortical organization
- Allow us to relate multifaceted feature similarity across measures and across species
- Provide an underutilized framework for studying how gradients change in development, aging, and illness

GRADIENTS: *HOW*?

1. Obtain input feature matrix from neuroimaging data
2. Calculate affinity (feature similarity) matrix
3. Embed the affinity matrix in low dimensional space

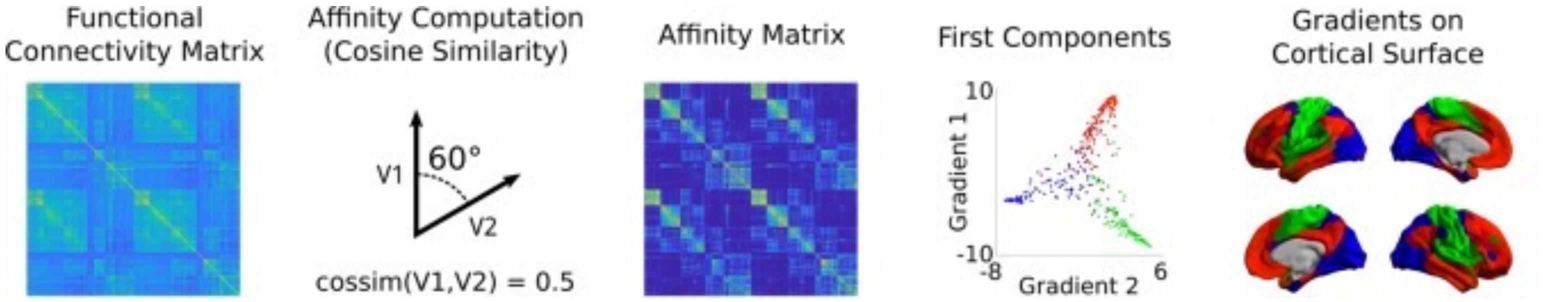
"Core to these techniques is the computation of an affinity matrix that captures inter-area similarity of a given feature followed by the application of dimensionality reduction techniques to identify a gradual ordering of the input matrix in a lower dimensional manifold space"- Vos de Wael, 2020, Communications Biology, BrainSpace

Vogt-Bailey Index
BrainSpace
LittleBrain

GRADIENTS: *HOW?*

Vogt-Bailey Index
BrainSpace
LittleBrain

1. Obtain input feature matrix from neuroimaging data
2. Calculate affinity (feature similarity) matrix
3. Embed the affinity matrix in low dimensional space



GRADIENTS: *HOW?*

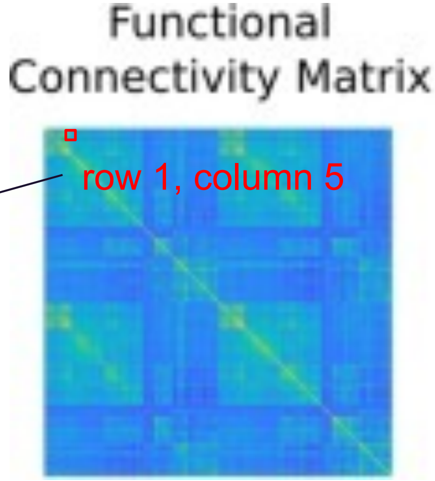
1. **Obtain input feature matrix from neuroimaging data**

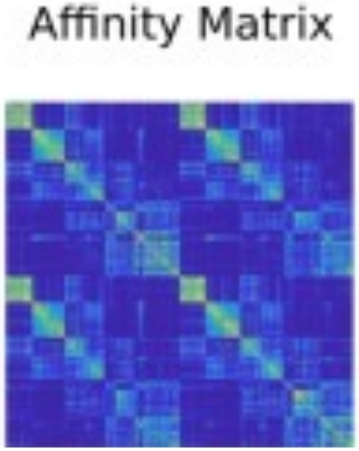
Vogt-Bailey Index
BrainSpace
LittleBrain

GRADIENTS: *HOW?*

2. **Calculate affinity (feature similarity) matrix**

An affinity matrix contains information about how similar each area (vertex, voxel, ROI) of the brain is to every other area of the brain





