NEUROPARTI: EVOLUTIONARY TRADE-OFF ANALYSIS OF HUMAN NEUROCHEMISTRY

08/10/2024 I ELIANA NICOLAISEN-SOBESKY & DR. KAUSTUBH R. PATIL

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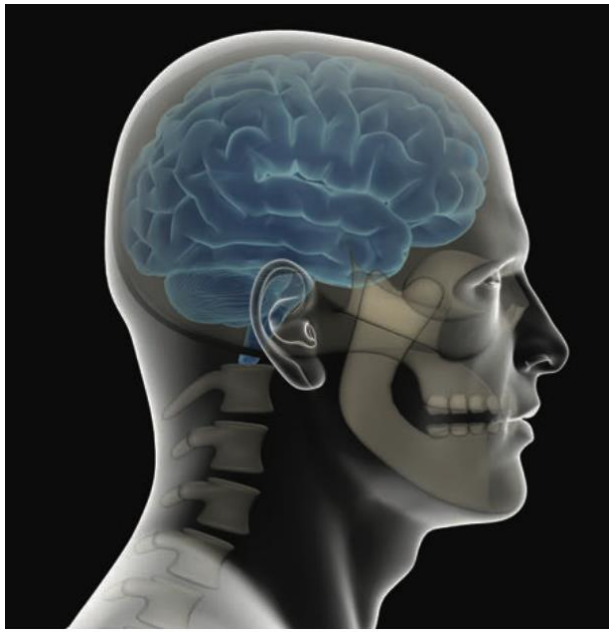
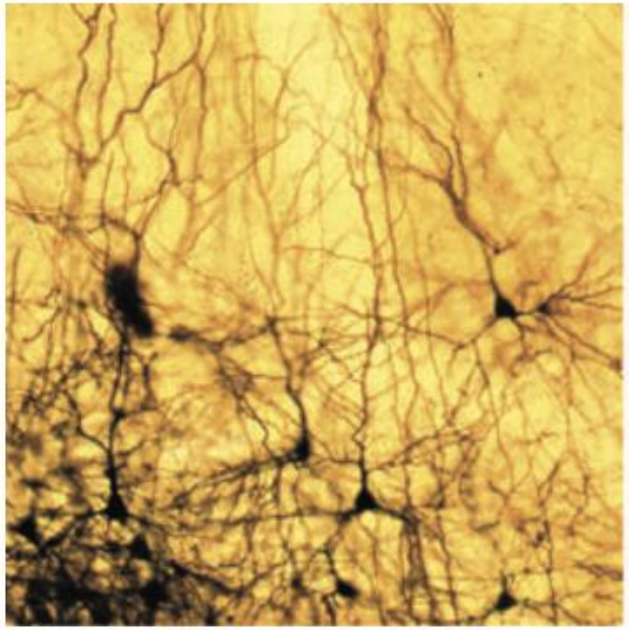
THE HUMAN BRAIN

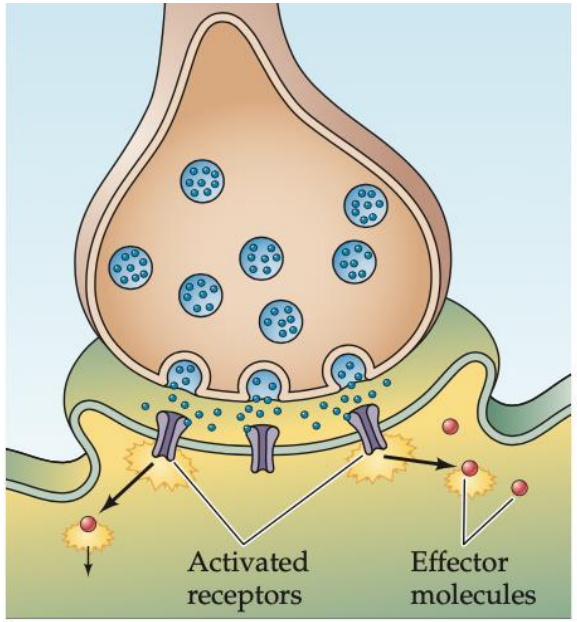
Brain



Neurons



Neurotransmitter systems



Purves et al., 2001, Neuroscience

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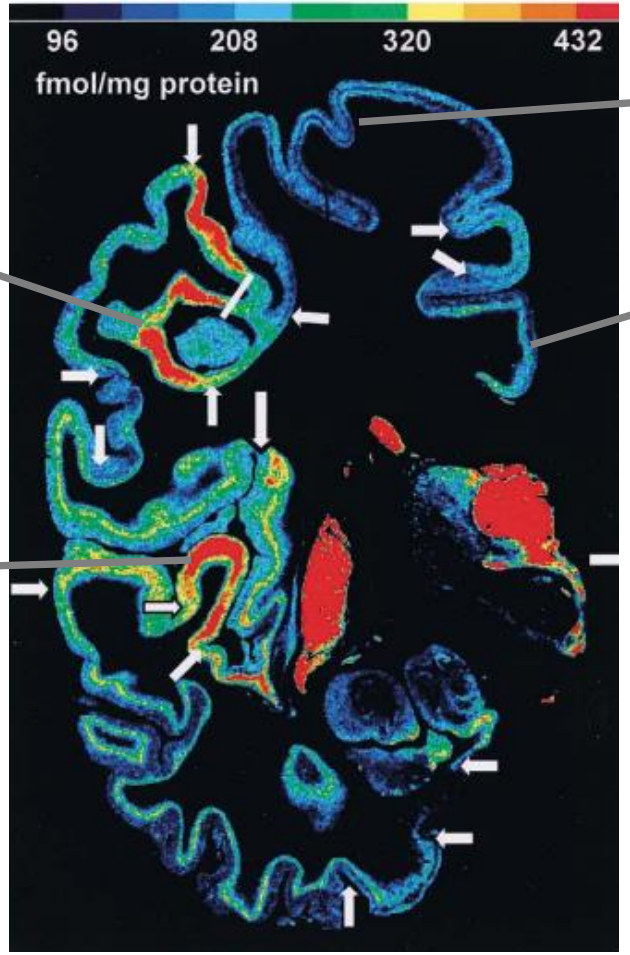
NEUROTRANSMITTER RECEPTORS AND TRANSPORTERS

Receptor autoradiography, Cholinergic muscarinic M2 receptors

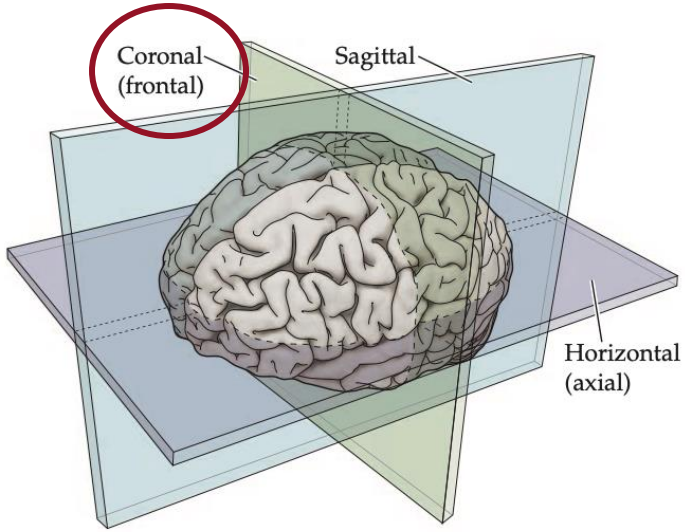


Primary motor cortex

Primary somatosensory area

Anterior cingulate cortex

Primary auditory area



Zilles et al., 2002, *European Neuropsychopharmacology;* Purves et al., 2001, Neuroscience

