Dynamic connectivity clusters reflect progressive learning and fast strategy shifts
Outline of the talk

- CDPC: A method to find connectivity clusters in fMRI
  - Density Peak Clustering (DPC): the basics
  - Applying DPC to fMRI: Coherence DPC

- An application of CDPC to a task with two strategies
  - Clustering frequency
  - Effects of learning and strategy-switching
Identifying short-term activity patterns

• **Original idea**: identify brain activity patterns associated to non-repeatable cognitive events

• **Example**: find brain areas co-activated in finding solution of complex problem

• **Goal**: be able to identify patterns in fMRI data with high accuracy in short time windows (<30 s)
Identifying short-term activity patterns

• Supervised methods (GLM) need many repetitions and well-defined model (design matrix)

• Unsupervised methods (ICA) may need long windows for reliable source identification

• Try Density Peak Clustering, developed within our group
  [A Rodriguez, A Laio, Science 344, 1492 (2014)]

• Idea: cluster BOLD time series of different voxels, finding groups of voxels with similar BOLD time-series (connectivity clusters)
DPC(1): density-based clustering

• start from a metric $d_{ij}$ that defines distances

• reconstruct density around each data point $i$
  [density = probability density from which data are sampled]

• count # of points in ball or radius $\varepsilon$ centered at $i$

\[
\rho_i = \sum_{j \neq i} \chi(d_{ij} - \varepsilon)
\]

\[
\chi(a) = \begin{cases} 
1 & a \leq 0 \\
0 & a > 0 
\end{cases}
\]

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DPC(2): Density-based clustering

• Reconstruct the density

• Standard algorithms (dbscan) identify clusters as disconnected regions of “high density”

• What is high? Results depend on the chosen density threshold!

• Cannot resolve structures at different density scales
DPC (3): finding peaks

Instead, one can associate a cluster to each density peak

Density peaks are local maxima in the density

**Density peaks are far from any point with higher density**

Compute for all points min distance from point at higher density \( \delta_i = \min_{j: \rho_j > \rho_i} d_{ij} \)

Peak are outliers in “decision graph” \( \rho_i \ vs \ \delta_i : \)

![Graph showing density peaks and decision graph](image)
Points are assigned to peaks by following a path of increasing density leading to one of the peaks.

Jump from one point to nearest point with higher density
Non density-based clustering methods (e.g. K-means) typically assign point to nearest center, and can only find roughly spherical clusters.

Density-based clustering methods allow to retrieve clusters of arbitrary shape.

K-means vs DPC

DPC (5): assigning points

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Density peak clustering: a new clustering method
[Rodriguez and Laio, Science 2014]

Advantages:

• Computationally cheap (no optimization involved)

• Works well in high dimension (no embedding required, only distances)

• Automatically finds number of relevant clusters

• Finds clusters of arbitrary shape

Disadvantages:

• Requires many data points (>100)

• One free parameter ($\varepsilon$) [solved in improved version, but highly nontrivial!]
Applying DPC to fMRI
Allegra et al., Hum Brain Mapp 2017

- apply DPC in the space of BOLD time series
- consider window of $T$ frames
- to each voxel corresponds a BOLD time series of $T$ values, $v_1, v_2, \ldots, v_T$
- consider $T$-dimensional space of time-series
- each voxel time series is a point in this space
- a cluster in this space is group of coherent voxels, i.e. with similar BOLD
- we call such clustering **Coherence Density Peak Clustering (CDPC)**
CDPC: finding a metric

- first, we need a metric $d_{ij}$ to define the distance between BOLD signals of voxels $i$ and $j$.

- simplest candidate: Euclidean metric

- remove average and normalize amplitude

\[ d_{ij} = \sqrt{\sum_t (\nu_i(t) - \nu_j(t))^2} \]

\[ d_{ij} = \sqrt{\sum_t (\nu_i'(t) - \nu_j'(t))^2} \]
CDPC: filtering noise

- Where do we “cut” clusters? Can we use a lower threshold on $\rho$?

- Problem: applying the method on imaging phantom, we find high values of $\rho$ (comparable to real data) **Noise can be (highly) coherent**

- in real images strong coherence between spatially close voxels, in phantom no (sparse coherence)

- Consider small sphere $S_i$ around each voxel $i$ and compute “number of coherent neighbor voxels”

  \[ n_i = \sum_{j \in S_i} \chi(d_{ij} - \epsilon) \]

- $n_i$ is low for phantom, high for real images
Assumption: coherence in a task induces coherence among small (possibly disconnected) regions, not isolated voxels.

Let $n_0$ be $\max n_i$ found in phantom: use this as threshold on $n_i$.

Only voxels with $n_i > n_0$ are considered in the computation of $\rho$ and assigned to clusters.

This (empirical) noise filter removes spurious clusters in phantom and simulated data affected by high noise.
Simple validation of CDPC: motor experiment

- First test in motor experiment (alternative trials left/right clenching, visually cued)

- Can we reconstruct activity patterns in single trials?

