NeuroLang

ERC Starting Grant Application 2017

Demian Wassermann, Ph.D.
Inria, France

NeuroLang’s PI: Demian Wassermann

UBA
2006
Inria
2010
Harvard
2014
Inria

Education

- 2003-2005: **MsC. in Computer Sciences**, Universidad de Buenos Aires
- 2006-2010: PhD in **Signal Processing with Applications to Neuroimaging** (with highest honours)

Research Positions

- 2010-2013: Post-Doc **Harvard Medical School** and Brigham and Women’s Hospital
- Since 2014: Research Scientist, Inria

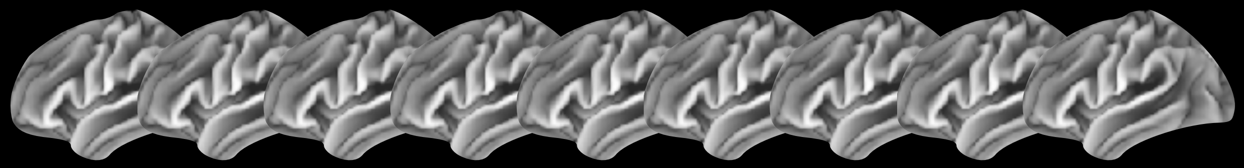
Research Interests

- Computational Neuroanatomy:
  Geometric and Semantic representations of Brain Structure and Function

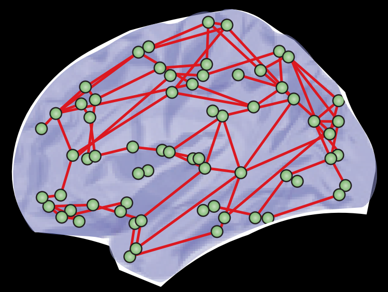
Early Achievements and Impact

- 15 journal publications; 30 conference publications; >550 citations (25% citation increase in the last year)
- Mentoring 2 post-docs; 3 PhD students; 9 masters’ students
- Raised more than **500k€ in research funding** as PI or co-PI since 2014

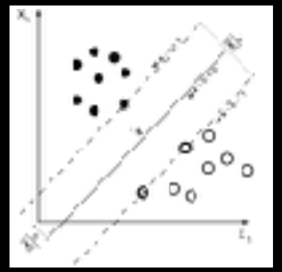
Large Scale / Big Data Studies



Network theory

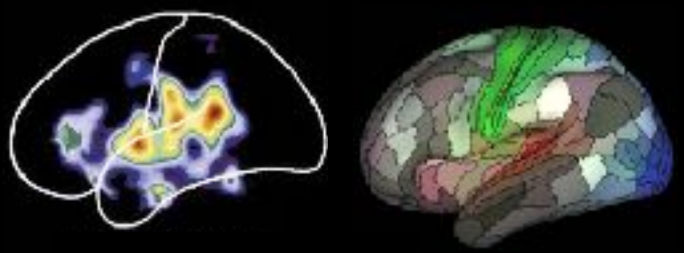


Machine Learning

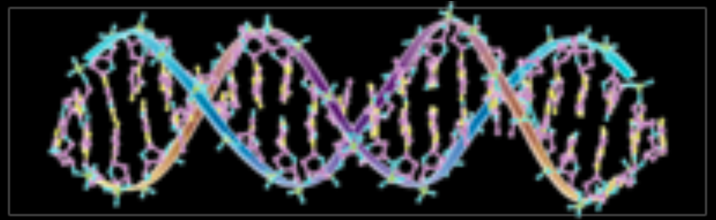


Computational Neuroanatomy

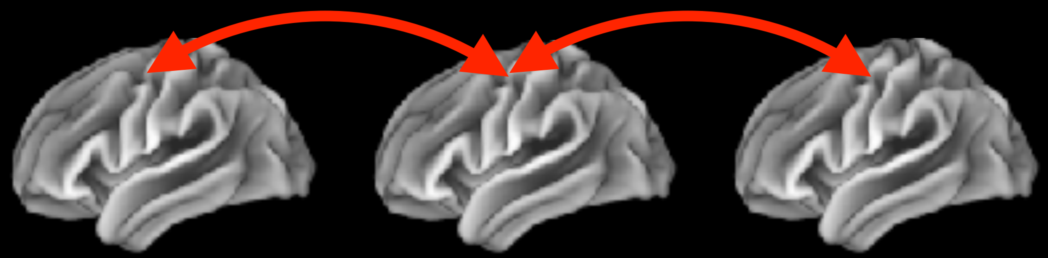
Neuroanatomy



Genetics

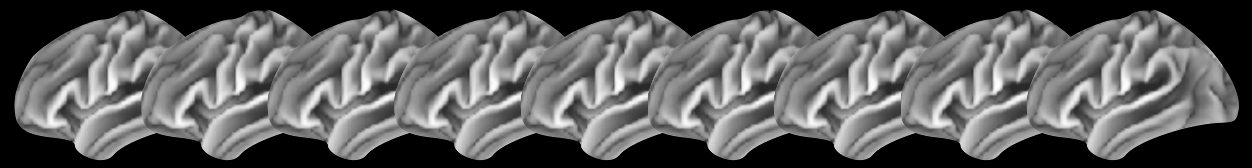


Shape Spaces

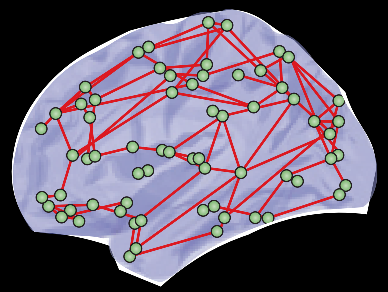


x

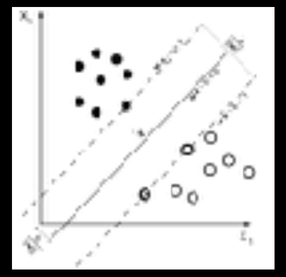
Large Scale / Big Data Studies



Network theory

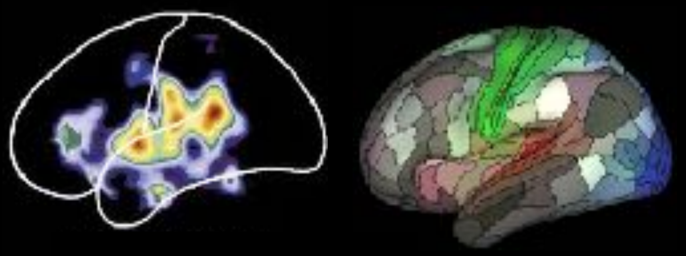


Machine Learning



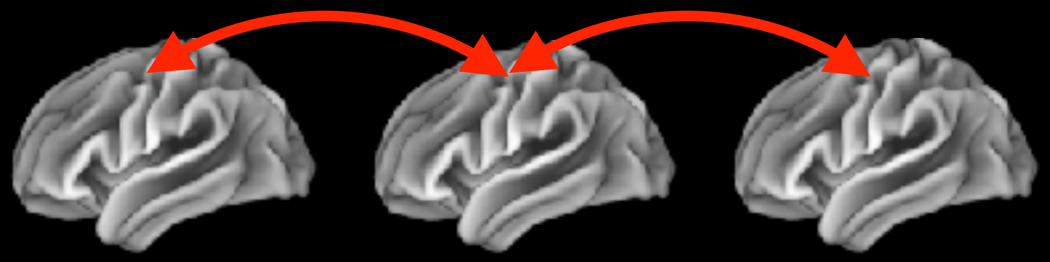
There is a growing need for a **unifying formalism** across all sub-areas of **computational neuroanatomy**