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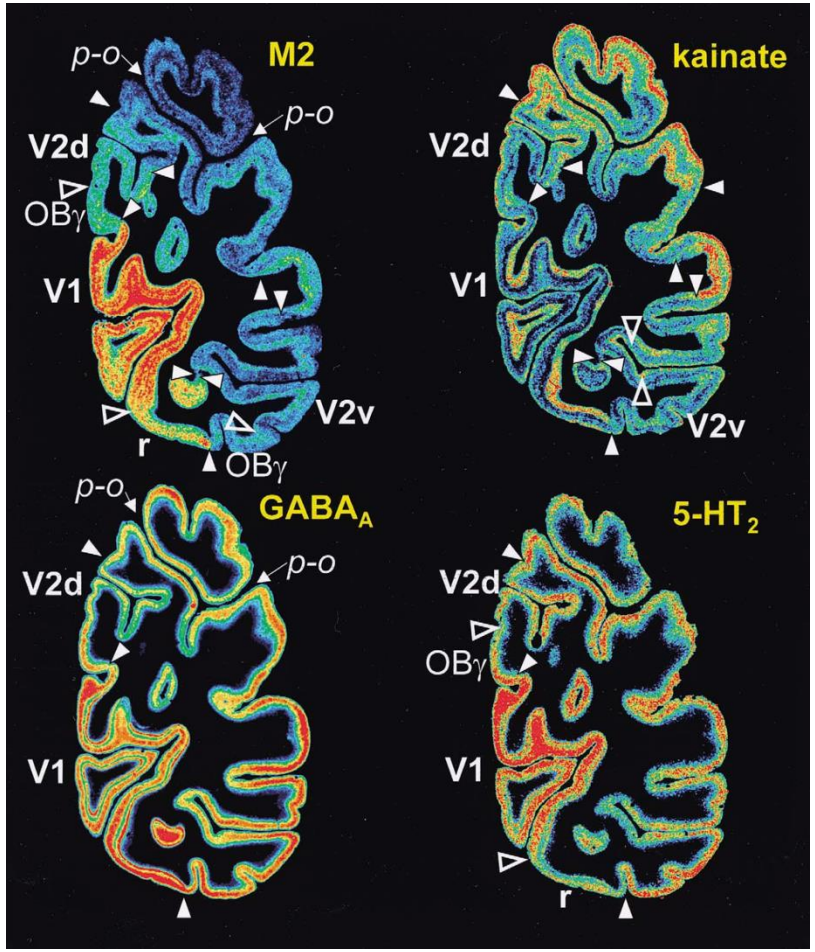
DISTRIBUTION OF MOLECULES TROUGH THE BRAIN

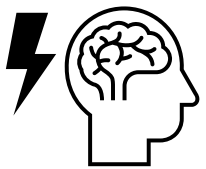
Multivariate and whole-brain analyses



Zilles et al., 2002, *European Neuropsychopharmacology*

- Physiological functions (heart rate, respiration)

- Cognition and emotion



- Imbalances:
  - Epilepsy: glutamate hyperexcitation

  - Depression: disfunctions in GABA, glutamate, serotonin, dopamine and norepinephrine

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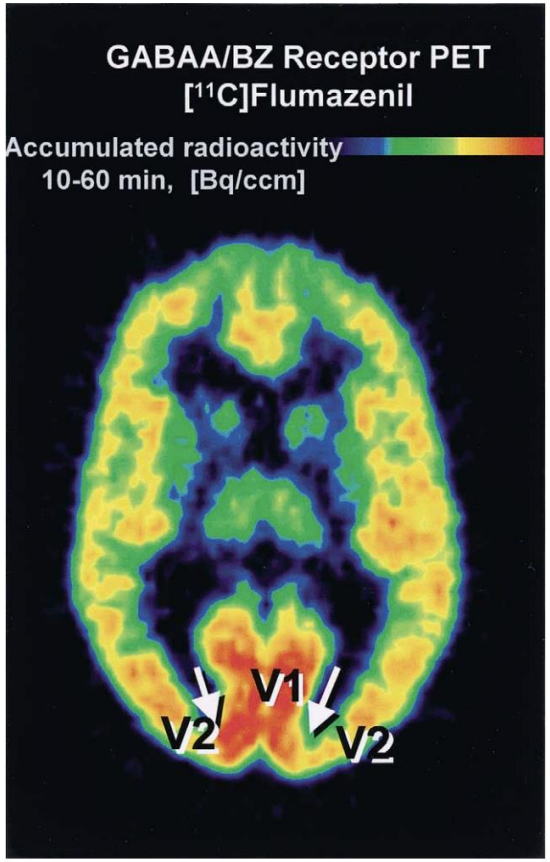
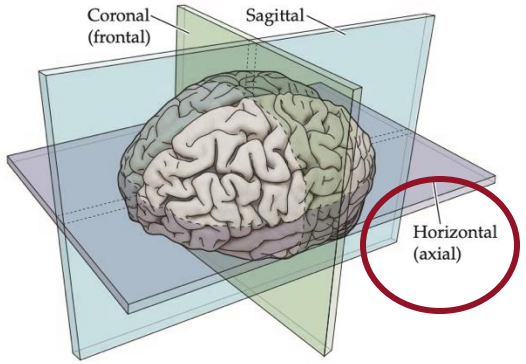
POSITRON EMISSION TOMOGRAPHY (PET)





Zilles et al., 2002, *European Neuropsychopharmacology;* Purves et al., 2001, Neuroscience; Wikipedia

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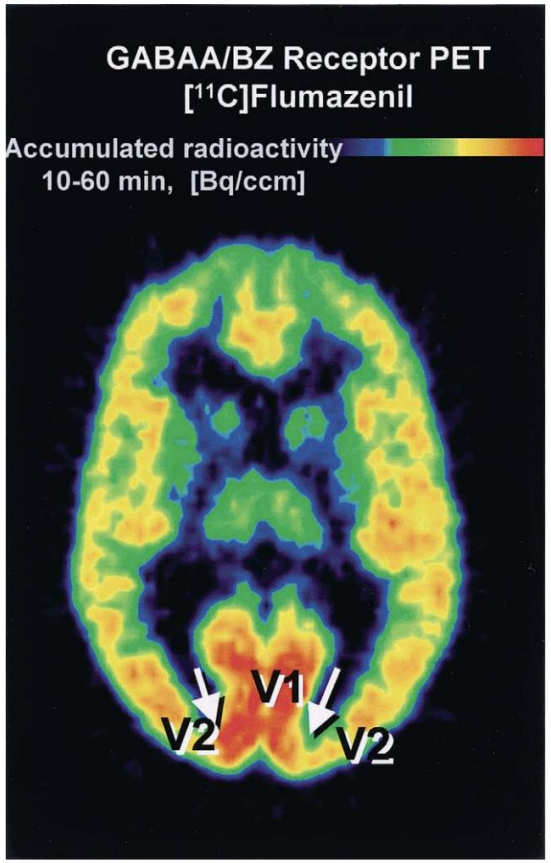
THE HUMAN BRAIN AND EVOLUTION

- The brain is a product of evolution
- Critical evolutarionary adaptations: beneficial for solving tasks
- We want to understand how evolution shaped the brain
- Enhance our understanding of neural information processing



Zilles et al., 2002, *European Neuropsychopharmacology*

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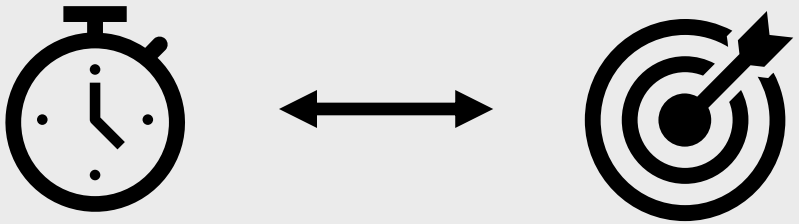
HOW TO STUDY EVOLUTIONARY SIGNALS?

