Revisiting Multi-Subject–Random-Effect in fMRI

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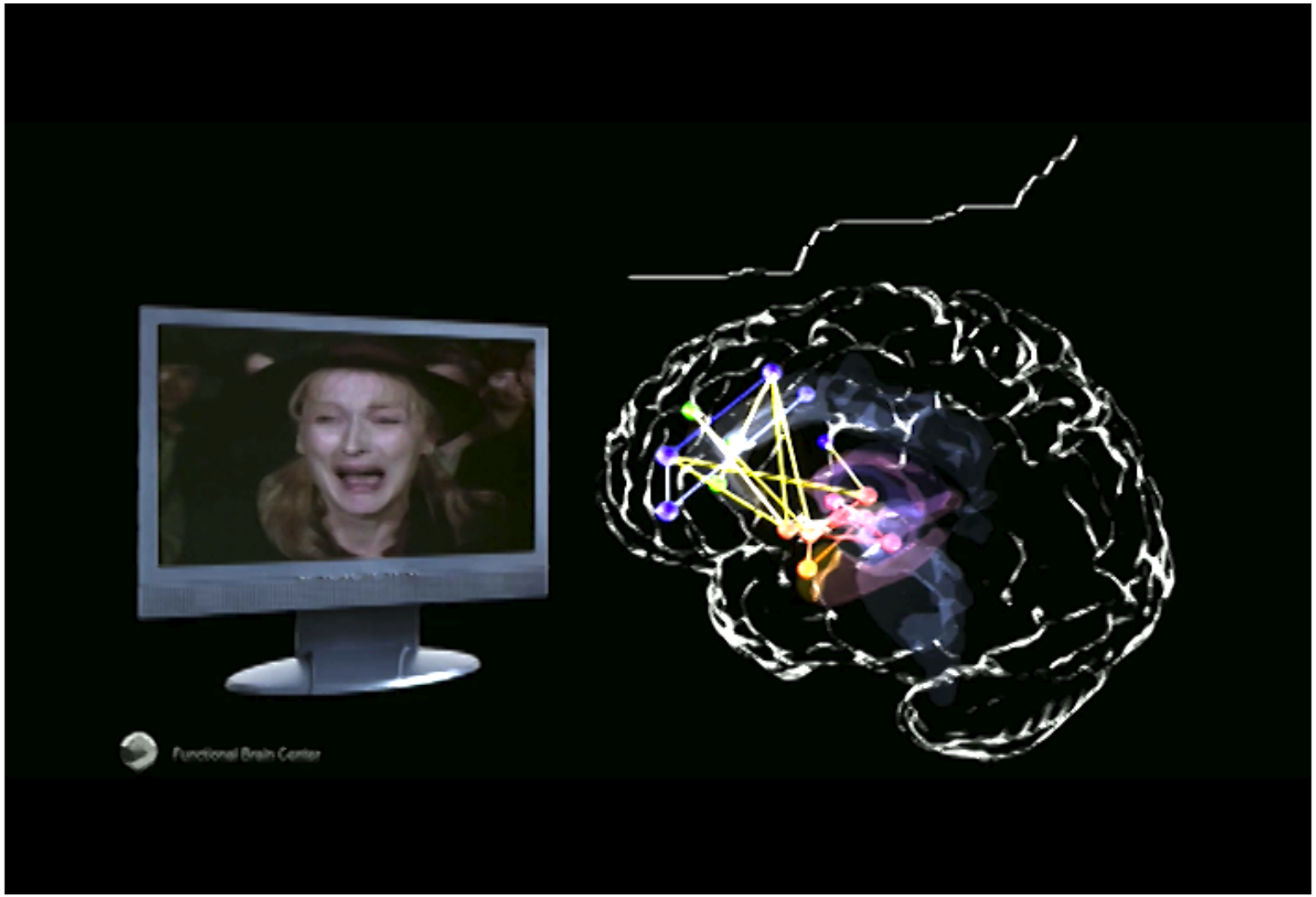
Outline

