Connectivity-Based Brain Parcellation

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Structural and Functional Maps on Cortex

Brodmann, 1909

Fritsch & Hitzig, 1870
Structural and Functional Maps on Cortex

Distribution of muscarinergic M2 receptor in human visual cortex

Eickhoff et al., Cereb Cortex 2008

Orientation preference in cat visual cortex

Carandini & Sengpiel, J Vis 2004

Cytoarchitectonic parcellation of human hippocampal formation

Amunts et al., Anat Embryol 2005

Spatial frequency preference in bush baby visual cortex

Xu et al, J Comp Neurol 2007

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Structural and Functional Maps on Cortex

Each neuron, column, area etc. is tuned to a region in that feature space (e.g. receptive field).

Knösche & Tittgemeyer, Front Syst Neurosci 2011
Similarity Mapping and Parcellation

Cortex

connectivity
cytoarch.

receptors
e etc.

similarity

correlation

Euklidian dist.
Mahalanobis dist.

similarity matrix
(after spectral reordering)
Similarity Mapping and Parcellation

Connectivity similarity matrix (after spectral reordering)

cortex correlation

euklidian dist.
mahalanobis dist.

correlation

connectivity

cytoarch.

receptors

etc.

connectivity

cytoarch.

receptors

etc.

similarity
Similarity Mapping and Parcellation
Characterization of Structure

- Structural MRI (T1, T2, diffusion)
- Chemical Tracing
- Autoradiography
- Staining and Microscopy

- Global connectivity
  (fiber architecture in white matter)
- Local connectivity
  (myeloarchitecture in grey matter)
- Receptorarchitecture
  (arrangement and morphology of cells)
- Cytoarchitecture
  (arrangement and morphology of cells)

- grey value
- grey matter fraction
- “cortical thickness”
- fractional anisotropy
- tractogram
- “in vivo cytoarch”
- receptor fingerprint
- “cortex layering”

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**Similarity Mapping and Parcellation**

- Clustering is an unsolvable problem
- Parcellations only approximate the similarity structure of the cortex.

The particular choice of parcellation depends on ...

- ... the required level of detail, i.e. the magnitude of difference that is just considered relevant for the particular purpose.
- ... the achievable level of detail, i.e. the magnitude of difference that just can be reliably detected by the available technique.
- ... the particular structural criteria the parcellation is based upon.
- ... the resolution at which we can sample.
Connectivity in the Brain

Effective Connectivity embodies **causality** and **information transfer** between cells, populations, areas ...

Functional Connectivity describes **correlative relationship** between brain activities.

Anatomical Connectivity summarizes **physical basis** for effective connectivity.

suggests, but does not prove

quantifies potential for
Anatomical Connectivity

Dendritic trees
- morphology
  (determines influences of local PSPs on membrane potential at axonal hillock)

Synapses
- number per presynaptic projection neuron
- distribution at target cells
- synaptic efficacies

Postsynaptic area
- number of target neurons
- local circuitry

Presynaptic area
- number of projection neurons
- local circuitry

Axons
- myelination and caliber
  (determines transmission speed)
- fiber course, distance

Axonal hillock
- firing threshold

Knösche & Tittgemeyer, Front Syst Neurosci 2011
Estimation of Anatomical Connectivity

Disection

Tracing

Not possible in living humans.
Estimation of Anatomical Connectivity

... using diffusion weighted MRI and tractography.

Heidemann, Anwander, Feiweier, Knösche, Turner, NeuroImage 2011
Grey matter parcellation based on intrinsic fibre architecture

**local model**
- fractional anisotropy
- eigenvector direction
- number fiber bundles

- complexity
- Mean diffusivity

clustering
Subdivision of the Human Putamen
Subdivision of the Amygdala

Structure and Connectivity of Human Caudate

Kotz, Anwander, Axer, Knösche, submitted
Connectivity-Based Parcellation

A. Seed Points
   - Cortex: grey/white matter interface
   - Grey matter volume

B. Target Point
   - Whole brain
   - Grey matter
   - Predefined areas

C. Tractographic Fingerprints
   - Probabilistic tractography

D. Similarity Structure
   - Similarity matrix
   - Hierarchical tree

E. Mapping Areas

Knösche & Tittgemeyer, Front Syst Neurosci 2011
Target-based Clustering

Parcellation of the thalamus according to cortical targets

Behrens et al., Nat Neurosci 2003
k-means clustering of Broca’s area using predefined number of parcels