Trade-off analysis



Inter-species comparison

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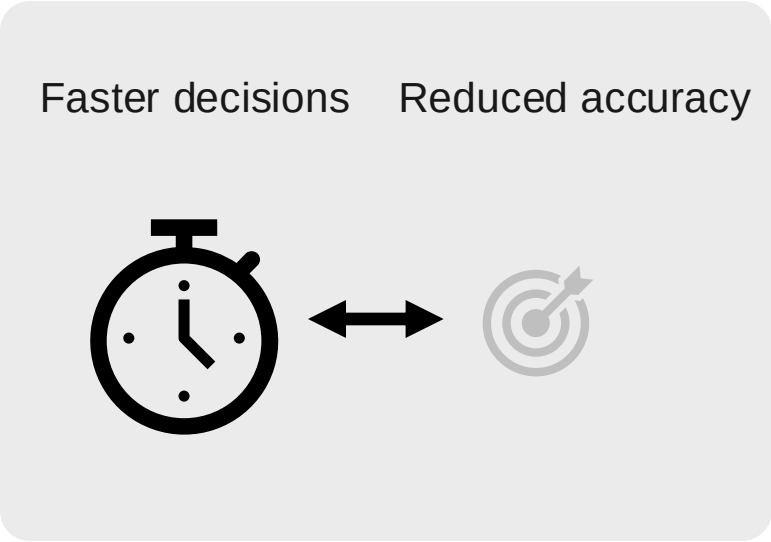
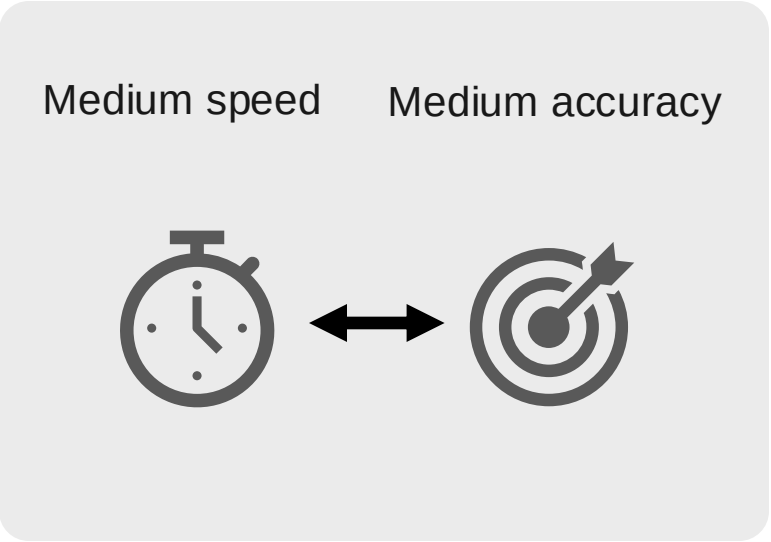
TRADE-OFFS

- Biological systems that need to perform multiple tasks face a trade-off: no system can be optimal for all tasks
- Trade-offs affect the range of phenotypes found in nature





Hart et al., 2015, *Nature Methods*; Shoval et al., 2012, *Science*

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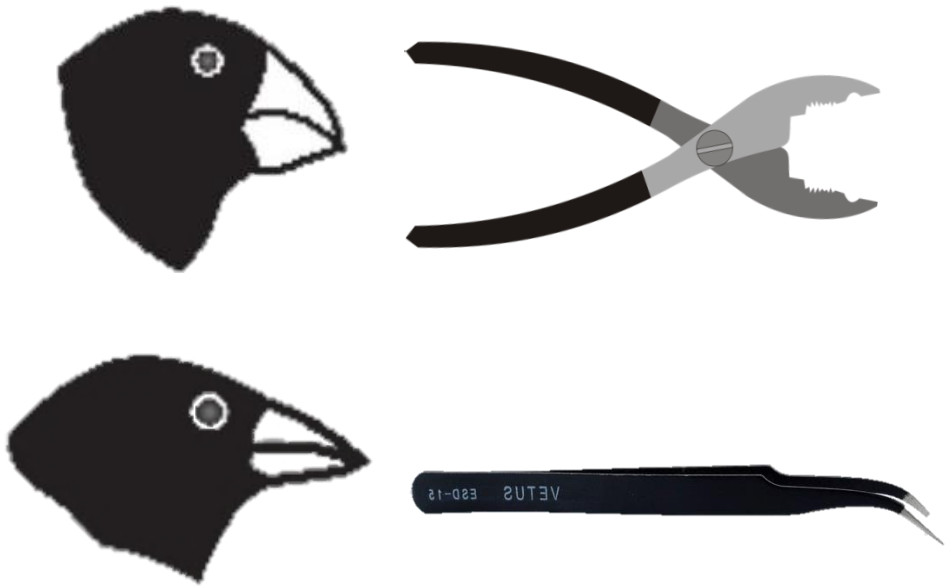
PHENOTYPES AND TASKS

Phenotypes



Tasks

Alon, 2019, An introduction to systems biology; Hart et al., 2015, *Nature Methods*; Shoval et al., 2012, *Science*
Photo by Ksenia on Unsplash; Photo by Kristine Weilert on Unsplash; Imagen de Aixklusiv en Pixabay; Imagen de Alejandra Jimenez en Pixabay

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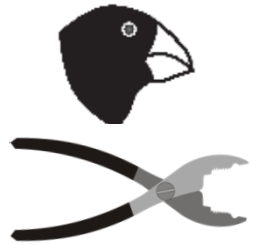
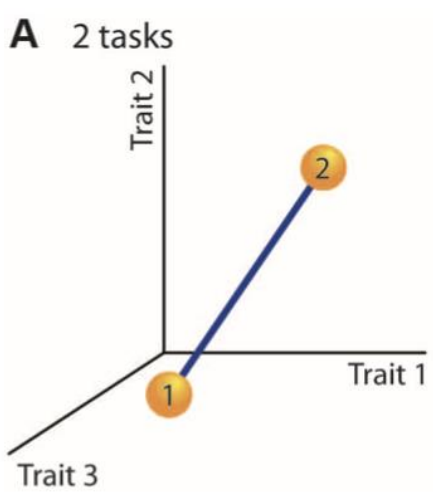
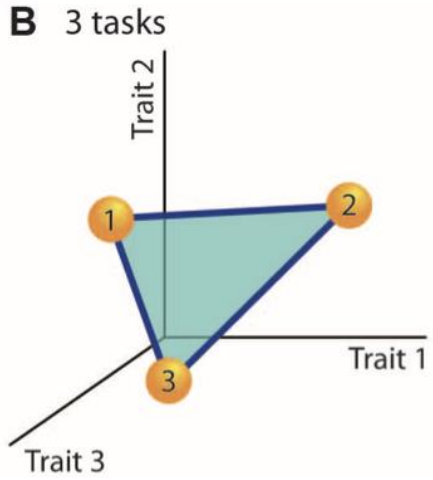
PARETO TASK INFERENCE

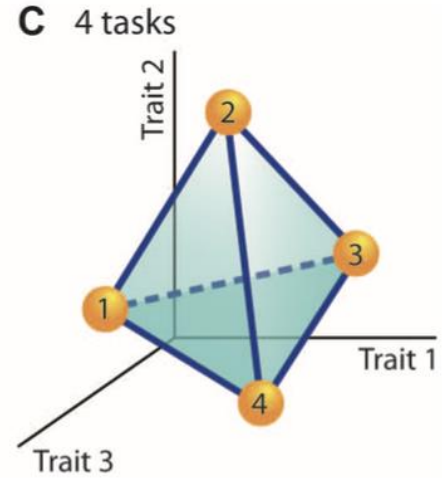
(ParTI)

- Inference of tasks from multi-dimensional data
- A polytope significantly fits the data → evolutionary trade-offs









Shoval et al., 2012, *Science;* Alon, 2019, An introduction to systems biology; Hart et al., 2015, *Nature Methods*
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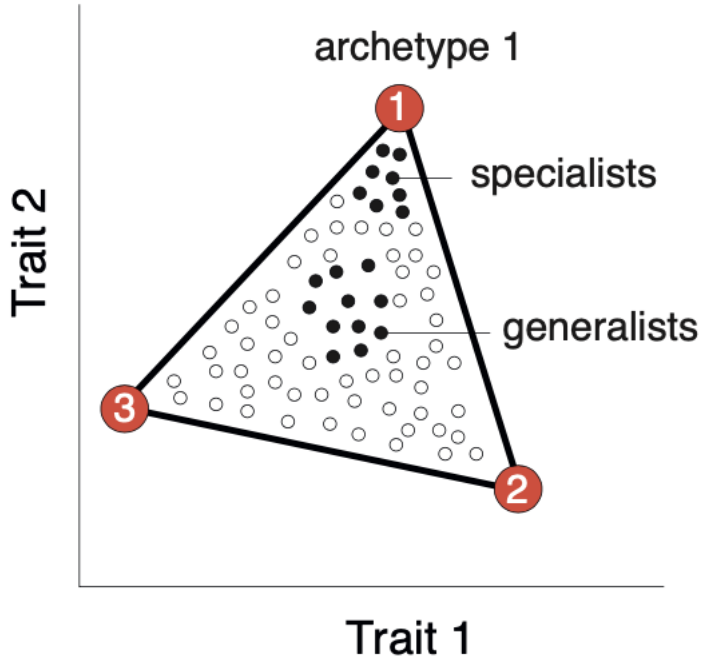
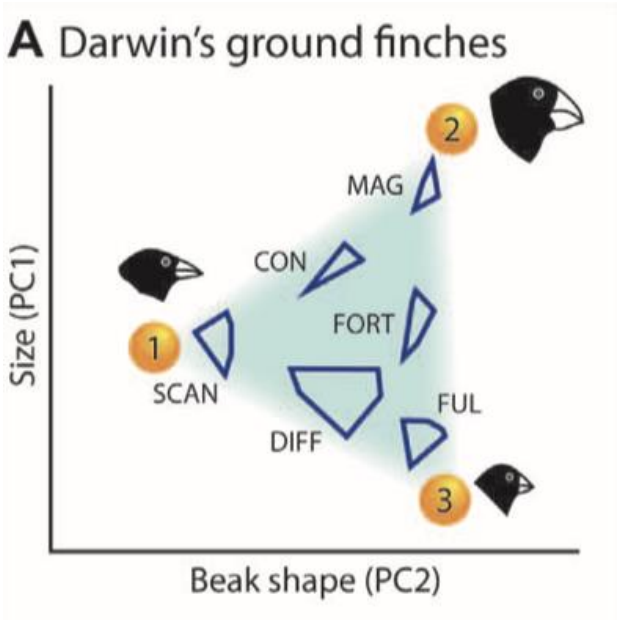
ARCHETYPES AND DISTANCES