Fundamental Questions of Cognitive Sciences

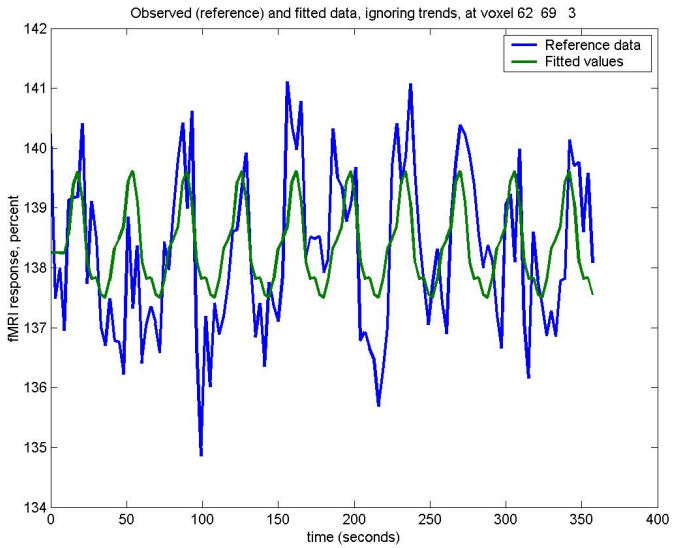
1. How does the brain work?
2. What happens where?