Neuroanatomy



Genetics

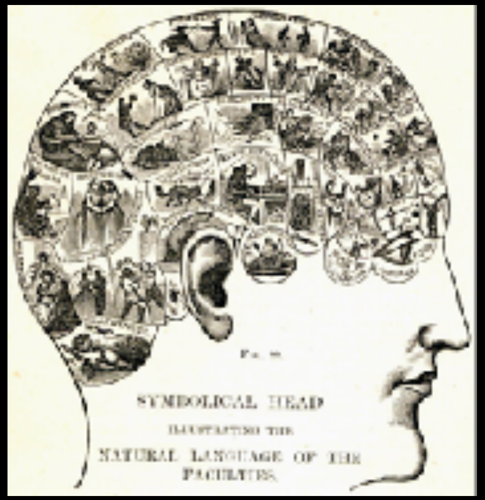
Shape Spaces



x

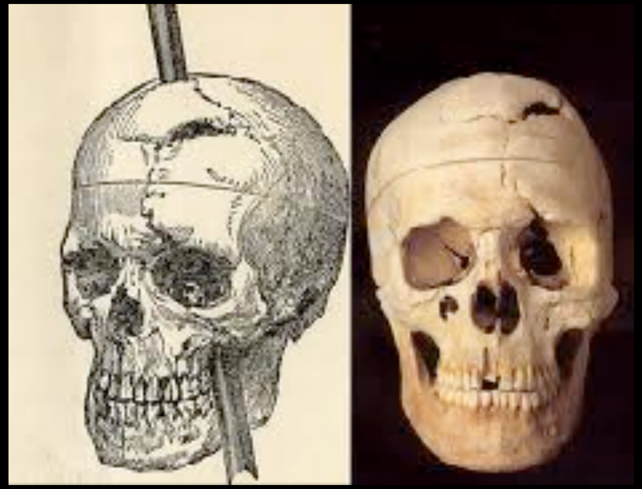
Current Neuroanatomy

Bicentennial quest for the relationship between brain location and function



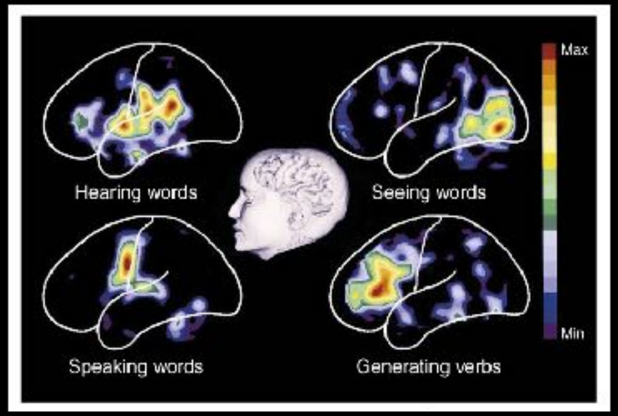
Francis Gall [1810]

Paul Broca [1861]

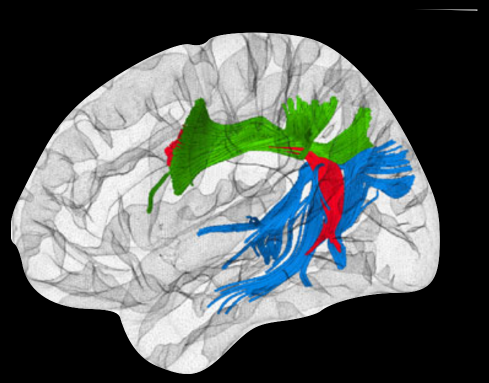


Phineas Gage case [1848]

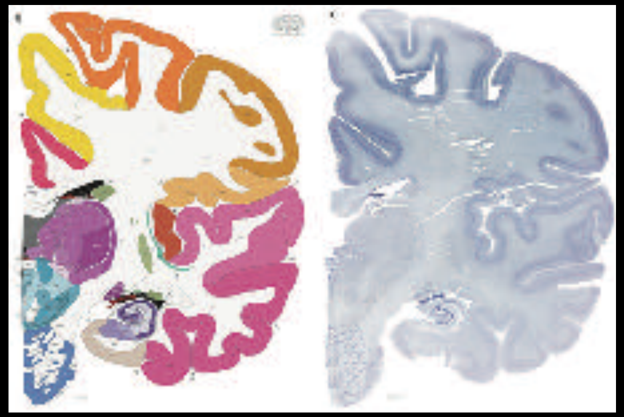
Advent of Brain Imaging: resurgence of the spatial specialization paradigm



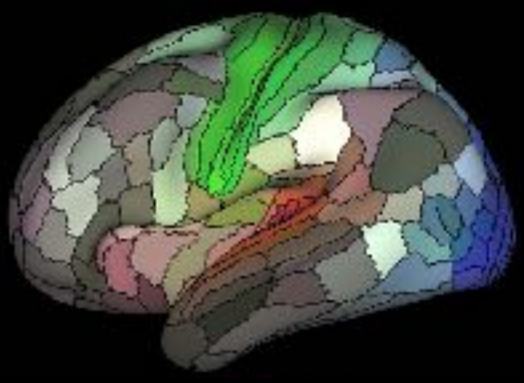
Activity Related to Function
Petersen et al [1988]



Structural Connectivity
Wassermann et al [2016]



Cellular Structure
Ding et al [2016]