Specialization at a particular task

- Archetype: Optimal phenotype for a certain task
- Distances to the archetype
- Specialists: Phenotypes close to an archetype
- Generalists: Phenotypes not specialized for a particular task





	Archetypes	Task (Diet)
1	Long beak, medium body	Insects, nectar
2	Large thick beak, large body	Large, hard seeds
3	Small thick beak, small body	Small, soft seeds

FORT: Medium ground finch

MAG: Large ground finch

FUL: Small ground finch

SCAN: Cactus finch

Alon, 2019, An introduction to systems biology; Hart et al., 2015, *Nature Methods;* Shoval et al., 2012, *Science;*

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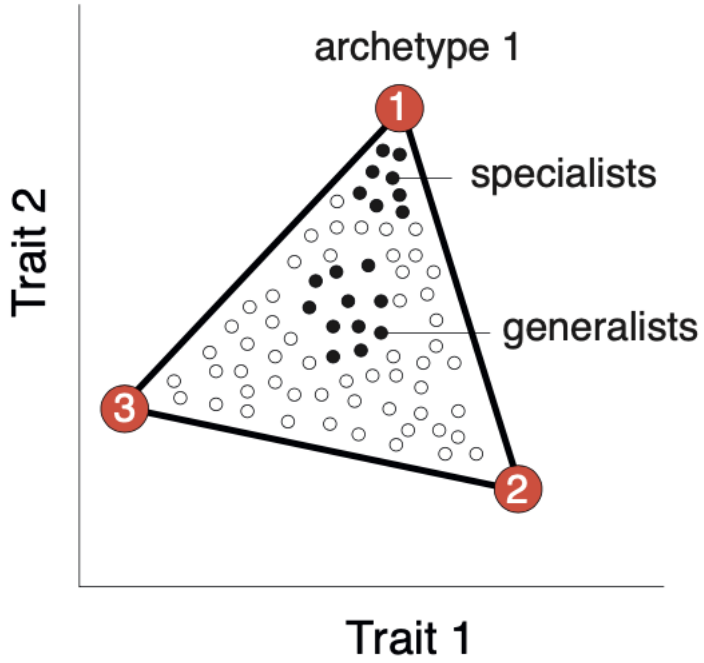
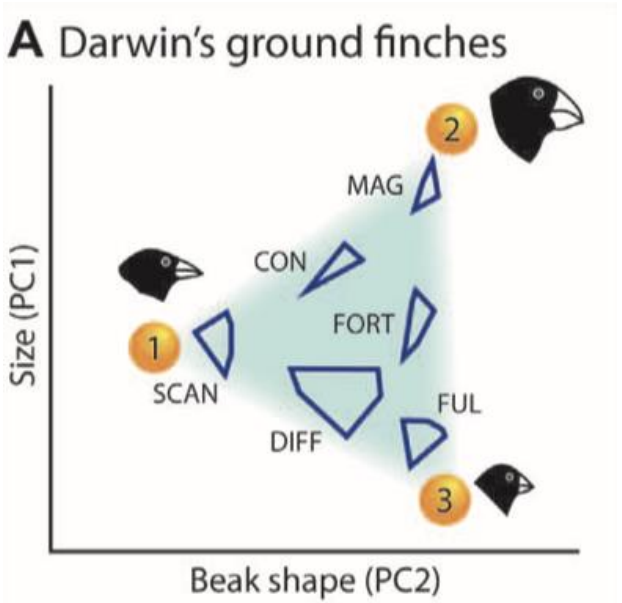
BETWEEN-SPECIES AND WITHIN-SPECIES

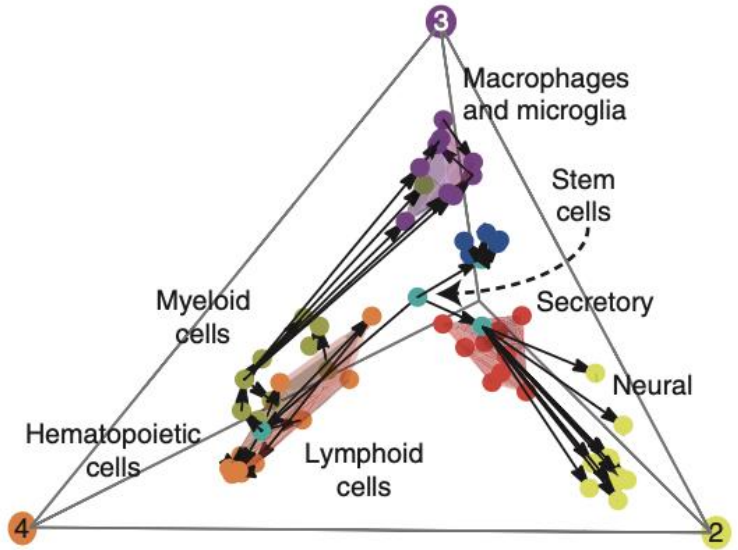
Each dot is an element



Each dot is a species



Each dot is a cell



Alon, 2019, An introduction to systems biology; Hart et al., 2015, *Nature Methods;* Shoval et al., 2012, *Science;*