Single Subject Cognitive fMRI Study

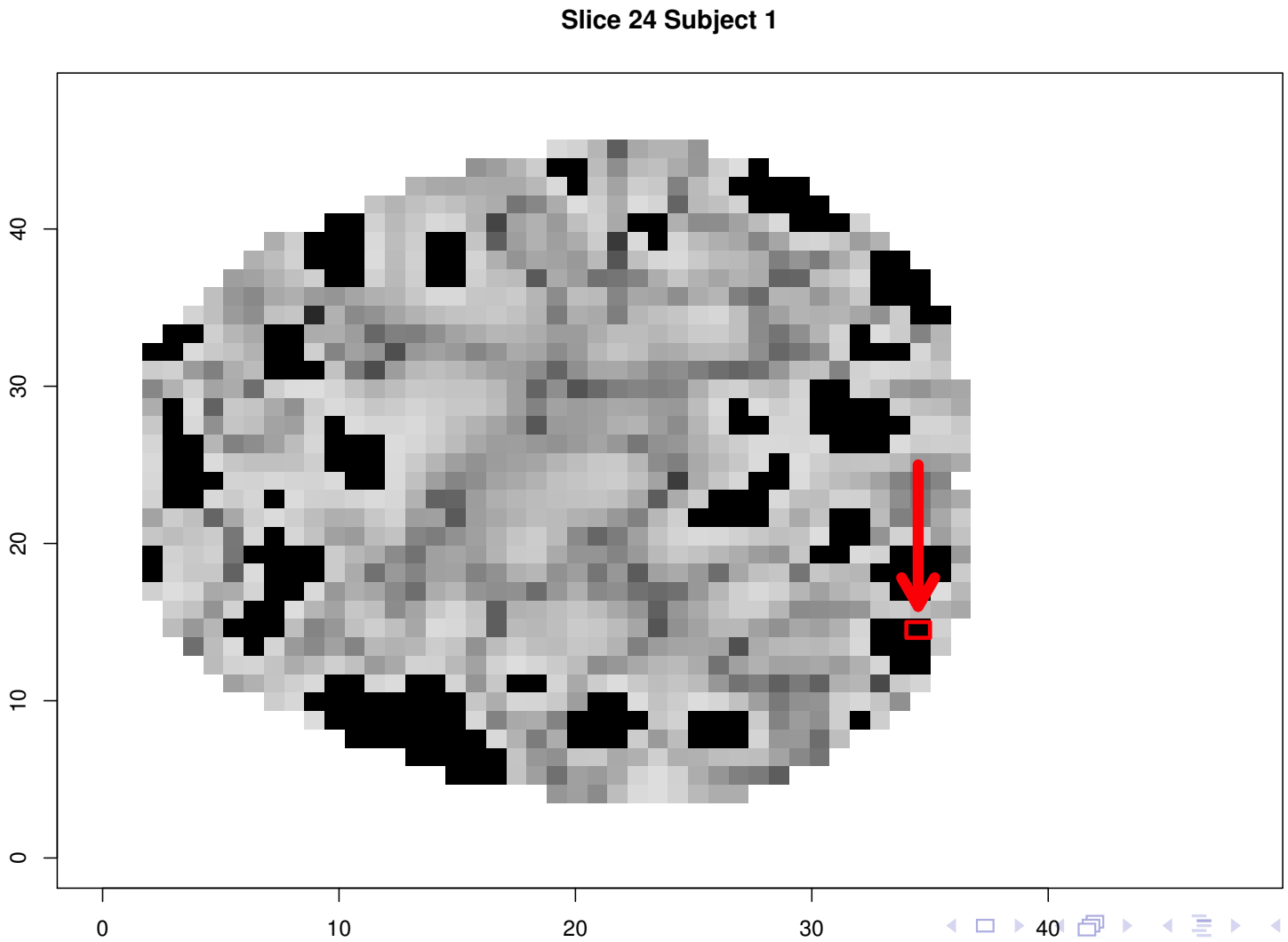


Statistical Analysis of BOLD Signal

