Statistical Inference on Brain Dynamics

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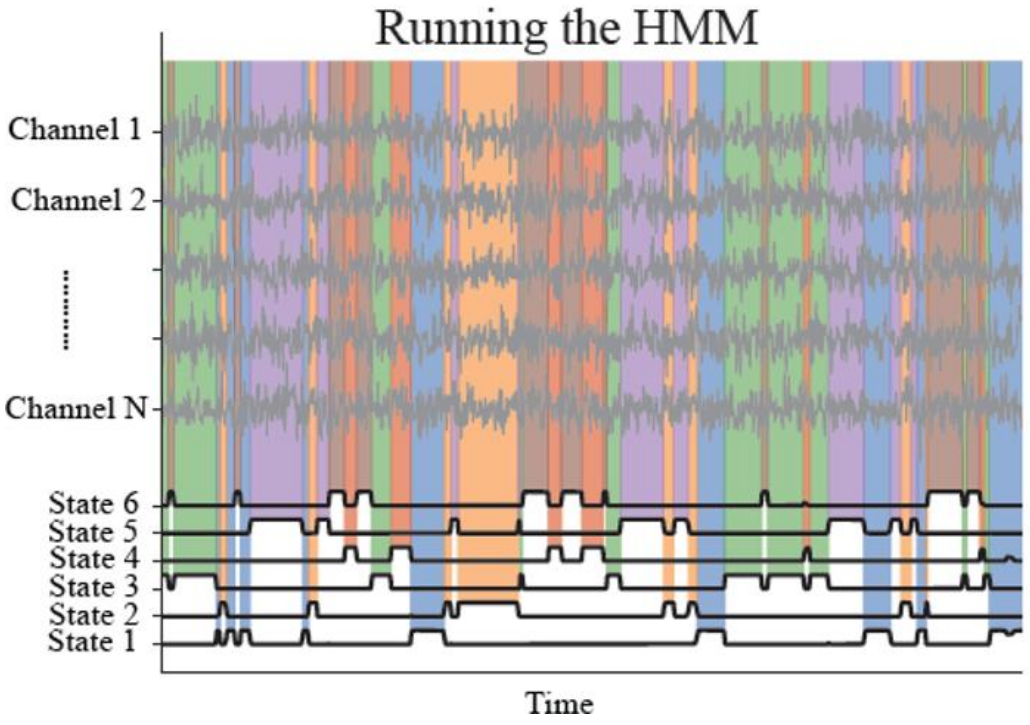
How do brain states relate to behavior?

- HMM decodes brain activity into dynamic state time courses
- We want to know: do these brain states relate to task behaviour or physiology?

- Brain activity fluctuates over time, across individuals and sessions
- We need statistical tools capable of taking that into account