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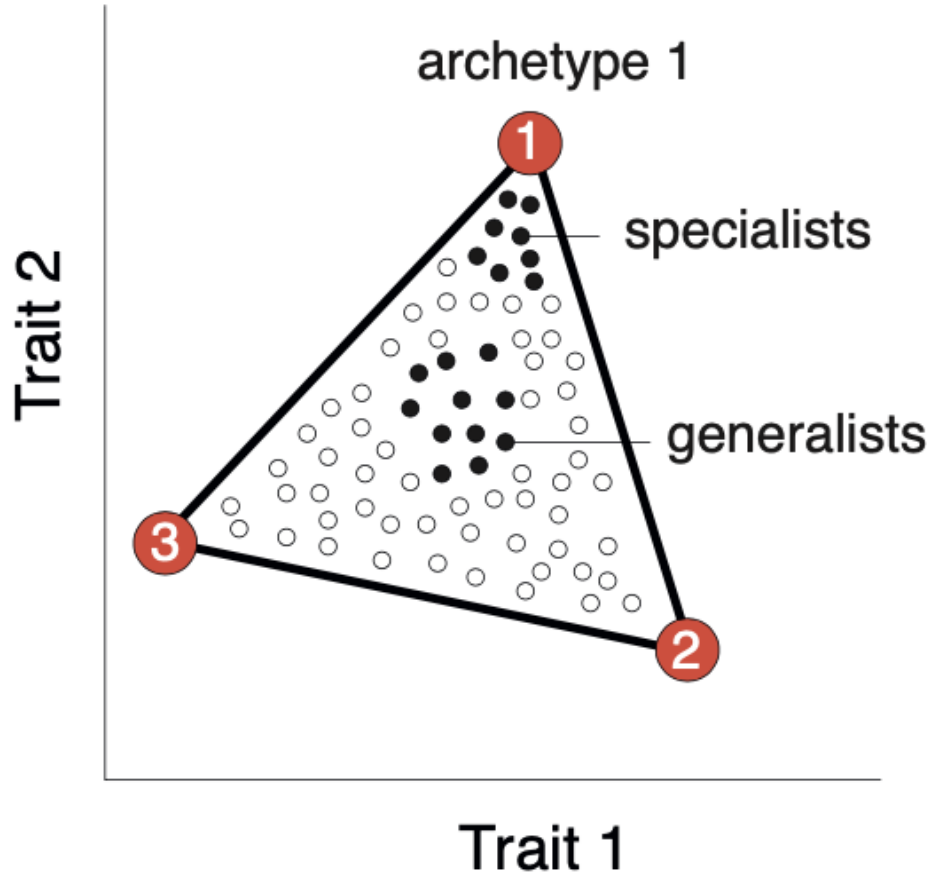
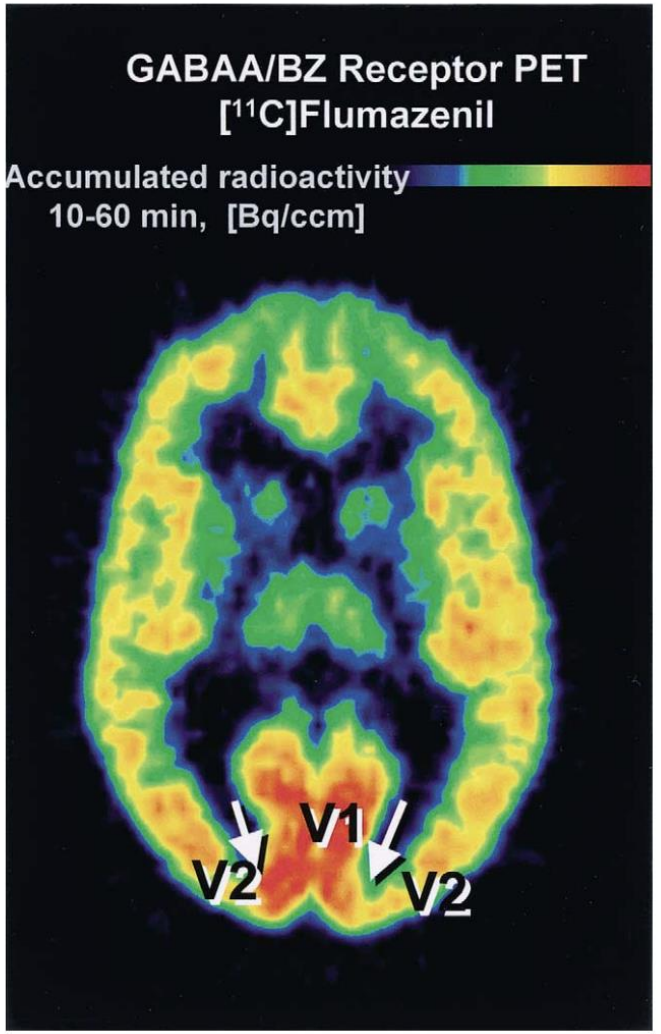
COMING BACK TO THE BRAIN





Alon, 2019, An introduction to systems biology; Zilles et al., 2002, *European Neuropsychopharmacology;*

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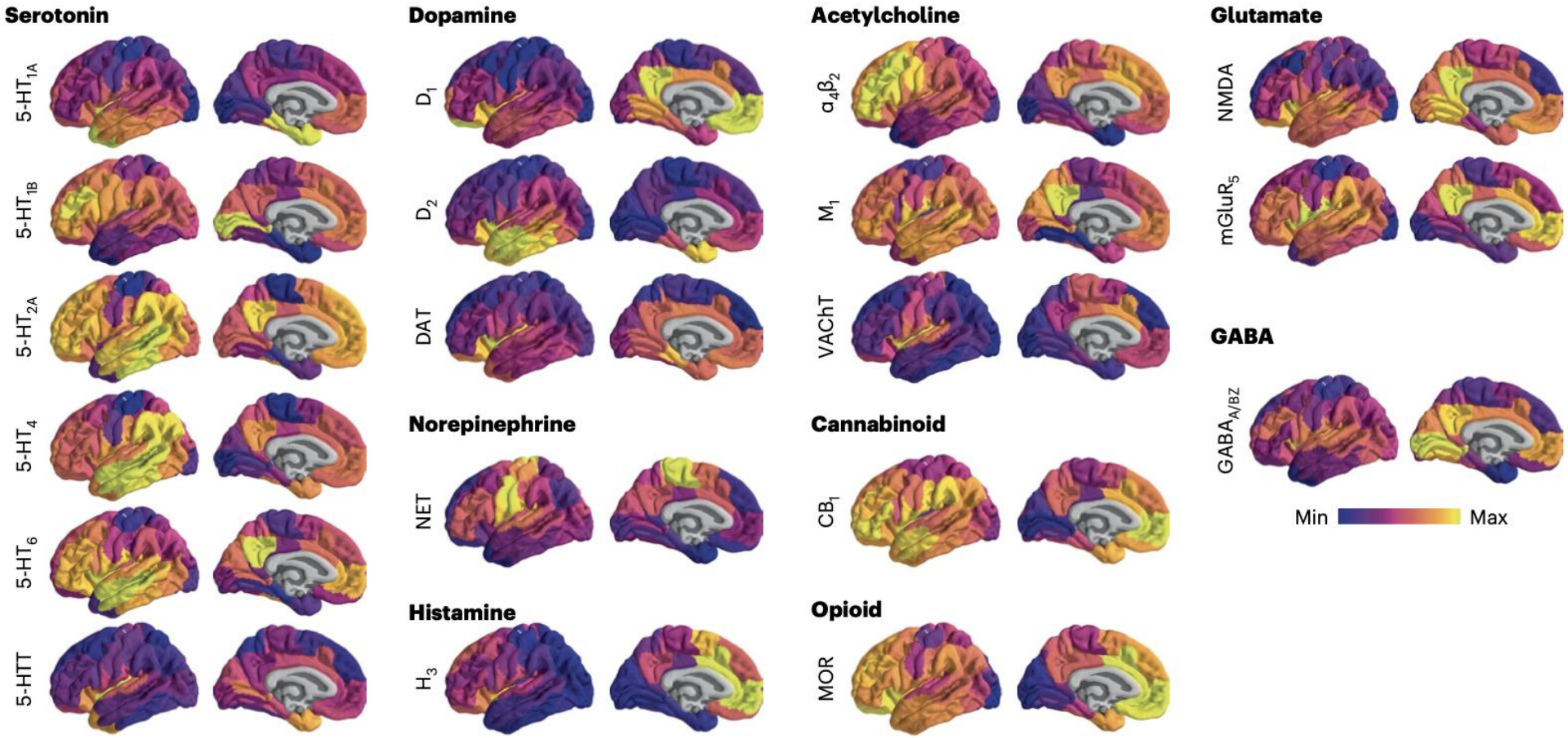
OPENLY AVAILABLE PET DATA

Tools like JuSpace or neuromaps



Hansen, et. Al., 2022, *Nature Neuroscience;* Dukart, et al., 2020, *Hum Brain Mapp*