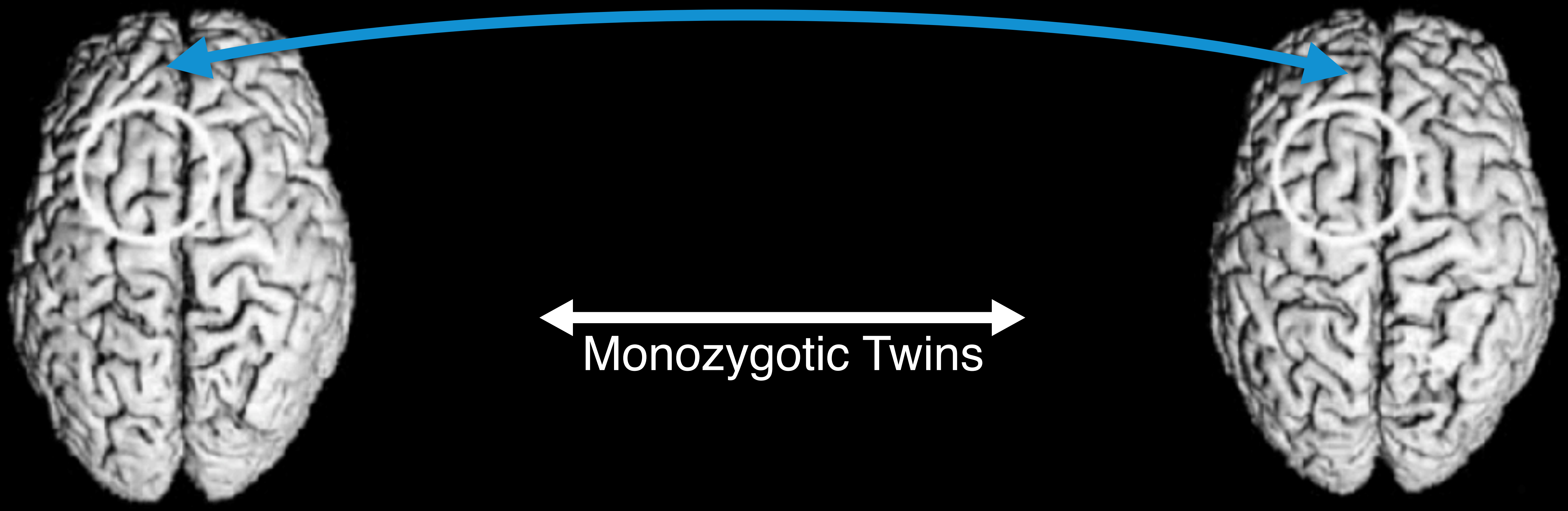


Multi-Modal
Glasser et al [2016]

x

Spatial Specialization in Neuroanatomy

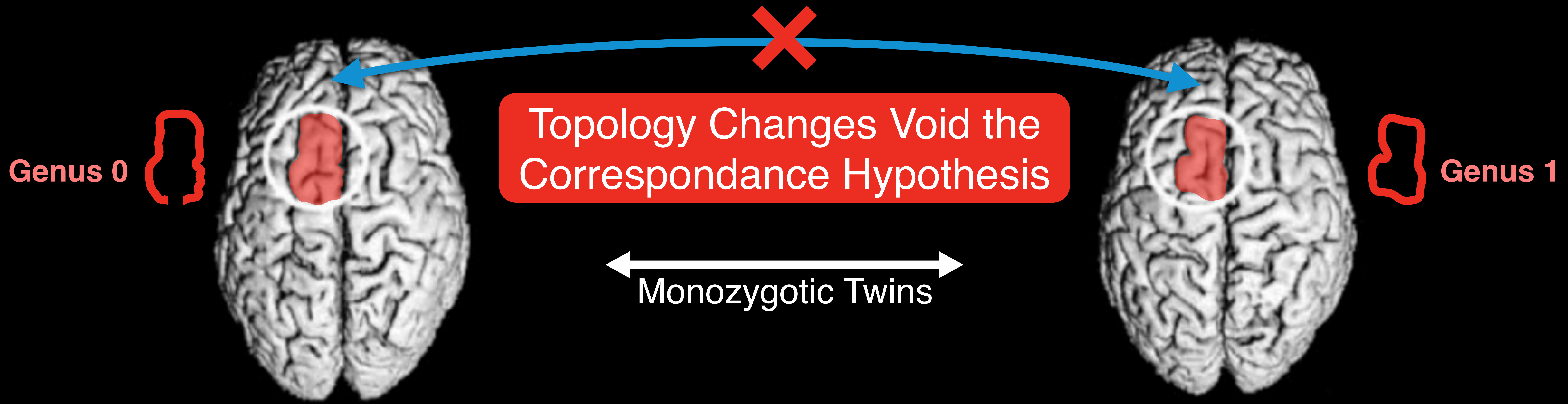
The current driving hypothesis is the existence of a
Spatial Correspondance across Individuals



x

Spatial Specialization in Neuroanatomy

The current driving hypothesis is the existence of a
Spatial Correspondance across Individuals

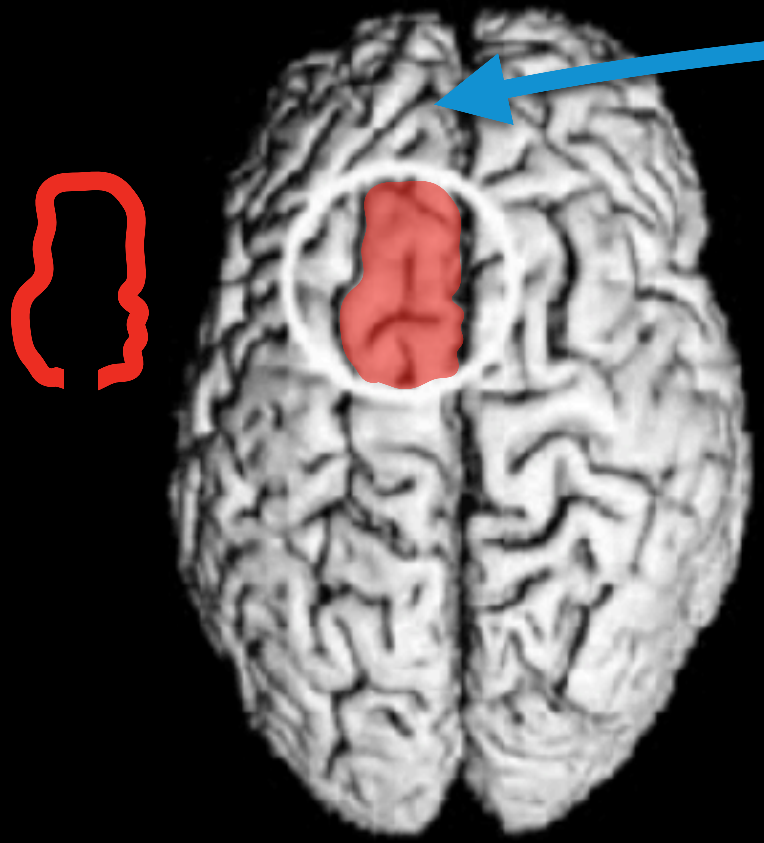


Spatial correspondance misrepresents individual characteristics **limiting 1000s of studies yearly**.