Source: [Larsen et al., 2025] arxiv

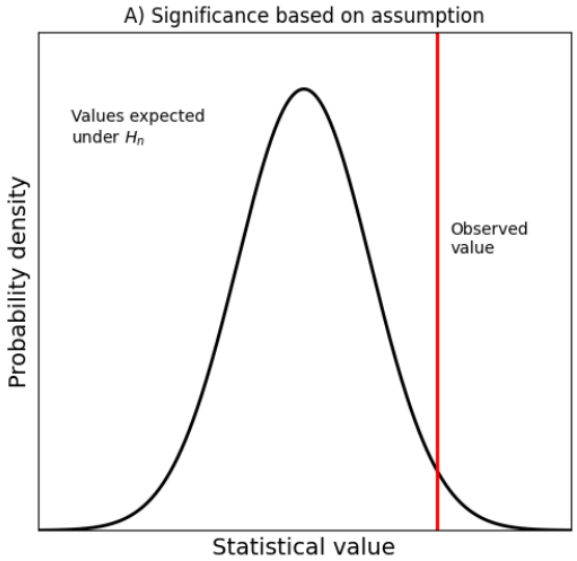
Parametric vs Non-parametric

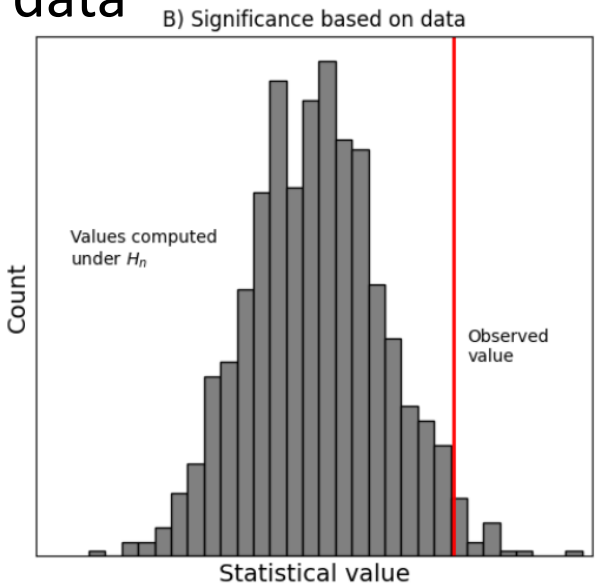
Parametric statistics

- Assume the data follows a known distribution (often Gaussian)
- Expect the variability to stay constant across measurements
- Assume each observation is independent from the rest

Non-Parametric statistics

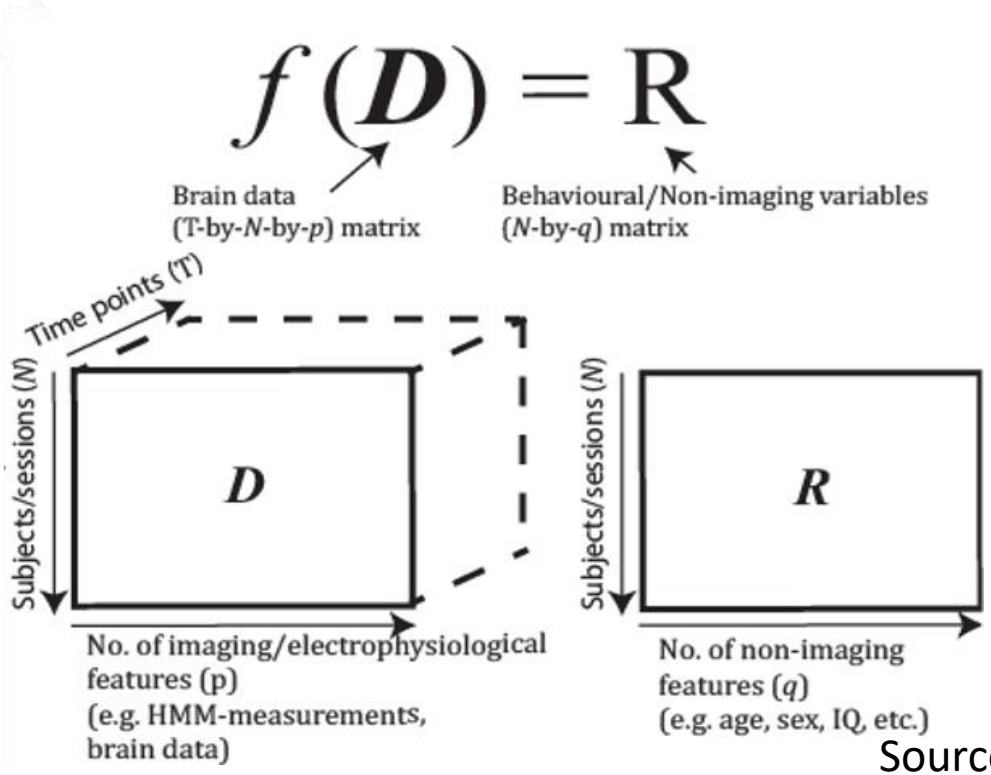
- Don’t rely on a specific shape or distribution of the data
- Build a null distribution directly from your data (no formulas needed)
- Common choice for high-dimensional or time-varying brain data





