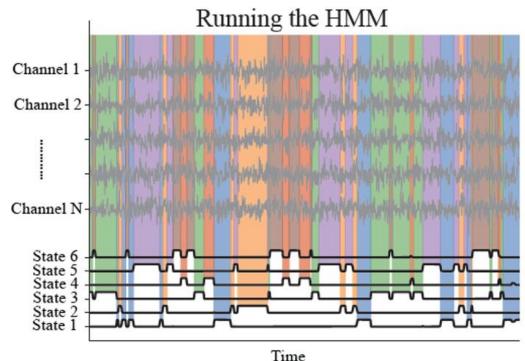
Statistical Inference on Brain Dynamics

Nick Yao Larsen Postdoc

How do brain states relate to behavior?

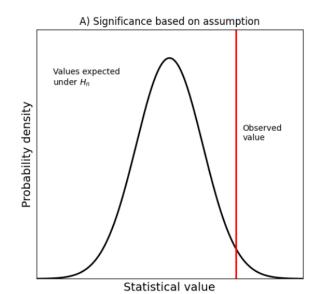
- HMM decodes brain activity into dynamic state time courses
- We want to know: do these brain states relate to task behaviour or physiology?
- Brain activity fluctuates over time, across individuals and sessions
- We need statistical tools capable of taking that into account



Parametric vs Non-parametric

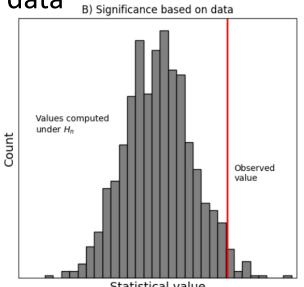
Parametric statistics

- 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



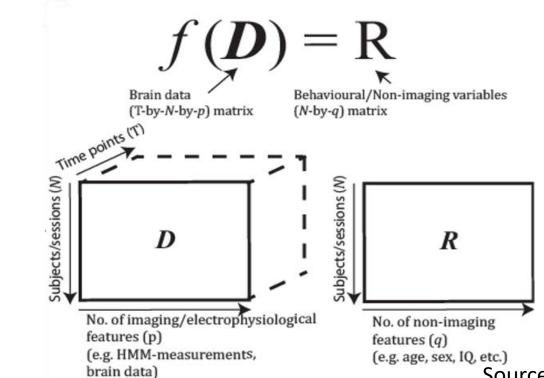
Non-Parametric statistics

- 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 highdimensional 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



What we test

Many-to-one (Multivariate):

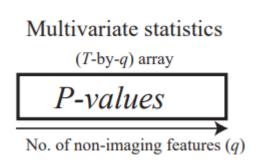
Test whether multiple brain features together relate to one outcome (e.g. do all state time courses together relate to age?)

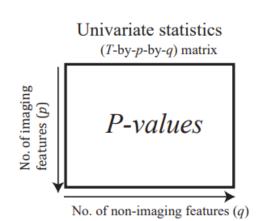
One-to-one (Univariate):

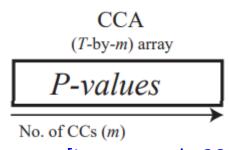
Test one brain feature at a time against one outcome (e.g. does State 1 relate to age?)

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?)