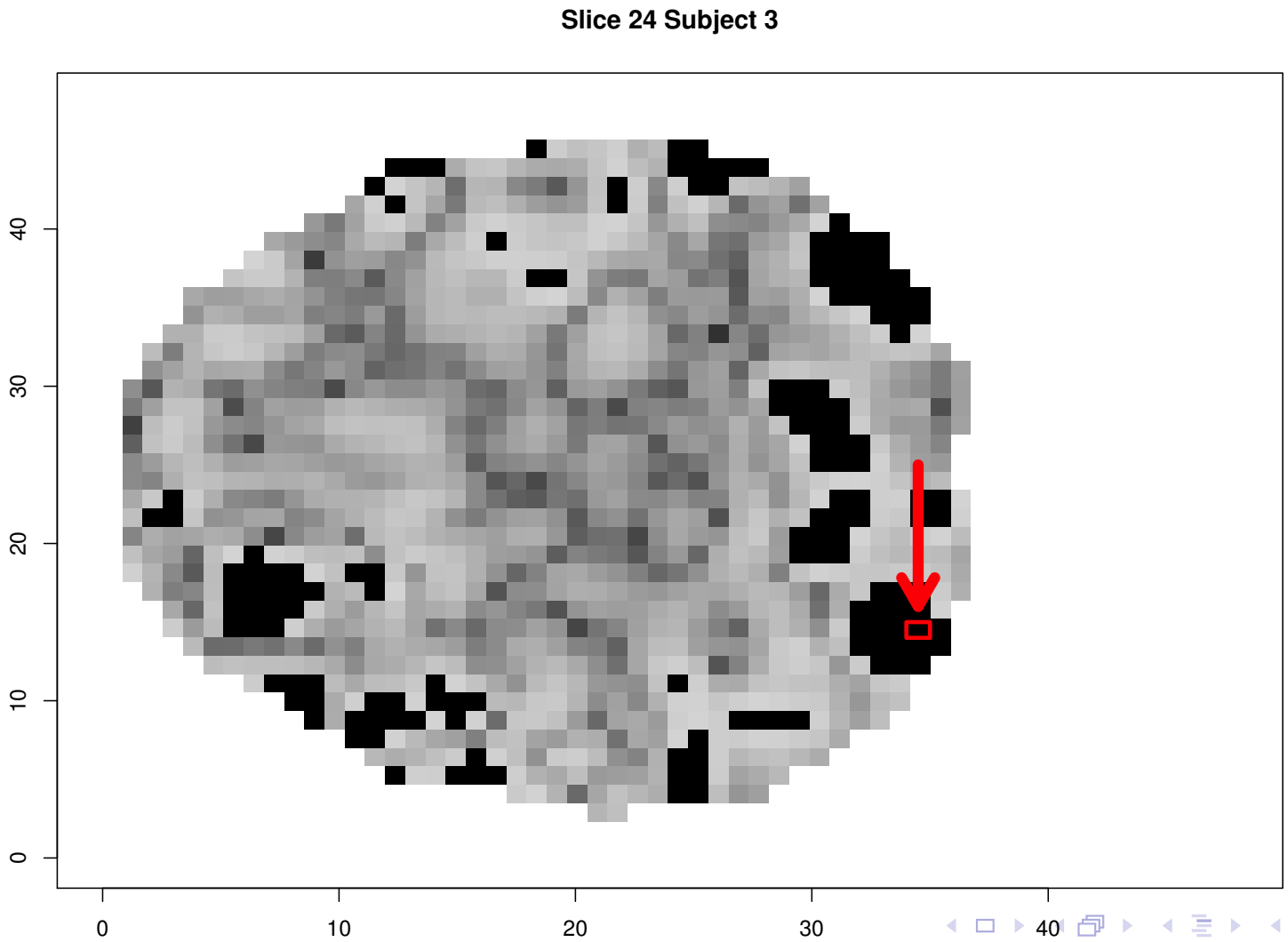
- Mass Univariate analysis (voxelwise). [Worsley et al., 1996]
- Multiplicity Control.