Linking brain activity to behaviour

- **D**: Brain-derived variable (independent/predictor)
- **R**: Behavioural or physiological variable (dependent/outcome)
- Goal: Test if **D** is associated with **R**, using different study designs



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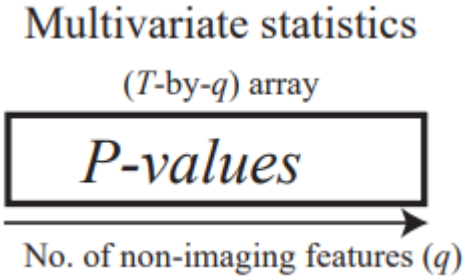
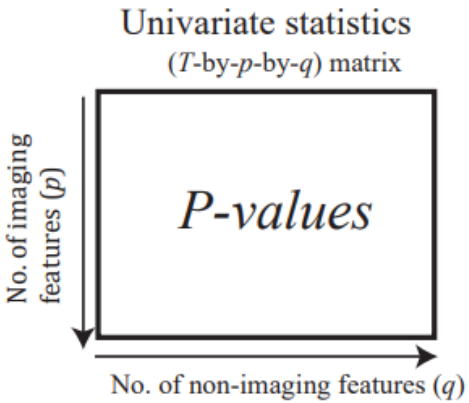
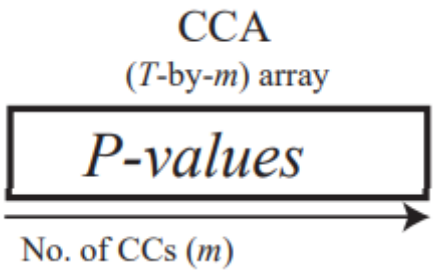
What we test

- **Many-to-one (Multivariate)**:
  Test whether multiple brain features together relate to one outcome
  (e.g. do all state time courses together relate to age?)
- **One-to-one (Univariate)**:
  Test one brain feature at a time against one outcome
  (e.g. does State 1 relate to age?)
- **Many-to-many (Canonical Correlation Analysis)**:
  Link multiple brain features to multiple behavioural variables
  (e.g. how do brain states relate to a profile of cognitive traits?)







Source: [Larsen et al., 2025] arxiv

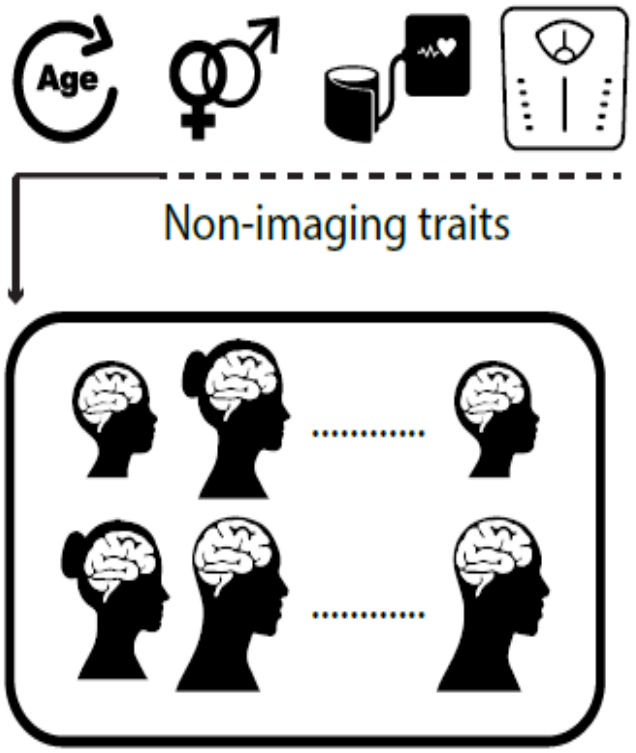
Overview of 4 types of tests

- Across-Subjects
- Across-Trials
- Across-Sessions
- Across-State-Visits

Overview of 4 types of tests

Notebook: [Across-Subjects Notebook]