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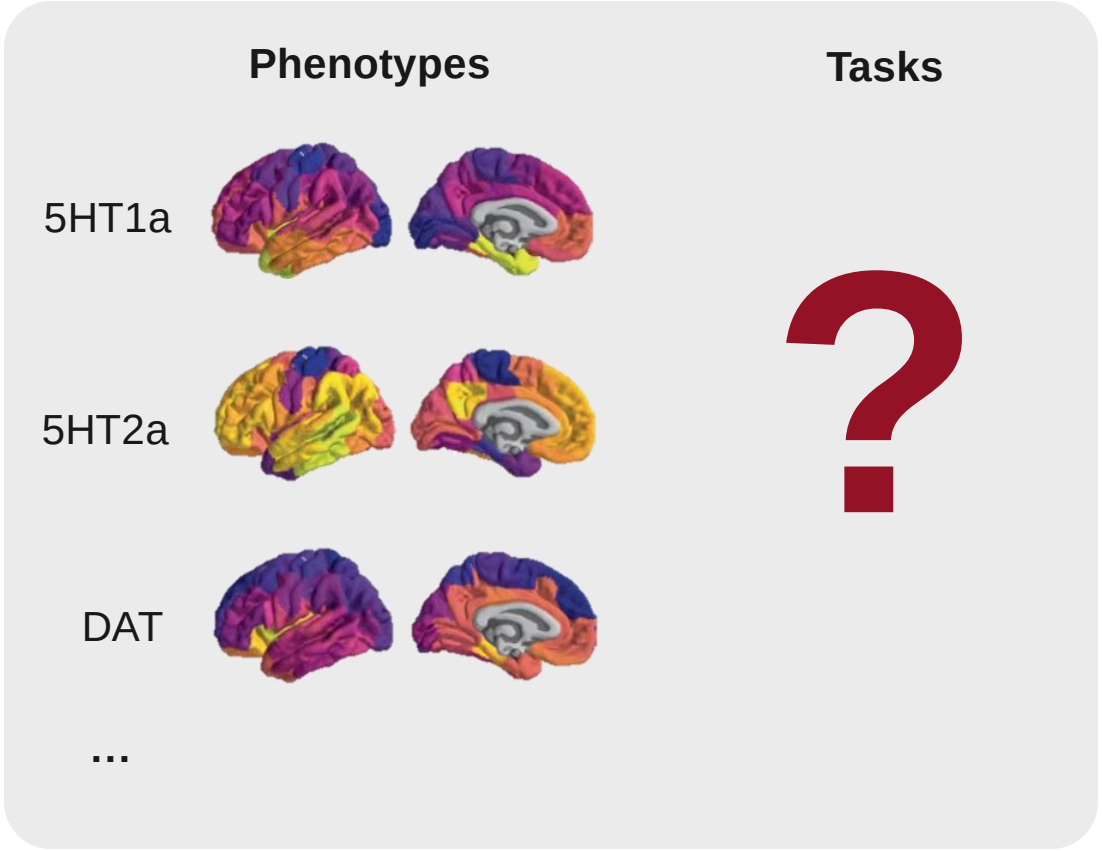
AIM



- Is there a trade-off in these distributions?
- Identify evolutionary trade-off patterns of neurotransmitter and receptor distribution in the human brain.
- Analyse PET data from several neurotransmitter systems with ParTI.

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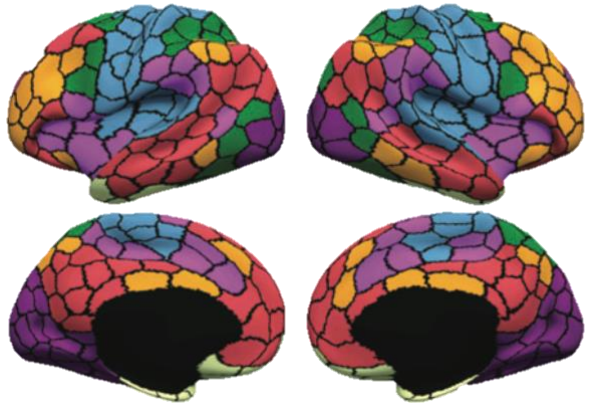
DATA

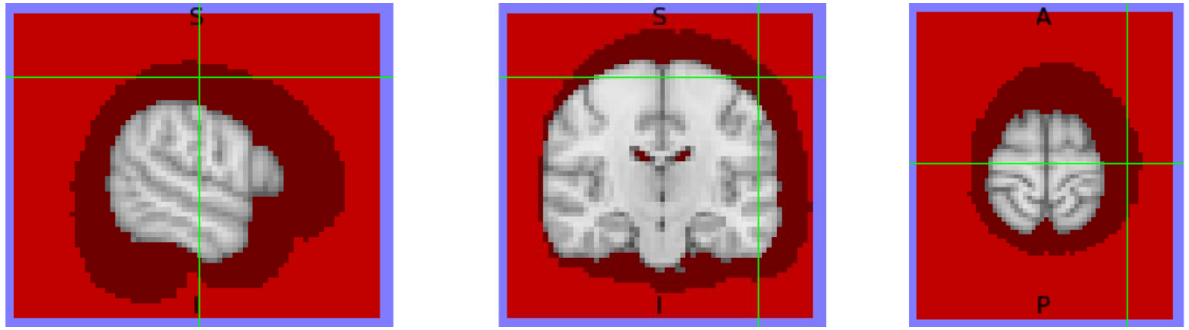
PET data:

- 5HT1a
- 5HT2a
- 5HT4
- 5HTT
- mGluR5
- DAT
- FDOPA
- GABAa
- CBF (cerebral blood flow)
- CMR (cerebral metabolic rate of glucose)

PET preprocesing

- Resampling (3mm)
- Registration to MNI template
- Standardization
- Parcellation with Schaefer atlas (1000)





Schaefer, et al., 2018, *Cereb. Cortex*

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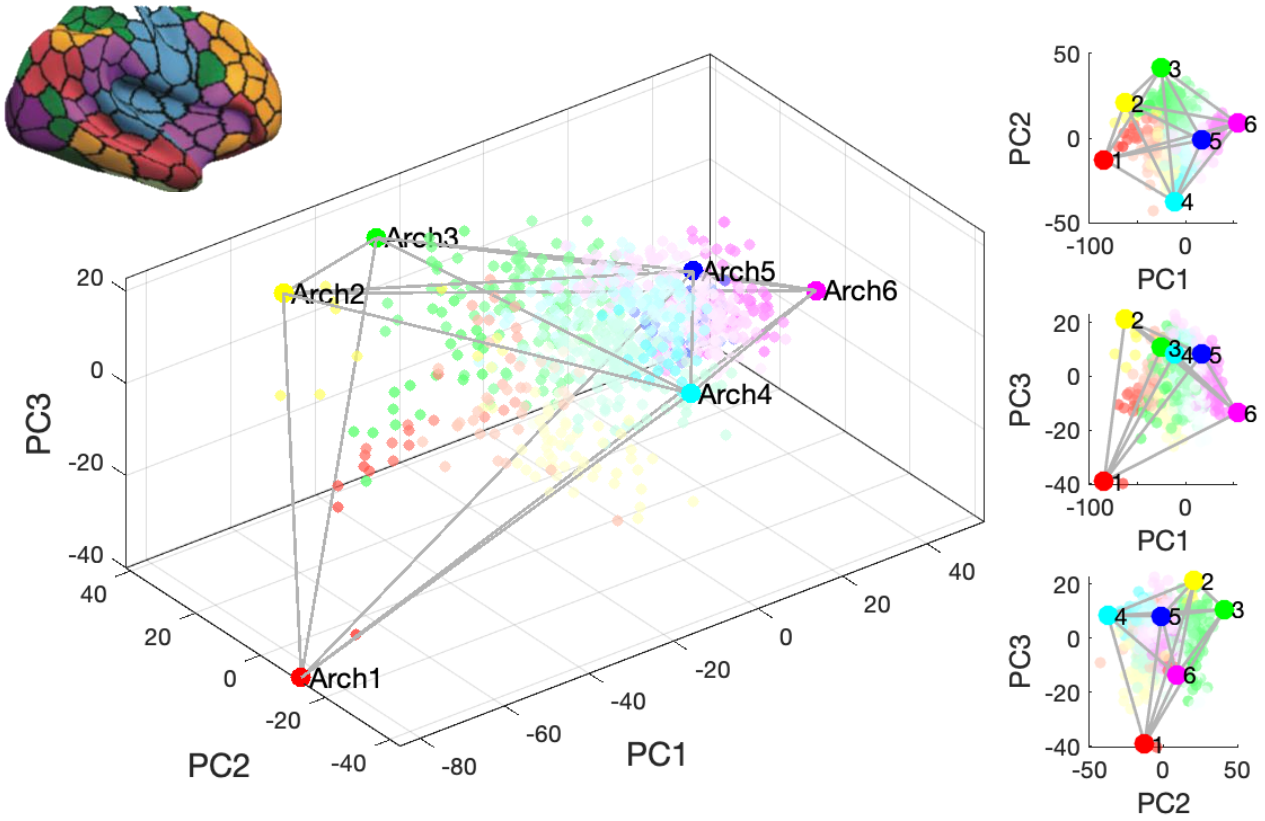
PRELIMINARY RESULTS