- Apply CDPC to short time windows (~12 volumes, ~20 s) corresponding to single clenching trials
In window corresponding to left/right clenching trial we find main cluster including right/left motor cortex

The cluster also includes part of occipital cortex (clenching was visually cued)
Results:

- Proof-of-principle of coherent pattern detection in single trials
- Accurate retrieval of coherent patterns, little noise even in single subjects and short time windows
- Results are consistent over subjects

Limitations:

- No null model to perform inference on clustering results
- Two free parameters ($n_i$ and $\varepsilon$)
Many windows together: clustering frequency map

- With CDPC we can in principle retrieve connectivity in single trials

- Looking at several time windows we can track dynamic connectivity in a task

- Apply CDPC on running windows of ~20 s (scans 1-12, 2-13,...)

  ![Graph showing transient coherence](graph.png)

  - This allows to detect *transient coherence*, different from global coherence over all windows

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Many windows together: clustering frequency map

- Hypothesis: a brain area participating to the task will be often involved in coherent clusters

- Put together many windows: Clustering frequency map

  \[ \Phi_i = \frac{1}{N_t} \sum_t \chi(c_i(t)) \]

- High-\( \Phi \) regions for the motor experiment reflect areas involved in the task: motor, parietal, visual, frontal

![Brain images](A) ![Brain images](B)
Applying CDPC to more complex experiments

- **Q1:** by means of the clustering frequency map $\Phi$, can we find areas involved in a task?

  If yes, CDPC may be used to find task-relevant areas without supervision

- **Q2:** for a task with several sessions, can we track variations in the functional response by looking at how $\Phi$ varies in different sessions?

  If yes, CDPC may be used to track learning and task-switching effects

- **A:** we try to apply CDPC to a task where there is both progressive learning and a sudden behavioral shift,

A task with two strategies

At each trial, subjects are shown a cloud of dots inside a square.

Visual stimulus has **two features**: **corner** (position of dots closer to one corner of the square) and **color** (color of dots, rd or green).

“Judge in which corner of the frame the little squares are. The squares are colored and can be either red or green.”

**Instructed S-R Mapping**

*Corner determines response*

4 corners map onto 2 buttons:

- **Upper left**: press right
- **Lower right**: press right
- **Upper right**: press left
- **Lower left**: press left

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A task with two strategies

- There are 12 runs of 5 min each; in each run, ~180 trials

- Instructed S-R mapping requires effort: 4-2 mapping, conflict when corner is contralateral to button

- Without telling participants, starting from third run a perfect color-corner correlation is introduced, so that UL/LR are always red and UR/LL always green

- Then an alternative, cheaper strategy based on color becomes possible

**Learned S-R Mapping**

*Color determines response*

2 colors map onto 2 buttons

- Any Corner
  - Red
    - press right

- Any Corner
  - Green
    - press left
A task with two strategies

- 11/36 subjects ("color users") spontaneously realize correlation and switch to color strategy in the mid of the experiment

  The switch can be identified with a temporal resolution of 0.5 run (1 block) based on several behavioral markers, e.g. drop in RT, drop in error rate, ...

- 25/36 subjects ("corner users") continue to rely on corner information, and are told about the correlation before last two runs
A task with two strategies

Both color and corner users exhibit learning effects:

- Progressive drop in RT and error rate in corner phase
- Sudden drop in RT and error rate in the (spontaneous or instructed) switch to color phase
CDPC results (1): average $\Phi$

Allegra et al., in preparation (2018)

- we compute $\Phi$ for gray matter voxels and use max value found as cutoff for $\Phi$ map

- we obtain set of “high-$\Phi$ regions” comprising occipital, parietal, and frontal regions, plus deep region in temporal lobe
CDPC results (1): average $\Phi$

- Original work (Schuck et al.) focused on corner and color encoding areas (mVPA)

- high-$\Phi$ regions (found completely without supervision) largely overlap with regions found by mVPA (highly supervised)
CDPC results (2): changes in $\Phi$

- how does $\Phi$ vary with run?

- increase in $\Phi$ when subject is performing corner strategy, sudden decrease followed by increase after transition to color

- effect concentrated in parietal cortex and precuneus
CDPC results (2): changes in $\Phi$

- During incremental learning in corner phase, increase in in parietal and precuneus

- $\Phi$ increase is correlated with decrease in RT
CDPC results (2): changes in $\Phi$

- During instructed switch to color, sudden decrease in $\Phi$ in parietal and precuneus

- Same effect in spontaneous switch, although much weaker (lower stats?)
Global summary:

- We developed CDPC, an fMRI analysis method based on the recently introduced Density Peak Clustering

- The method can find groups of voxels with similar activation time series even in short windows and single subjects

- CDPC can be used with sliding windows approach to find a clustering frequency map (Φ) that represents areas that are recurrently involved in coherent patterns in a task

- CDPC is promising tool to find task-relevant regions in fully unsupervised way

- Variations of Φ can be related to incremental learning and sudden behavioral shifts in a task with two strategies

- Task-relevant areas seem to become more synchronized during incremental learning, while such synchronization is disrupted by the strategy change
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