- Across-Subjects
  - **Ask**: Are differences in brain features associated with behavioural traits, like age, diagnosis, or cognitive scores?
  - Take summary measure per person
  - Suitable for testing across people



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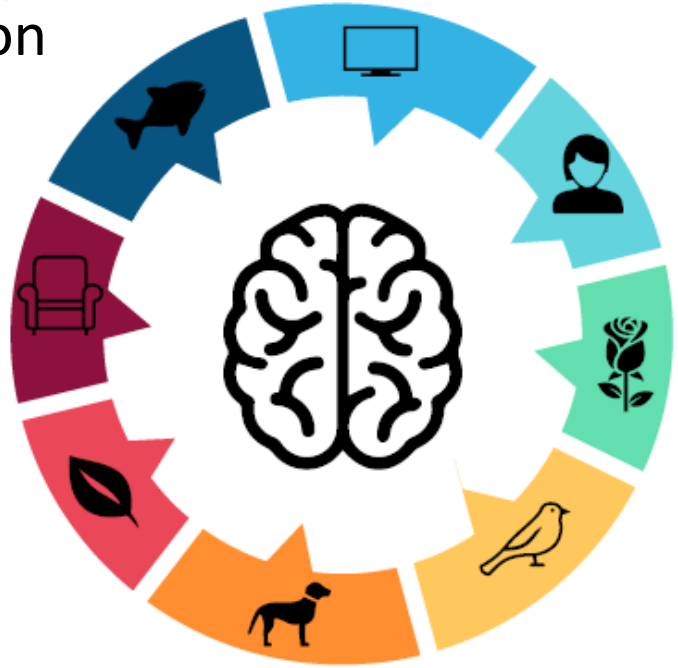
Overview of 4 types of tests

Notebook: Across-Trials Notebook

- Across-Trials
  - **Ask**: Does brain activity change depending on what condition or stimulus is presented on a trial?
  - Treat each trial as its own observation
  - Suitable for stimulus-response or task designs