Polytope and Archetypes: 6 tasks

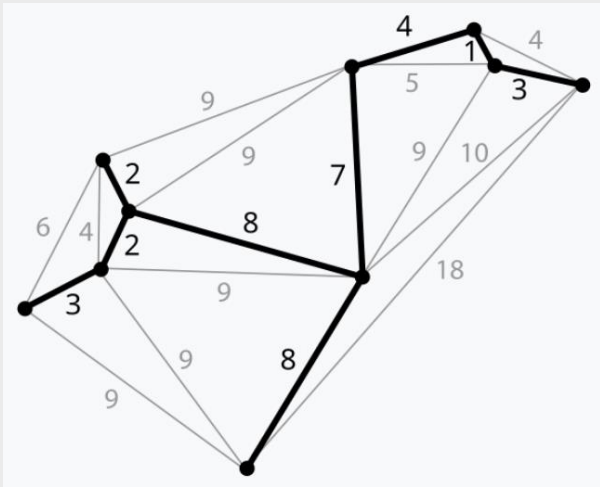


p-value=0.026

Wikipedia

Distances (can be calculated with different algorithms):

Minimum Spanning Tree (MST)



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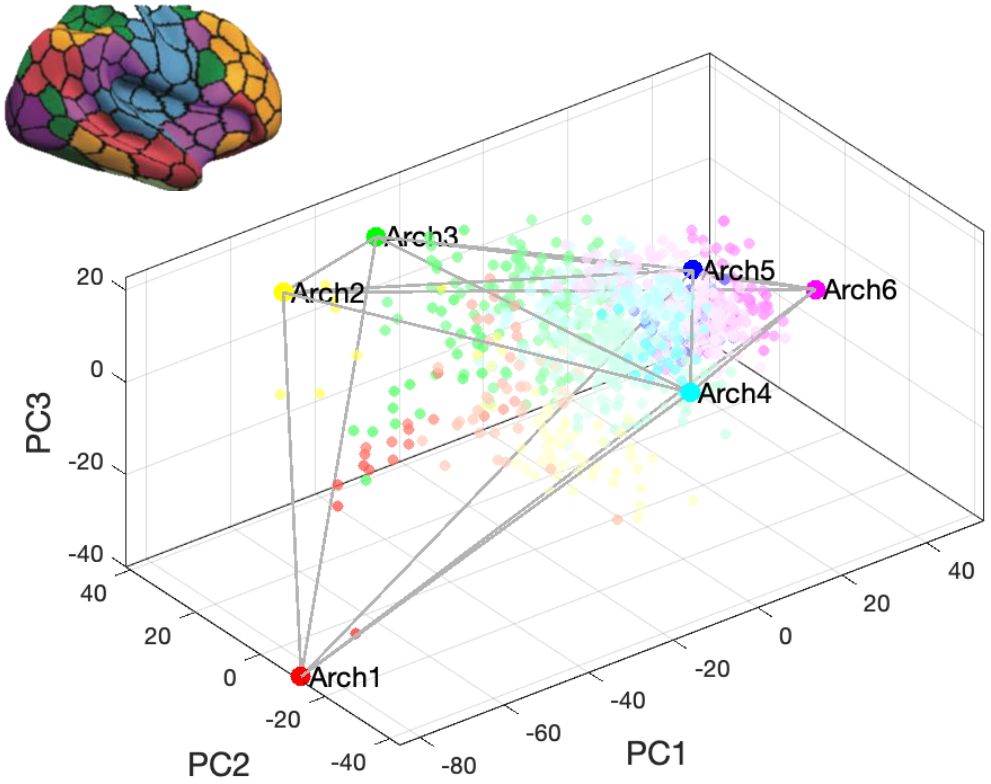
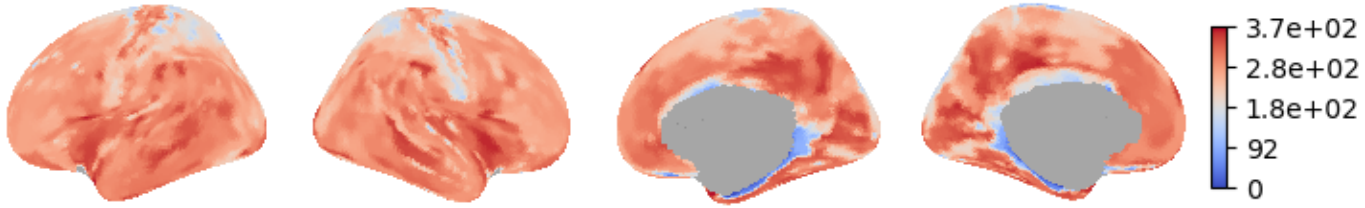
DISTANCES TO ARCHETYPES

What is the tasks associated with archetype 1? Step 1



Archetype 1 (distance of each region to vertex 1)



Limbic structures:

- Insula (emotion)
- Parahippocampal gyrus (memory)

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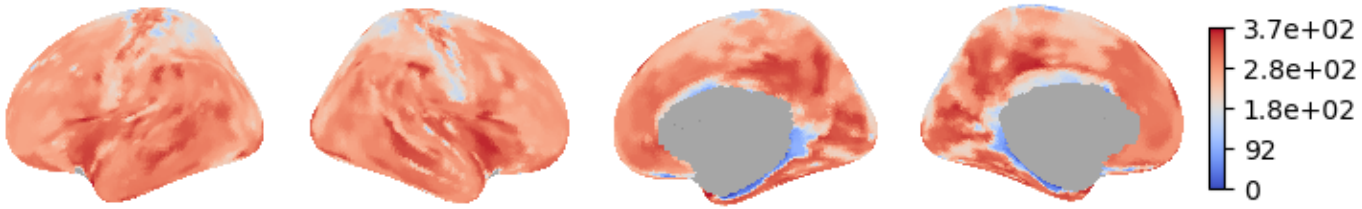
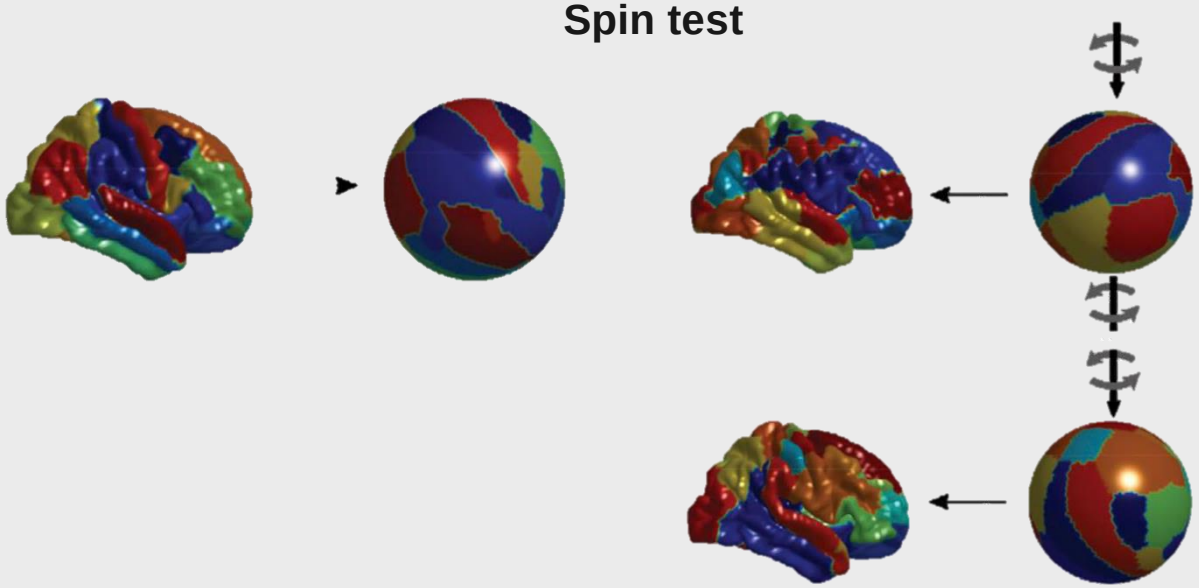
FEATURE ENRICHMENT

What is the tasks associated with archetype 1? Step 2

Archetype 1 distance of each region to vertex 1



Spin test



Significant associations

DAT (r=0.62, p-val<0.001)

GABAa (r=0.60, p<0.001)

5HT1a (r=0.60, p<0.001)

FDOPA (r=0.58, p<0.001)

5HT4 (r=0.58, p<0.002)

mGluR5 (r=0.58, p<0.002)

5HT2a (r=0.56, p<0.002)

5HTT (r=0.54, p<0.001)

CMR (r=0.37, p=0.021)