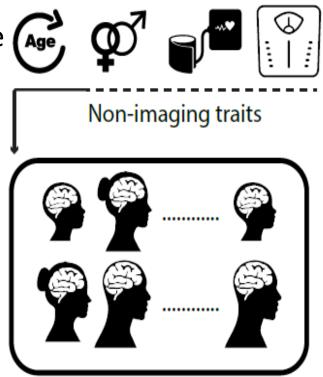




- Across-Subjects
- Across-Trials
- Across-Sessions
- Across-State-Visits

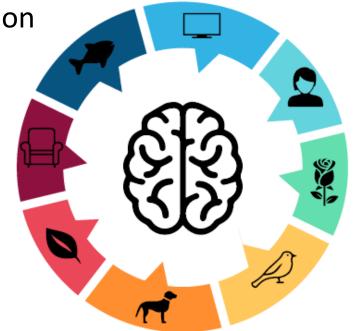
Notebook: Across-Subjects Notebook

- 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



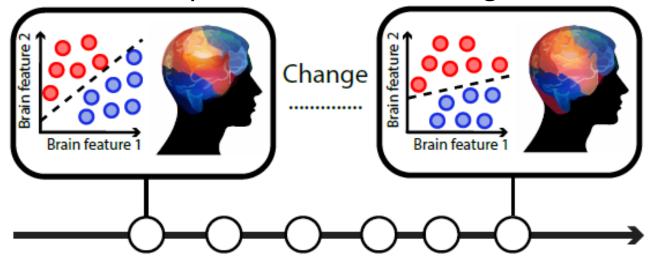
Notebook: Across-Trials Notebook

- 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



Notebook: Across-Sessions Notebook

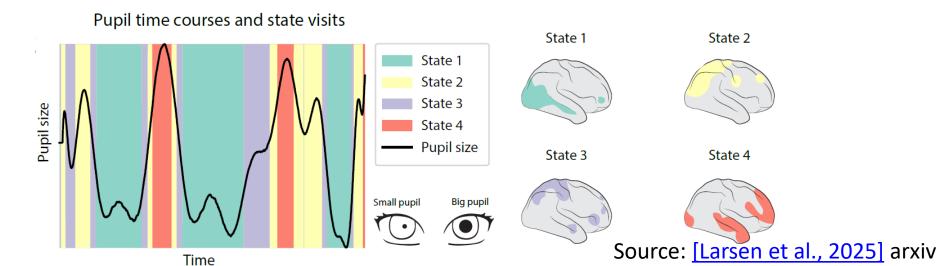
- Across-sessions
 - Ask: Do brain dynamics change across sessions for the same individual?
 - Treat session of measurements as its own observation
 - Suitable when you want to track changes over time



Sessions

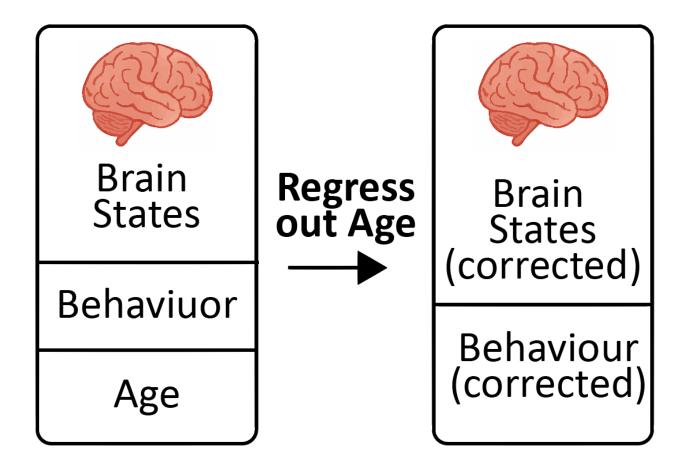
Notebook: Across-State-Visits Notebook

- 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



Handling confounds

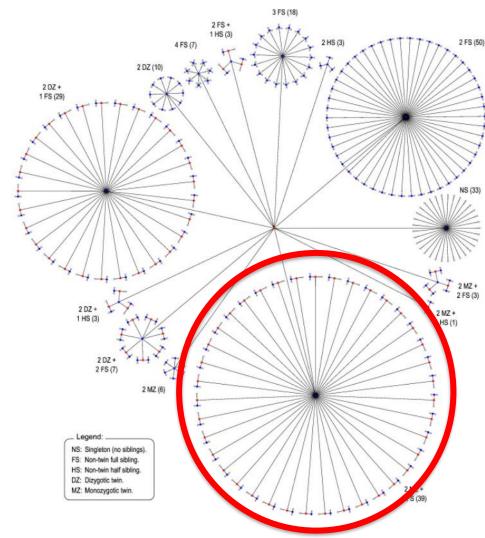
Control for age, motion, etc.