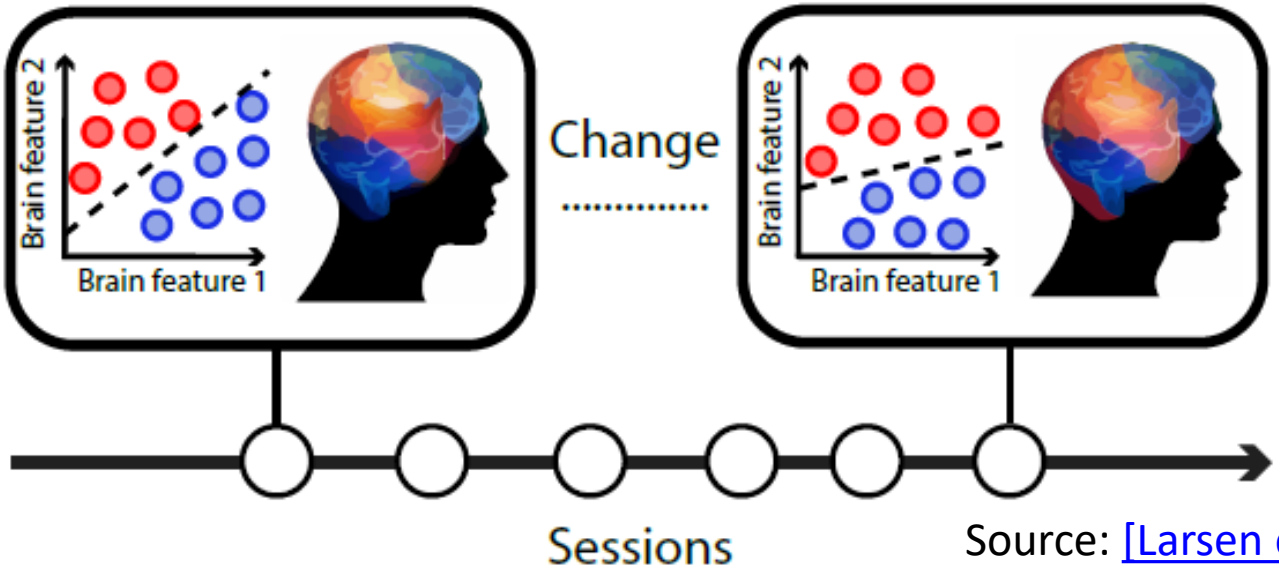


Source: [Larsen et al., 2025] arxiv

Overview of 4 types of tests

Notebook: [Across-Sessions Notebook]

- Across-sessions
  - **Ask**: Do brain dynamics change across sessions for the same individual?
  - Treat session of measurements as its own observation
  - Suitable when you want to track changes over time



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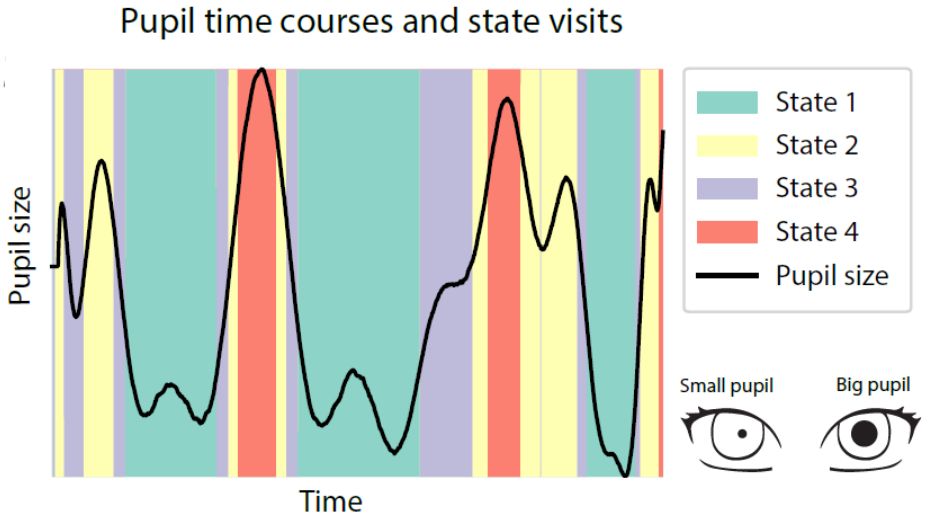
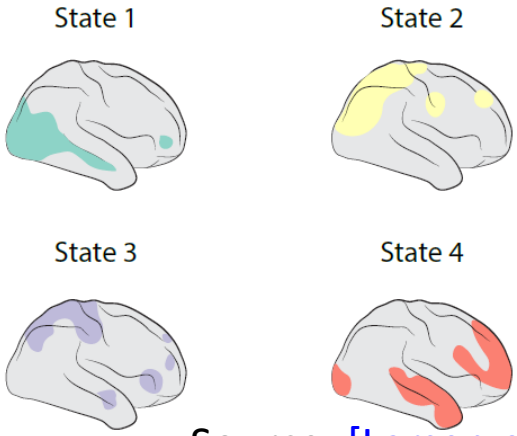
Overview of 4 types of tests

Notebook: [Across-State-Visits Notebook]

- Across-state-visits
  - **Ask**: Is another signal (e.g. pupil size, heart rate), behaving differently depending on which brain state the person is in?
  - Decode brain activity into state visits (Viterbi path)
  - Suitable when another signal is recorded at the same time