Anwander, Tittgemeyer, von Cramon, Friederici, Knösche, Cereb Cortex 2007
Free Clustering

Anwander, Tittgemeyer, von Cramon, Friederici, Knösche, Cereb Cortex 2007
Connectivity based parcellation of Broca’s Area

Probability maps of BA44 and BA45

Cytoarchitecture (N = 10)
DTI- Parcellation (N = 6)

Amunts et al., 1999
Anwander et al., 2007

Amwander, Tittgemeyer, von Cramon, Friederici, Knö sche, Cereb Cortex 2007
Connectivity based parcellation of the precentral gyrus – relation to the localization of function

Schubotz, Anwander, Knösche, von Cramon Tittgemeyer, NeuroImage 2010
Connectivity based parcellation of inferior parietal cortex – comparison with monkey findings

Ruschel, Anwander, Knösche, Turner, Geyer, submitted
Connectivity based parcellation of inferior parietal cortex – comparison with monkey findings

Ruschel, Anwander, Knösche, Turner, Geyer, submitted
Limitations

Target-based Parcellation

• Strong assumptions – each parcel should be mainly connected to one target area.

• Target areas maybe difficult to delineate.

Free Clustering

• Number of clusters, average size of clusters, or similar need to be known in advance → model selection problem.

• Parcellation is assumed to be unique and complete → boundaries may be fuzzy and there may be outliers.
Agglomerative Hierarchical Clustering

- Starting with seed points (leaves), a new element is created by joining the two most similar elements.
- New distances from the new nodes to the other ones are obtained.
- Operation is iterated until only one element remains.
Tree Quality Assessment

How similar the distances encoded in the tree are to the distances measured directly from the tractograms?

→ cophenetic correlation coefficient (0.0 ... 1.0)
Preprocessing – Tree Simplification

- Remove outliers
- Debinarization

- Information loss: 0.1%
- Complexity reduction by 97%
Preprocessing – Tree Simplification

![Bar chart showing information loss and complexity reduction for different preprocessing methods: Outlier Pruning, Max Granularity, and Debinarization.]

- **Information loss (%):**
  - Outlier Pruning: 0.031
  - Max Granularity: 0.092
  - Debinarization: 0.100

- **Complexity reduction (normalized):**
  - Outlier Pruning: 0.930
  - Max Granularity: 0.966

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Tree Comparison

Cophenetic similarity

- Distance values at which all possible pairs of leaves join
  → Emphasis on numerical distance values

Triples similarity

- Joining order of all possible triples of leaves
  → Emphasis on tree topology
Tree Comparison

left hemisphere

right hemisphere

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Assessment of Hierarchical Tree
Assessment of Hierarchical Tree

- In order to map tree information back to the cortex, the most important information has to be selected.
- In most cases, the similarity structure is best represented by a series of parcellations.

- Parcellations are collections of unemployed nodes.
- There are different possible criteria for selecting parcellations.
Assessment of Hierarchical Tree

Parcellation by joining distance (biggest distance between any pair of subclusters)
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Assessment of Hierarchical Tree

Parcellation by minimizing size difference
Assessment of Hierarchical Tree

Detecting most distinct boundaries (distance to next > 10\% of tree height)
Information-based Hierarchical Clustering

soft-constraint affinity propagation (SCAP)

Agglomerative information bottle-neck clustering

Gorbach et al., Frontiers in Neuroinformatics 2011
Conclusions

- Structural (and functional) feature maps are generally smooth with occasional (frequent?) sharp transitions.

- Parcellations are approximations of these maps at a given granularity level.

- Hierarchical trees capture the similarity structure of feature maps in a more complete way.

- Trees cannot be mapped on the cortex, therefore they should be interpreted by means of series of relevant partitions.

- For comparison of mappings, the entire trees should be used.
Outlook

• Open Challenge: finding most relevant partitions.

• Feature spaces are high-dimensional – different features result in different, but very often related parcellation

→ challenge: multimodal parcellation.

• Post mortem and animal methods (e.g., cytoarchitecture, receptor mapping) are accurate and precise, but mapping to individual human is problematic.

• Non-invasive methods (e.g., T1, dMRI) are possible in individual healthy human, but subject to lower accuracy and resolution.

→ challenge: integrate both types of data
Thank you

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