We need a new paradigm:
Semantic Representations of Neuroanatomy

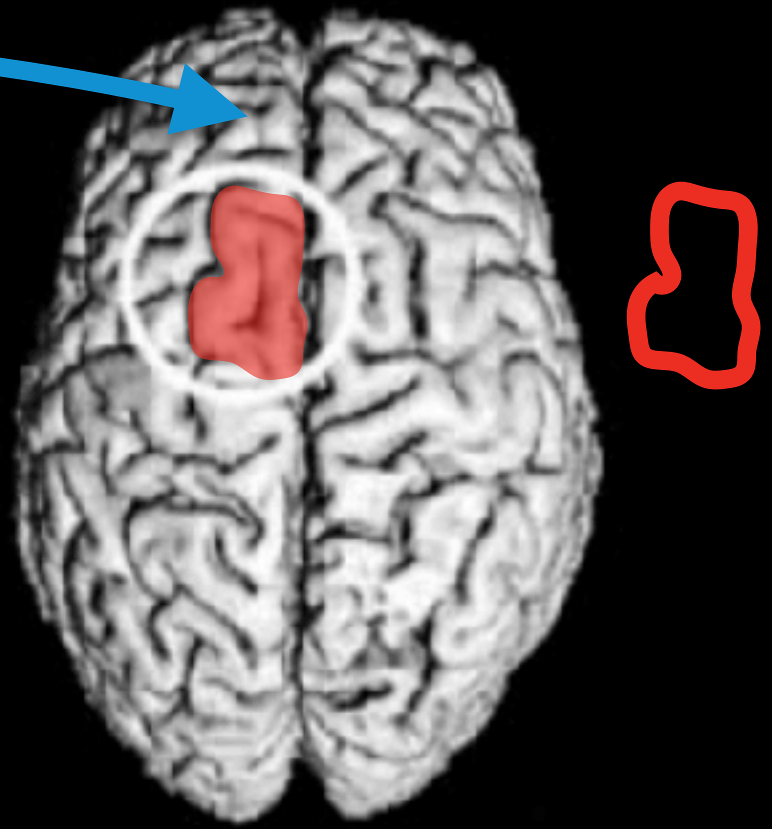
Spatial Specialization in Neuroanatomy

The current driving hypothesis is the existence of a
Spatial Correspondance across Individuals



Semantic Representation Example:

“The ***Supplementary Motor Cortical Area*** is on the **midline of** the **hemisphere anterior to** the **primary motor cortex leg representation**”



Spatial correspondance misrepresents individual characteristics **limiting 1000s of studies yearly**.

We need a new paradigm:
Semantic Representations of Neuroanatomy

NeuroLang: Semantic Neuroanatomy

The main challenge is to develop a specific language to unify neuroanatomy and apply it to solve cognitive and neurological problems

We propose to develop a Neuroanatomy Domain Specific Language (DSL).

DSLs are computer languages that:

- **Express solutions** in the idiom of the problem domain.
- **Produce programs** that are reusable & self documenting.
- **Embody domain knowledge**, enabling its conservation.

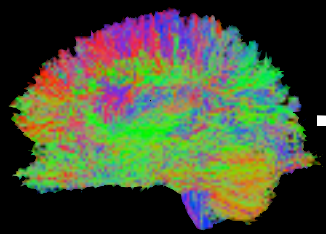
Semantic Representation of White Matter

"The **arcuate fascicle connects** the frontal and temporal lobes **coursing through** the parietal lobe"

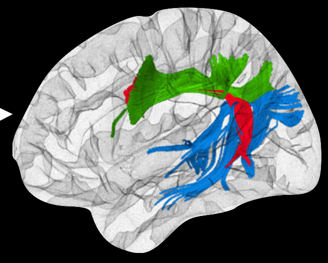
White Matter DSL Query

arcuate_fascile is
white matter tract **and**
connects temporal lobe with frontal lobe
and courses through parietal lobe

$$\{\mathbf{x} : \mathbf{x} \subset \mathcal{W} \leftarrow p_1(\mathbf{x}, C_1, C_2) \wedge p_2(\mathbf{x}, C_3)\}$$



White Matter DSL Engine



[Wassermann et al 2013, 2016]