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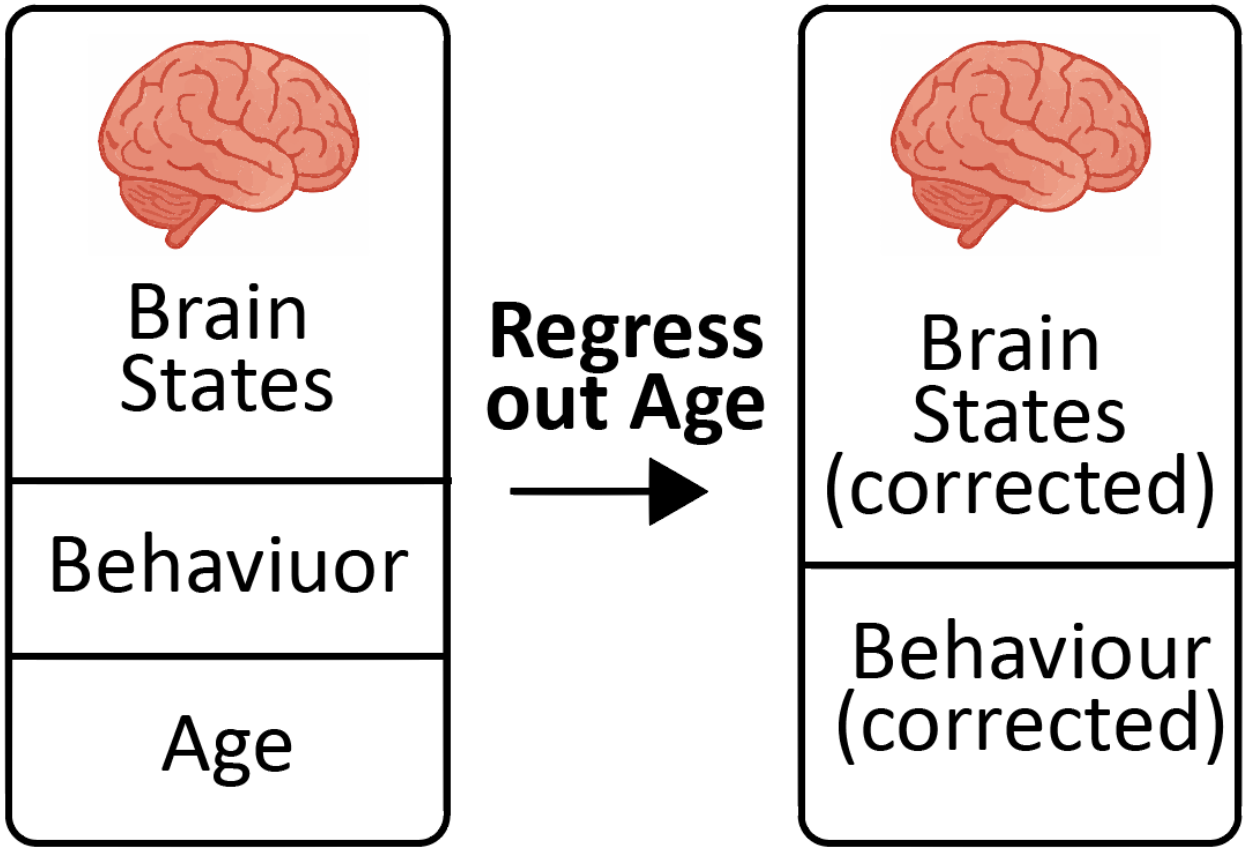
Handling confounds