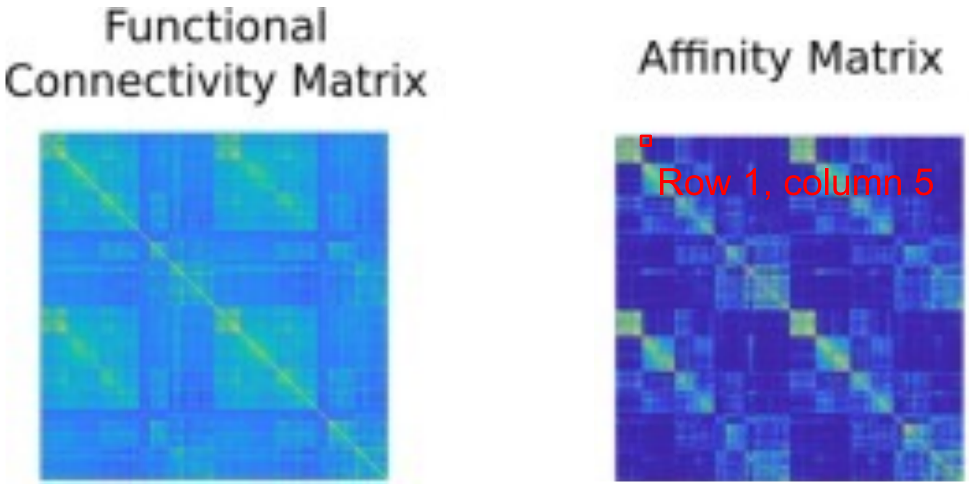
Pearson's correlation coefficient between BOLD time series in region 1 and region 5

GRADIENTS: *HOW?*

Vogt-Bailey Index
BrainSpace
LittleBrain

2. **Calculate affinity (feature similarity) matrix**

An affinity matrix contains information about how similar each area (vertex, voxel, ROI) of the brain is to every other area of the brain

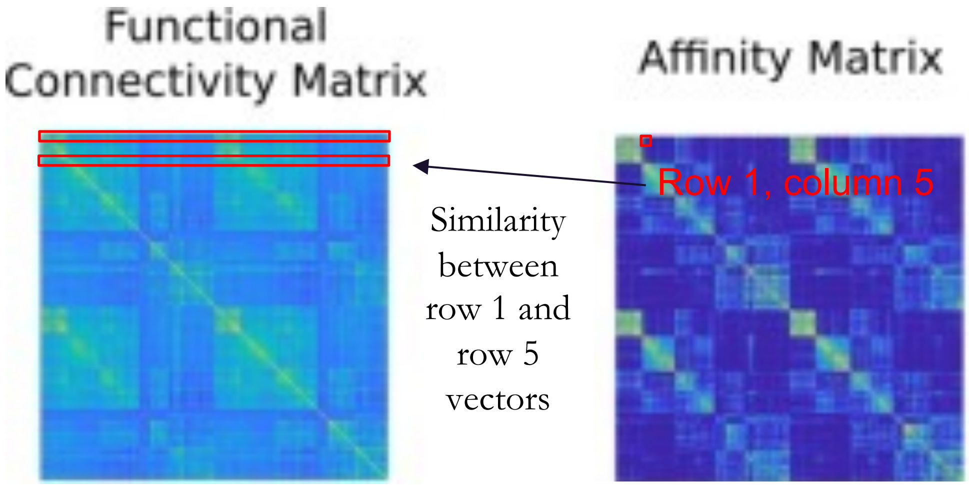


GRADIENTS: *HOW?*

Vogt-Bailey Index
BrainSpace
LittleBrain

2. **Calculate affinity (feature similarity) matrix**

An affinity matrix contains information about how similar each area (vertex, voxel, ROI) of the brain is to every other area of the brain



GRADIENTS: *HOW?*

Vogt-Bailey Index
BrainSpace
LittleBrain

2. **Calculate affinity (feature similarity) matrix**

An affinity matrix contains information about how similar each area (vertex, voxel, ROI) of the brain is to every other area of the brain

Computing feature similarity:

- **Cosine similarity** (centered data)
- **Normalized angle similarity** (arccosine, normalized by 90 degrees)
- **Pearson's** and **Spearman's** rank correlations

GRADIENTS: *HOW?*

Vogt-Bailey Index
BrainSpace
LittleBrain

2. **Calculate affinity (feature similarity) matrix**

Considerations:

- Input matrix values must be non-negative → drop negative values or add a scalar constant
- Can use entire input matrix or zero out values that fall below a given threshold (mitigate noise, sparsify matrix)

GRADIENTS: *HOW?*

Vogt-Bailey Index
BrainSpace
LittleBrain

3. **Embed the affinity matrix in low dimensional space**

The goal of this step is to create a one-dimensional ordering of brain areas based on how similar they are to one another. We penalize putting long distances between brain areas with high affinity, and find a final positioning where the sum of distance penalties amongst all areas is minimized

Linear dimensionality reduction methods: **PCA**
Non-linear dimensionality reduction methods: **Diffusion map embedding, Laplacian Eigenmaps**

GRADIENTS: *Vogt-Bailey Index*

The VB index: Is the transition between one brain area to another in low dimensional space gradual/continuous or sharp/discrete?

- Based on a measure of algebraic connectivity (second smallest Laplacian eigenvalue). Higher connectivity = more continuous; Low connectivity indicates potential clusters with discrete boundaries

- 1. Compute a whole brain, single gradient VB index
- 2. Compute an ROI-specific gradient and VB index (e.g. VB index within each functional network)
- 3. Identify boundaries via a vertex-wide searchlight (edge detection)