x

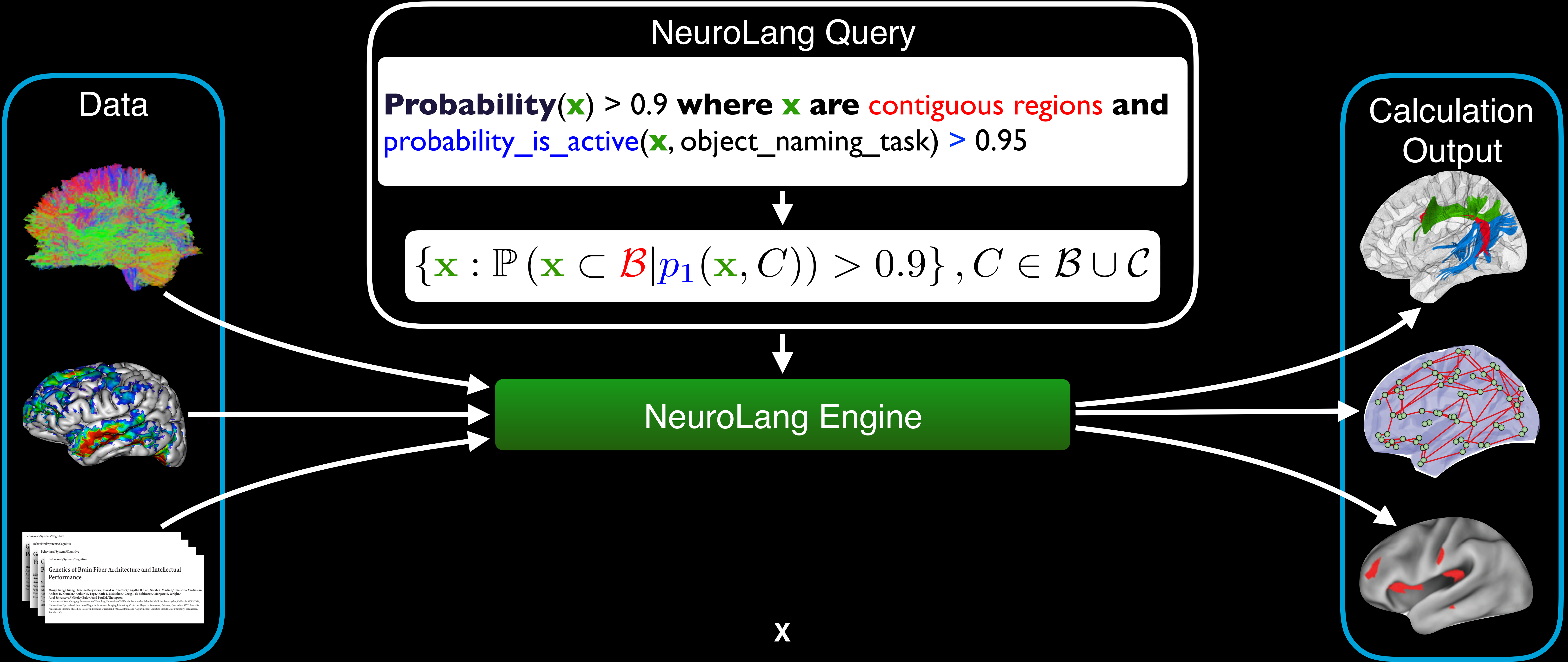
The NeuroLang DSL

"What cortical regions are involved in language processing?"

↓

"What were the most probably active contiguous regions under the simple object naming task?"

↓



NeuroLang: Challenges

The main challenge is to develop a specific language to unify neuroanatomy and apply it to solve cognitive and neurological problems

For this, NeuroLang will tackle the **specific challenges**:

1. Design a neuroanatomical Domain-Specific Query Language
2. Represent neuroanatomical organisation and data.
3. Enable large-scale statistical Inference in a neuroanatomical DSL.
4. Accelerate reproducible research and applications in clinical and cognitive research.

NeuroLang: Challenges

The main challenge is to develop a specific language to unify neuroanatomy and apply it to solve cognitive and neurological problems

For this, NeuroLang will tackle the **specific challenges**:

1. Design a neuroanatomical Domain-Specific Query Language
2. Represent neuroanatomical organisation and data.
3. Enable large-scale statistical Inference in a neuroanatomical DSL.
4. Accelerate reproducible research and applications in clinical and cognitive research.

x

Challenge 1: Design a Neuroanatomical DSL

Approach

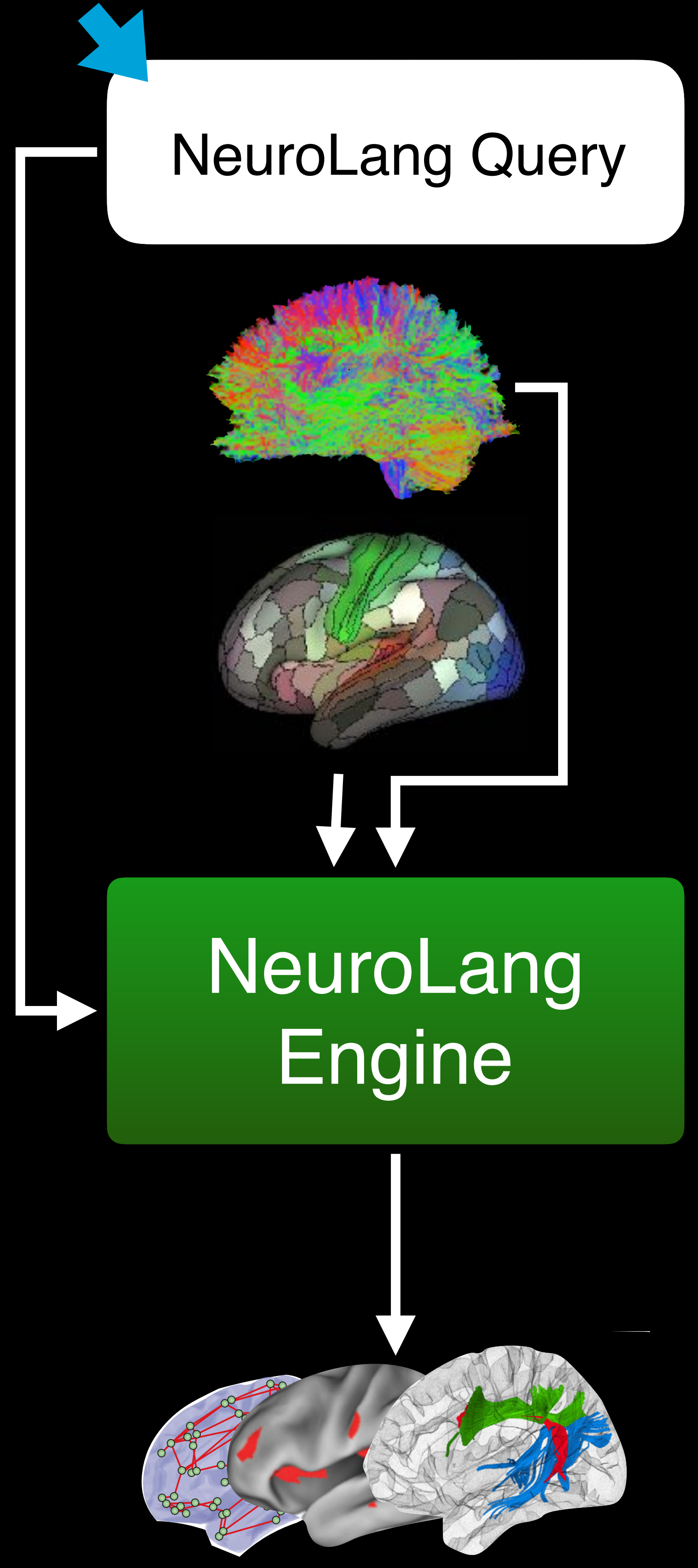
1. **Catalogue** the neuroanatomist's lexical phrases for characterising brain structures, connectivity, and function.

2. **Formalise** the neuroanatomist's lexicon as queries and design the corresponding query DSL.

3. **Enable** this DSL to use these queries to perform neuroimaging data analysis within and across databases.

Outcome

- DSL-based **formalisation of brain anatomy as a query language.**
- **Identification of neuroanatomical regions** beyond spatial matching.