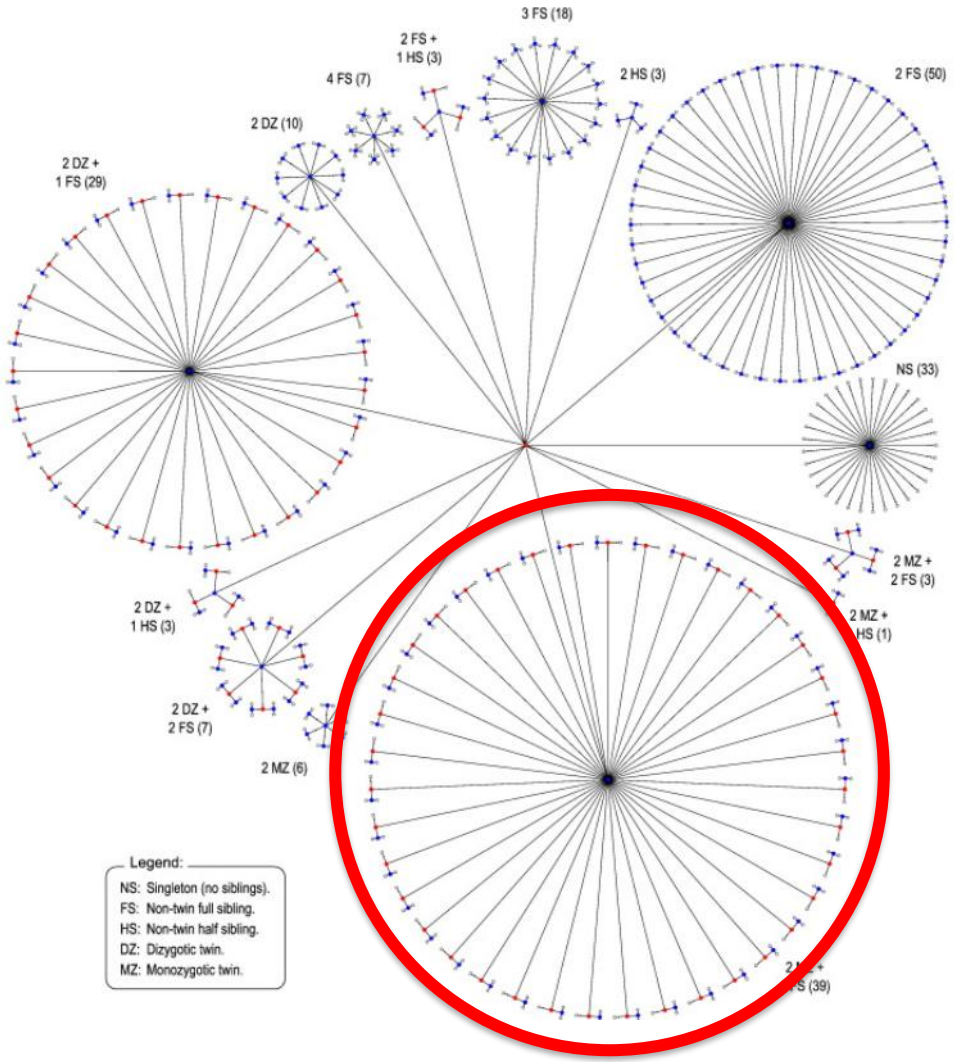
- Control for age, motion, etc.



Source: [Larsen., 2025]

Hierarchical data structures

- Accounts for related data (e.g. twins, families, repeated sessions)
- PALM is supported, with simpler built-in options available