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

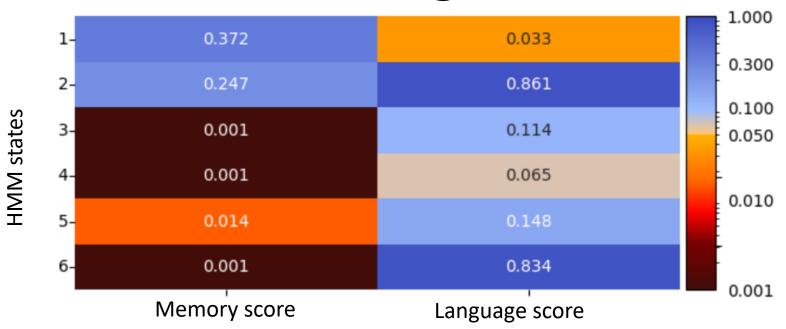


https://doi.org/10.1016/j.neuroimage.2015.05.092

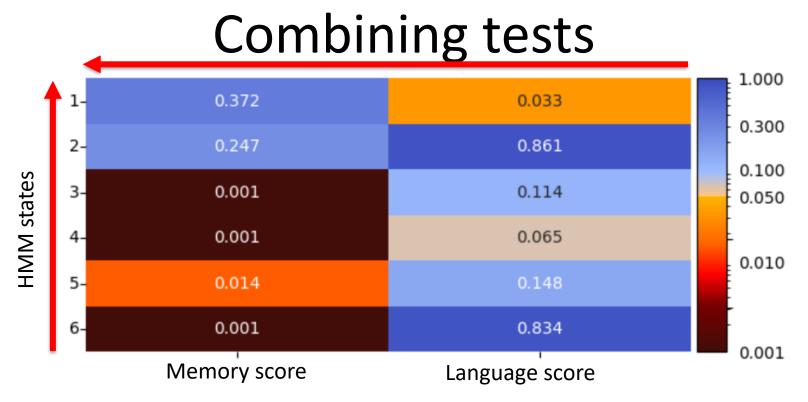
Multiple testing correction

- 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

Combining tests



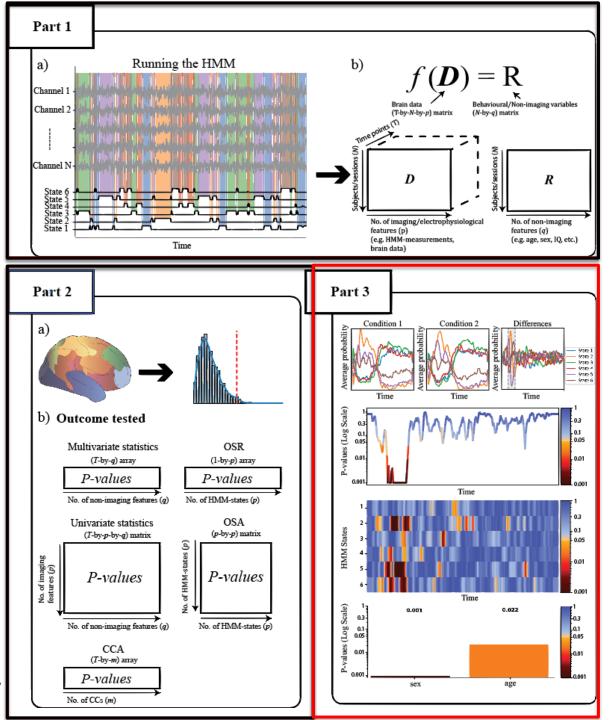
- Running tests across many states and traits gives a matrix of p-values
- This can be useful, but also hard to interpret all at once
- Sometimes we want a summary:
 Is there any relationship between these brain states and the behavioural traits overall?



NPC (Non-Parametric Combination) summarises multiple p-values

- Across rows ('across_rows') → One p-value per non-imaging trait
- Across columns ('across_columns') → One p-value per brain state
- All entries ('True') → One overall p-value
- Helps answer: which non-imaging trait matter? which state? is there a global effect?

Visual
Summary
of
Framework



Final Words + Resources

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