Challenge 1: Design a Neuroanatomical DSL, an Example

"The **arcuate fascicle connects** the frontal and temporal lobes **coursing through** the parietal lobe"

NeuroLang Query

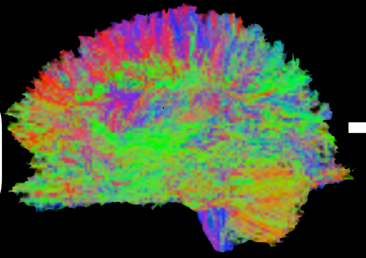
arcuate_fascile is white matter tract **and** connects temporal lobe with frontal_lobe **and** courses through parietal_lobe

$$\{\mathbf{x} : \mathbf{x} \subset \mathcal{W} \leftarrow p_1(\mathbf{x}, C_1, C_2) \wedge p_2(\mathbf{x}, C_3)\}\ C_1, C_2, C_3 \subset \mathcal{R}$$

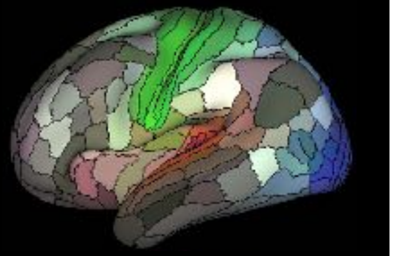
[Wassermann et al 2013, 2016]

NeuroLang Query

$\mathcal{W}$:

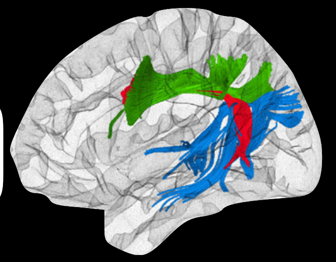


$\mathcal{R}$:



NeuroLang Engine

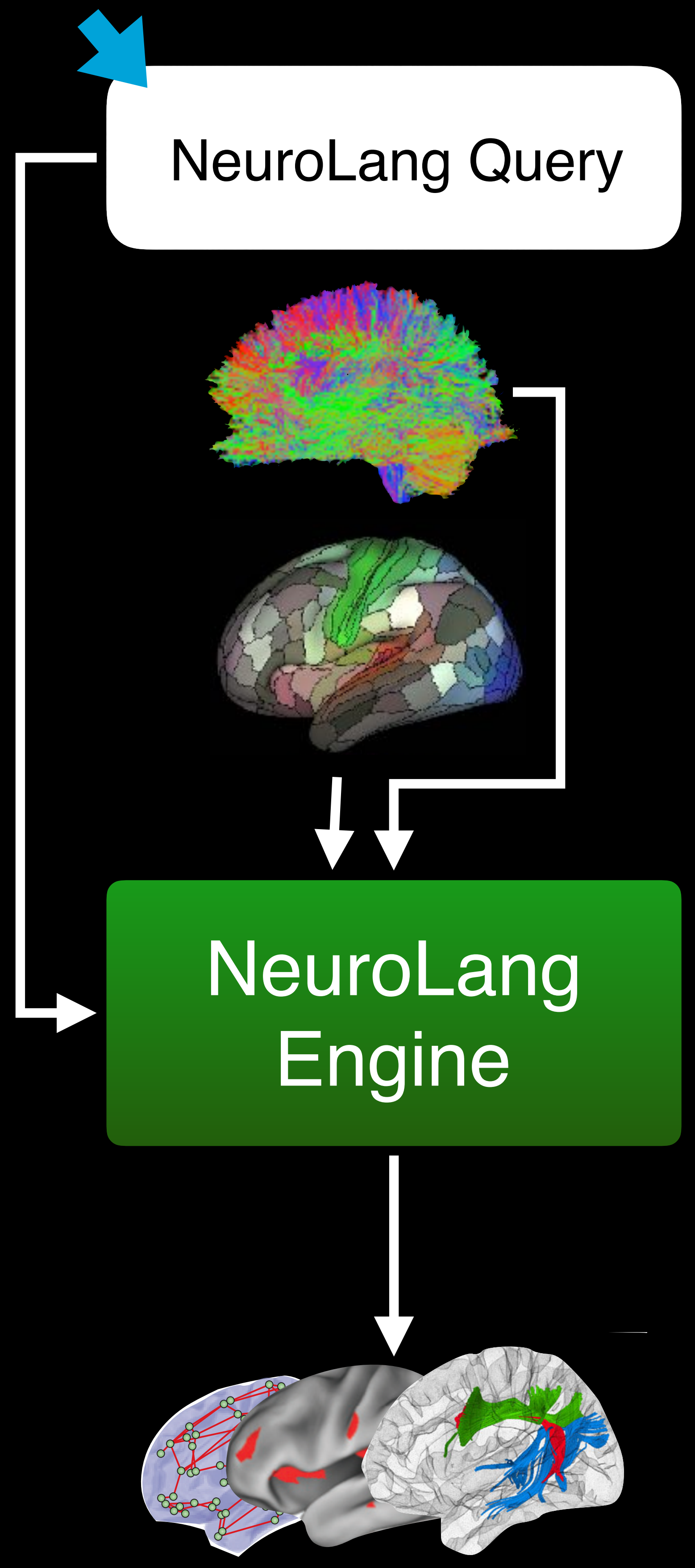
$\mathbf{x}$:



x

Challenge 1: Design a Neuroanatomical DSL: Language Properties

- **Modular and Compositional**: avoid unnecessary code duplication.
- **Well Behaved Formal Semantics**: to develop type systems and improve code quality.
- **Tractable**: solving queries should be feasible with the computing power of current architectures.
- **Programmable**: expressing neuroanatomical definitions should require little effort.

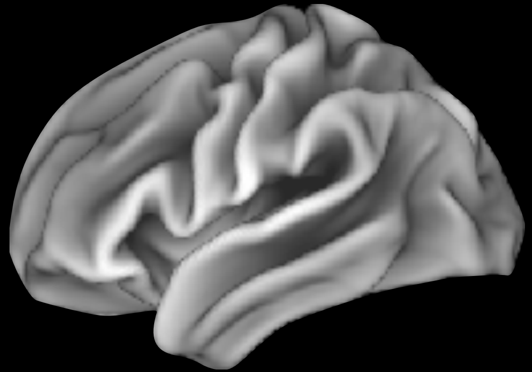


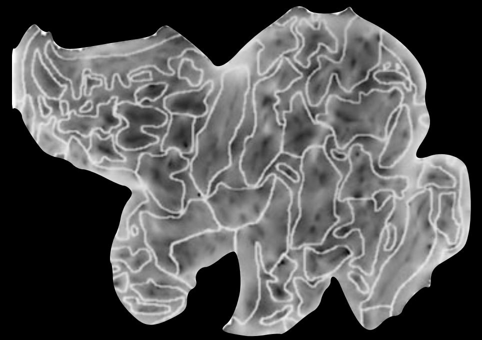
Challenge 2: Represent Neuroanatomical Organisation

Main Problem: Querying across Topologies

The brain is conceived as a **union of different entities with distinct topologies**:

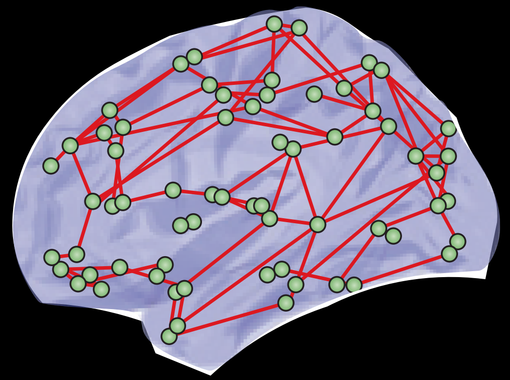
- The cortex is usually represented as a **3D-surface** or a **flat map**

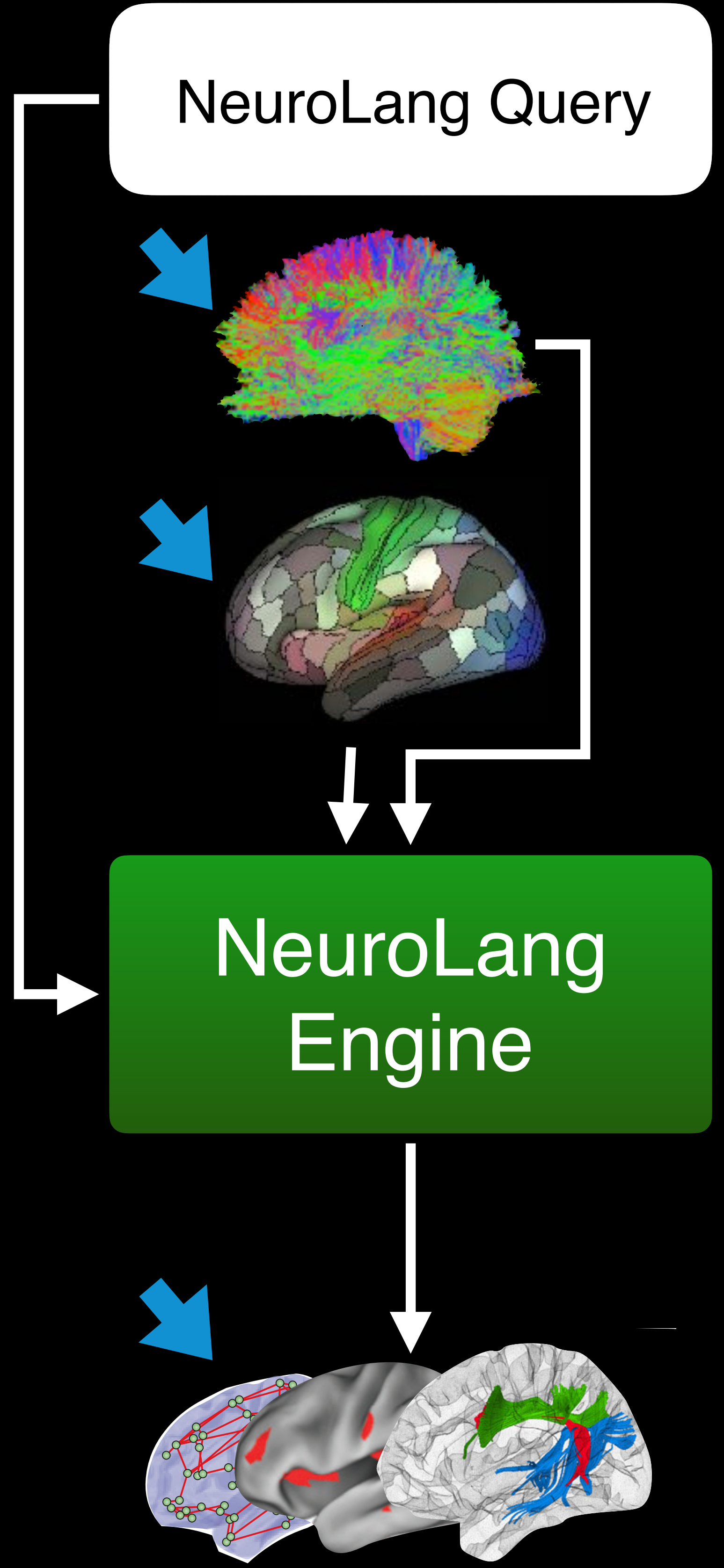




- The white matter as a set of **3D-curves**

- Brain Connectivity as a **graph**





x

Challenge 2: Represent Neuroanatomical Organisation

Approach

1. Elaborate a **type system** and representation for **spatial structures**

$$\{\mathbf{x_1} : \mathbf{x_1} \in \mathcal{B} \leftarrow p_1(\mathbf{x_1}, C_1) \ldots p_N(\mathbf{x_1}, C_N)\}, C_1 \ldots C_N \subset \mathcal{B} = \{\mathcal{W}, \mathcal{R}, \ldots\}$$