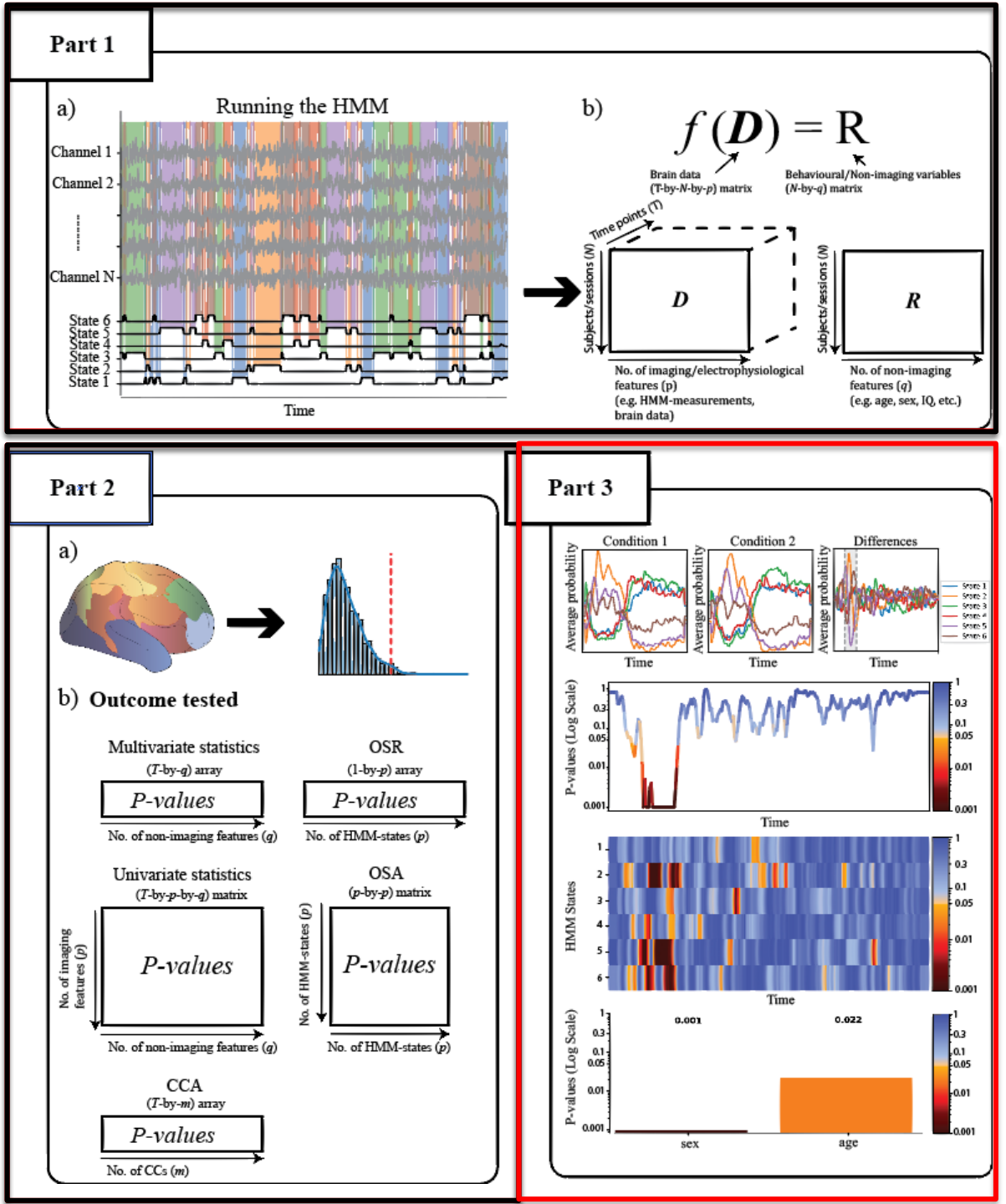


https://doi.org/10.1016/j.neuroimage.2015.05.092

Multiple testing correction

- Many comparisons inflate false positives
- Corrections methods available in GLHMM
  - **Classical methods**: Bonferroni, Benjamini–Hochberg (FDR) etc.
  - **Max-T correction**: Controls family-wise error across tests
  - **Cluster-based correction**: Groups neighbouring effects (e.g. space/time/frequency) to reduce false positives

Visual Summary of Framework



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Final Words + Resources

- GLHMM toolbox and tutorials available
  - Across-Subjects Notebook
  - Across-Trials Notebook
  - Across-Sessions Notebook
  - Across-State-Visits Notebook
- Ready to apply to your own dynamic brain data

https://github.com/vidaurre/glhmm