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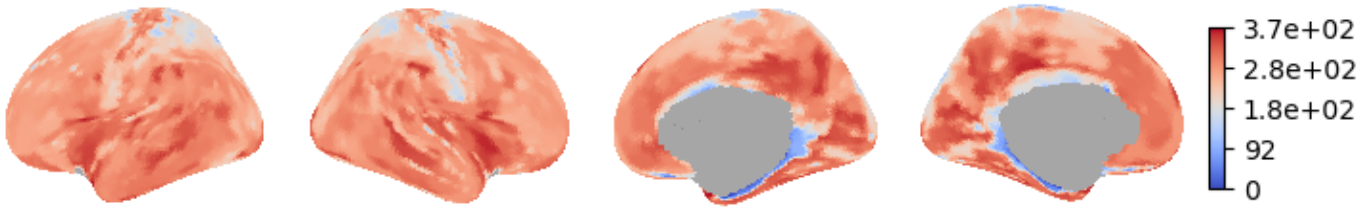
COMPARISON WITH OTHER BRAIN FEATURES

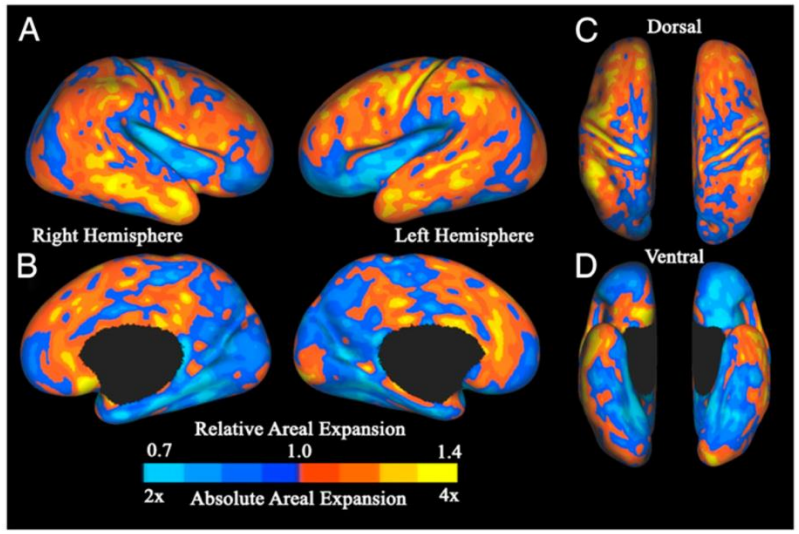
What are the tasks associated with archetype 1? Step 3

Archetype 1 distance of each region to vertex 1



Significant associations

- Expansion of brain cortex during human development and evolution ($p<0.001$)
- Differences in cortical thickness between depression and healthy controls ($p<0.001$)



- Evolutionary expansion (macaque → human)
- Brain structure
- MEG band frequencies
- Brain functional connectivity
- Geodesic distances

Hill et al., 2010, *PNAS*

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ONGOING AND FUTURE ANALYSES

- More PET datasets
- Distances to archetypes with other algorithms
- Comparison with other brain features (brain function, disorders, etc)
- Addition of subcortical data
- Cross-species comparison (macaques)

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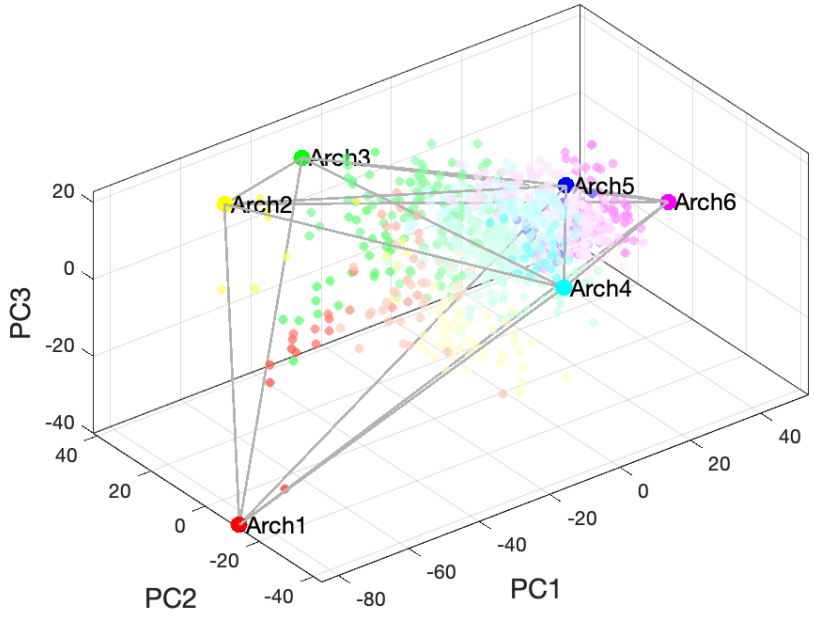
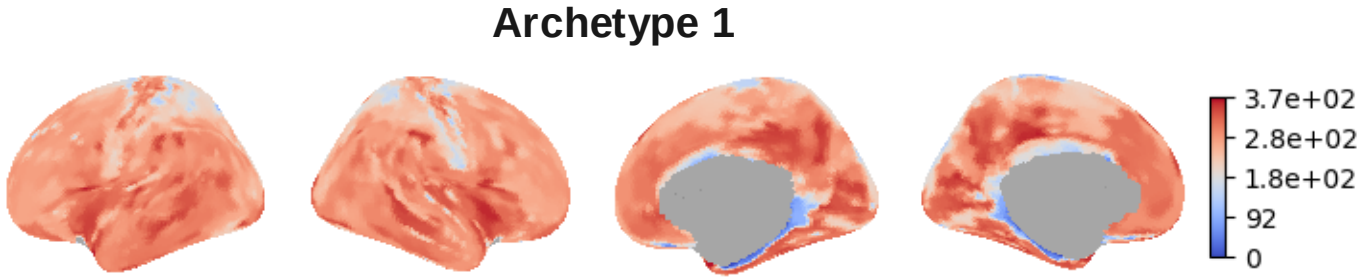
CONCLUSION

- Neurotrasmitter system might reflect evolutionary trade-offs that have influenced brain organistion
- Understanding of the spatial organisation of neurotransmitter systems
- Provide the association of such trade-off maps with other brain features, including maps of evolutariony expansion, brain function, etc





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THANK YOU!

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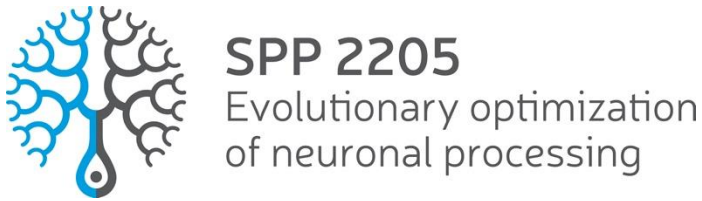
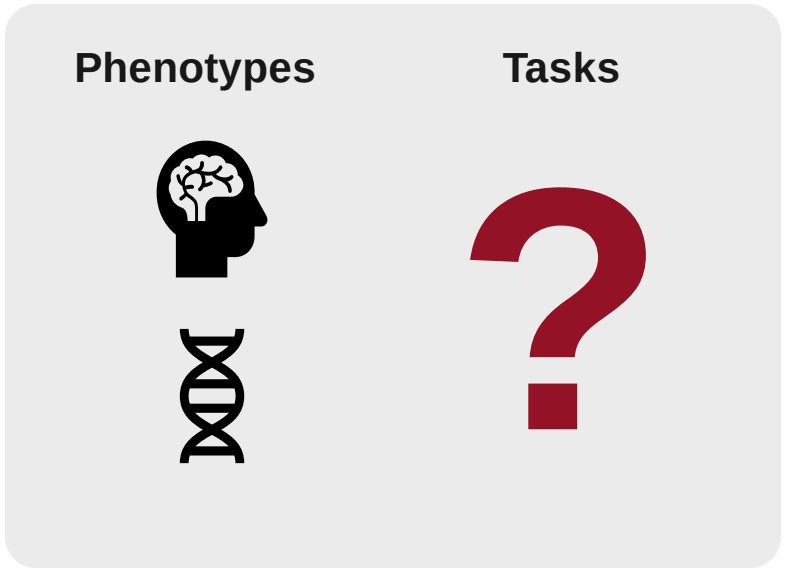
Dr. Federico Raimondo

Prof. Dr. Simon B. Eickhoff

Leonard Sasse





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