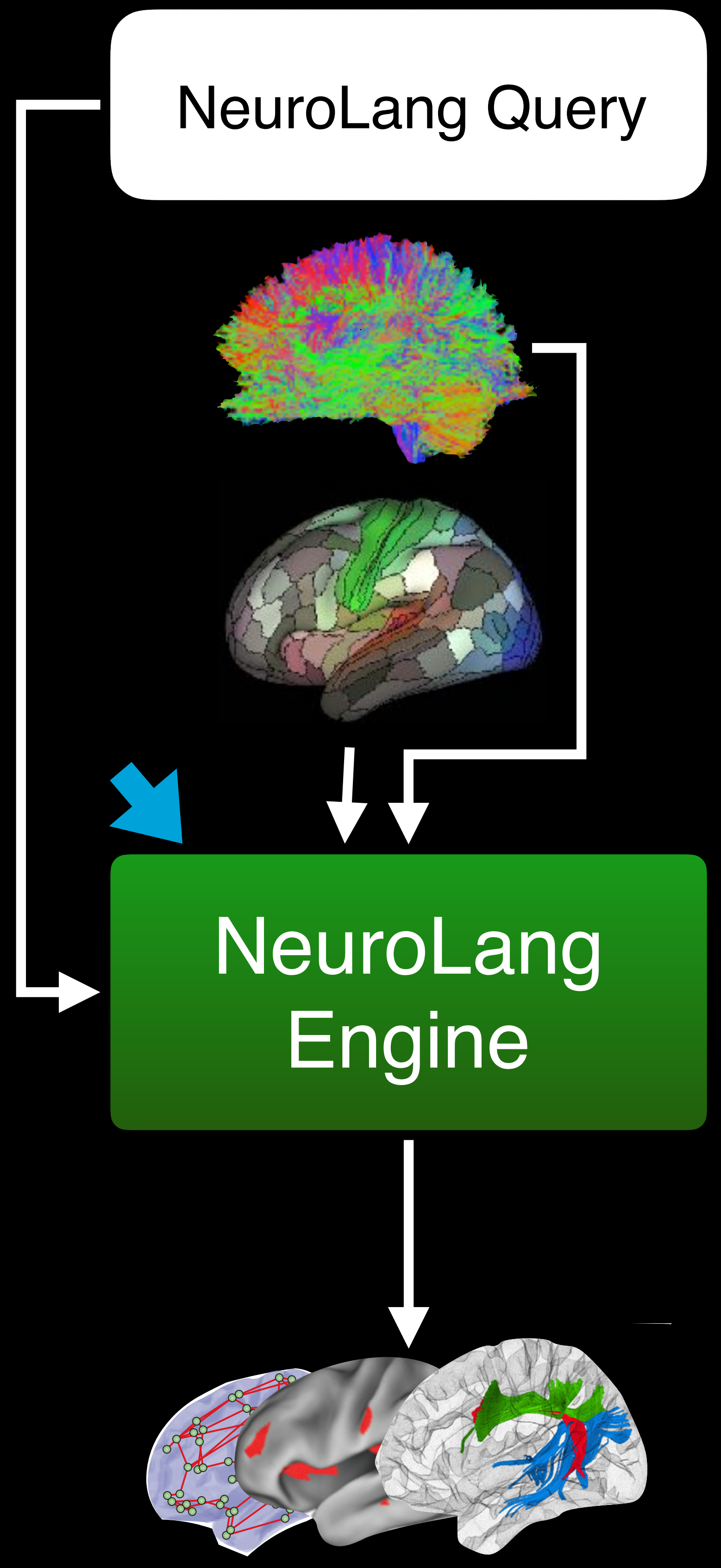
$$\Downarrow$$

$$\{(\mathbf{x_1}, \mathbf{x_2}) : \mathbf{x_1}, \mathbf{x_2} \in \mathcal{B} \leftarrow p_1(\mathbf{x_1}, \mathbf{x_2}, C_1) \ldots p_N(\mathbf{x_1}, \mathbf{x_2}, C_N)\}$$

2. Expand the **type system** to functions on **collections of structures**

$$\{f(\mathbf{x}, C) : \mathbf{x} \subset \mathcal{B} \leftarrow p_1(\mathbf{x}, C_1) \ldots p_N(\mathbf{x}, C_N)\}$$

3. Develop **efficient techniques** to evaluate $p_i(\mathbf{x}, C_i)$
   This will require **indexing across different topologies**.



Outcome

A DSL capable of formalising and inferring **relationships between objects of different topologies**.

X

Challenge 4: Accelerate Reproducible Research and Applications in Clinical and Cognitive Research

Brain Sciences Experience a Reproducibility Crisis

- Neuroanatomical protocols are **study-specific** and **hard to reproduce**.
- This makes **results harder to replicate**.


Behavioral/Systems/Cognitive

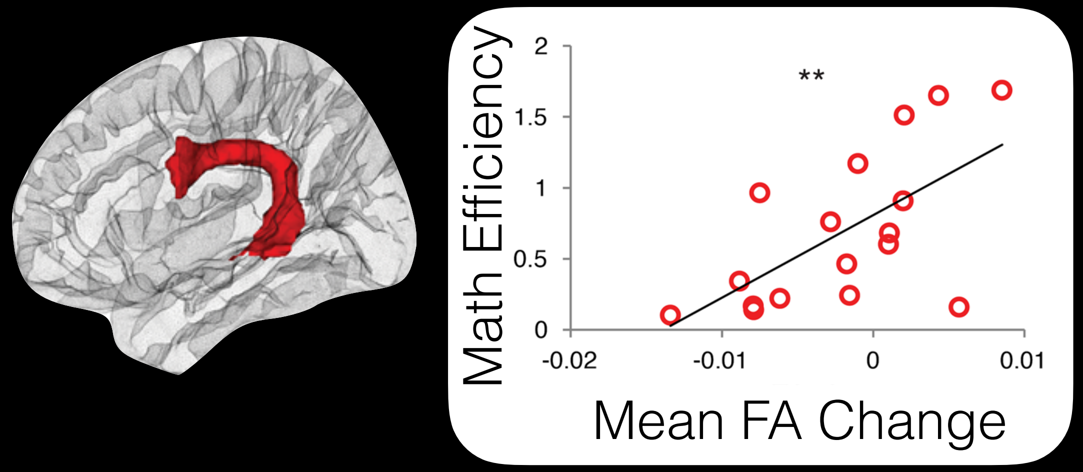
Genetics of Brain Fiber Architecture and Intellectual Performance

Ming-Chang Chiang,[1] Marina Barysheva,[1] David W. Shattuck,[1] Agatha D. Lee,[1] Sarah K. Madsen,[1] Christina Avedissian,[1] Andrea D. Klunder,[1] Arthur W. Toga,[1] Katie L. McMahon,[2] Greig I. de Zubicaray,[2] Margaret J. Wright,[3] Anuj Srivastava,[4] Nikolay Balov,[4] and Paul M. Thompson[1]

[1]Laboratory of Neuro Imaging, Department of Neurology, University of California, Los Angeles, School of Medicine, Los Angeles, California 90095-7334, [2]University of Queensland, Functional Magnetic Resonance Imaging Laboratory, Centre for Magnetic Resonance, Brisbane, Queensland 4072, Australia, [3]Queensland Institute of Medical Research, Brisbane, Queensland 4029, Australia, and [4]Department of Statistics, Florida State University, Tallahassee, Florida 32306

Approach

- Early application of NeuroLang to **cognitive and clinical problems**.
- Development of **high-quality software** for NeuroLang.



[Jolles, Wassermann et al 2015]

Outcome

A DSL and high quality software to **facilitate reproducibility** in neuroanatomical, cognitive and clinical research.

X

NeuroLang At a Glance

The main challenge is to develop a specific language to unify neuroanatomy and apply it to solve cognitive and neurological problems

Risks

- **Efficient handling** of neuroanatomical equations and structures
- **Stochastic modelling** of neuroanatomical data for large scale statistical inference

Impact

- A new generation of computational tools that will **unify neuroanatomy**
- New approaches for querying databases of **topologically and dimensionally varied large objects**
- Novel tools for understanding **neurological diseases**

The NeuroLang Team

- PI + 1 Junior Researcher + 4 PhD Students + 1 Engineer

Selected Collaborations

- Center for Brain Morphometric Analysis, Harvard Medical School, USA
- Stanford Cognitive & Systems Neuroscience Lab, Stanford, USA
- Core Facility for Clinical Research, Brain and Spine Institute, France
- Research Institute on Fundamental Informatics, CNRS / Paris 7, France