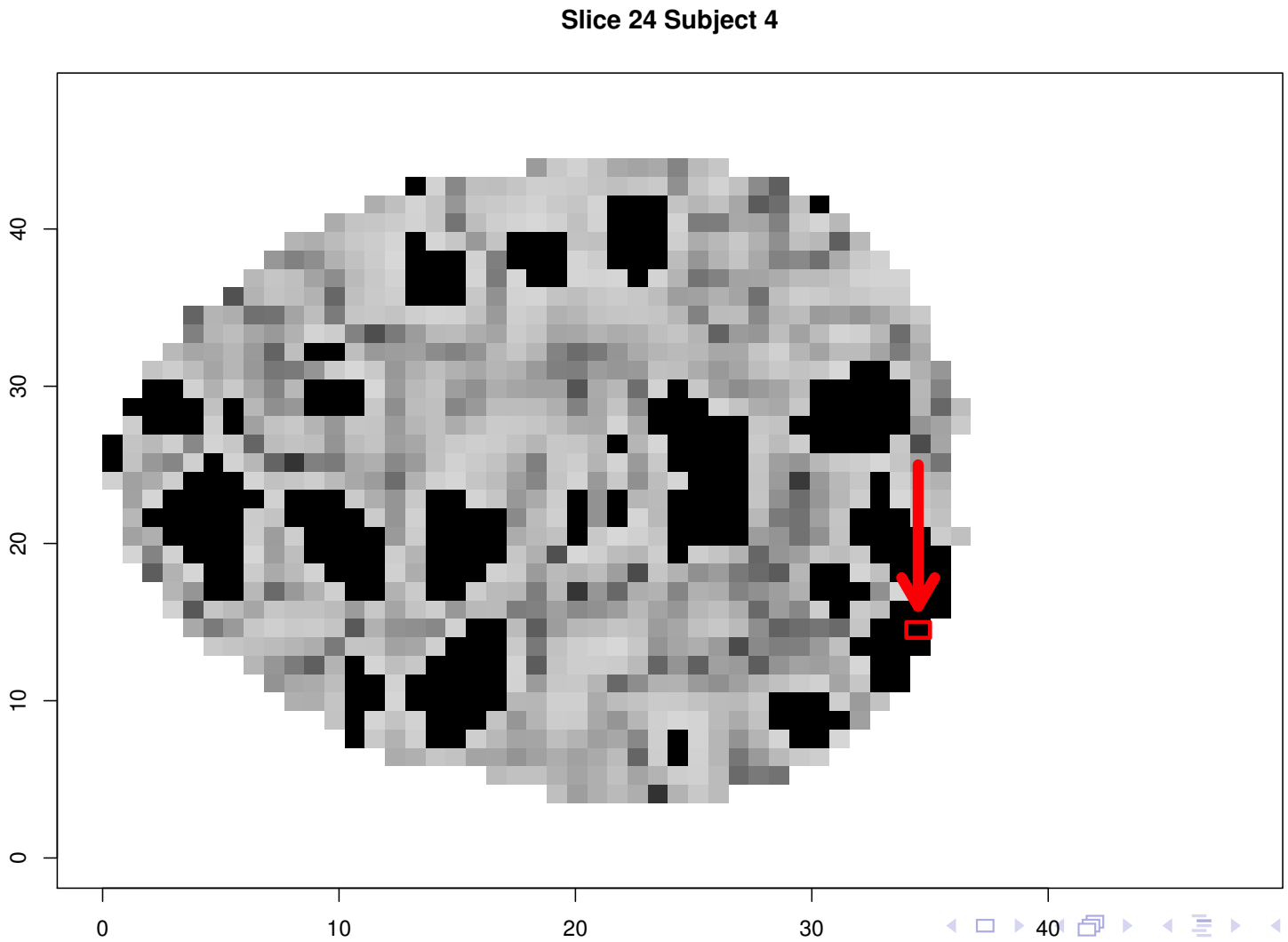
Partial Overlap Example



Partial Overlap Example



Partial Overlap Example



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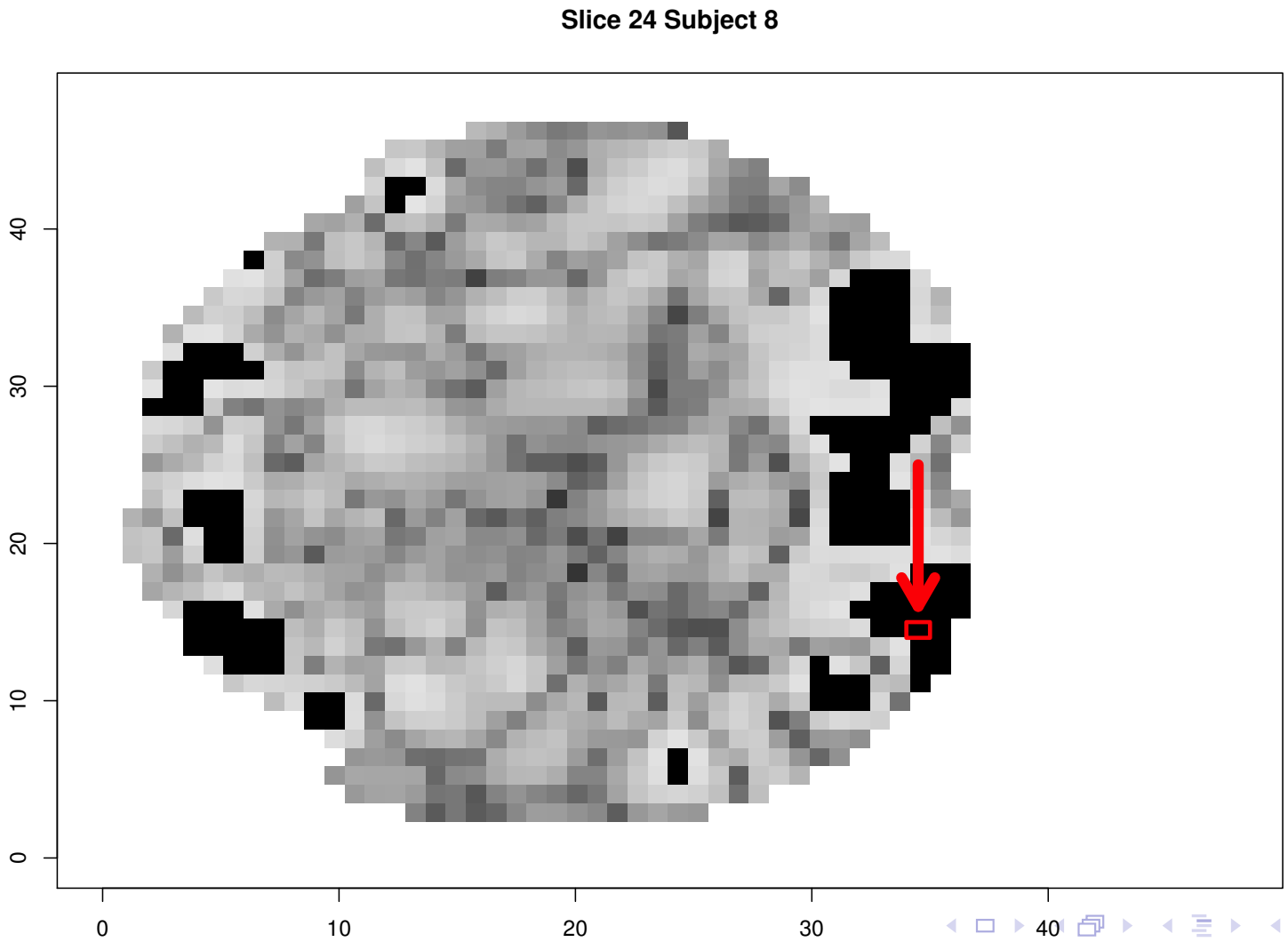

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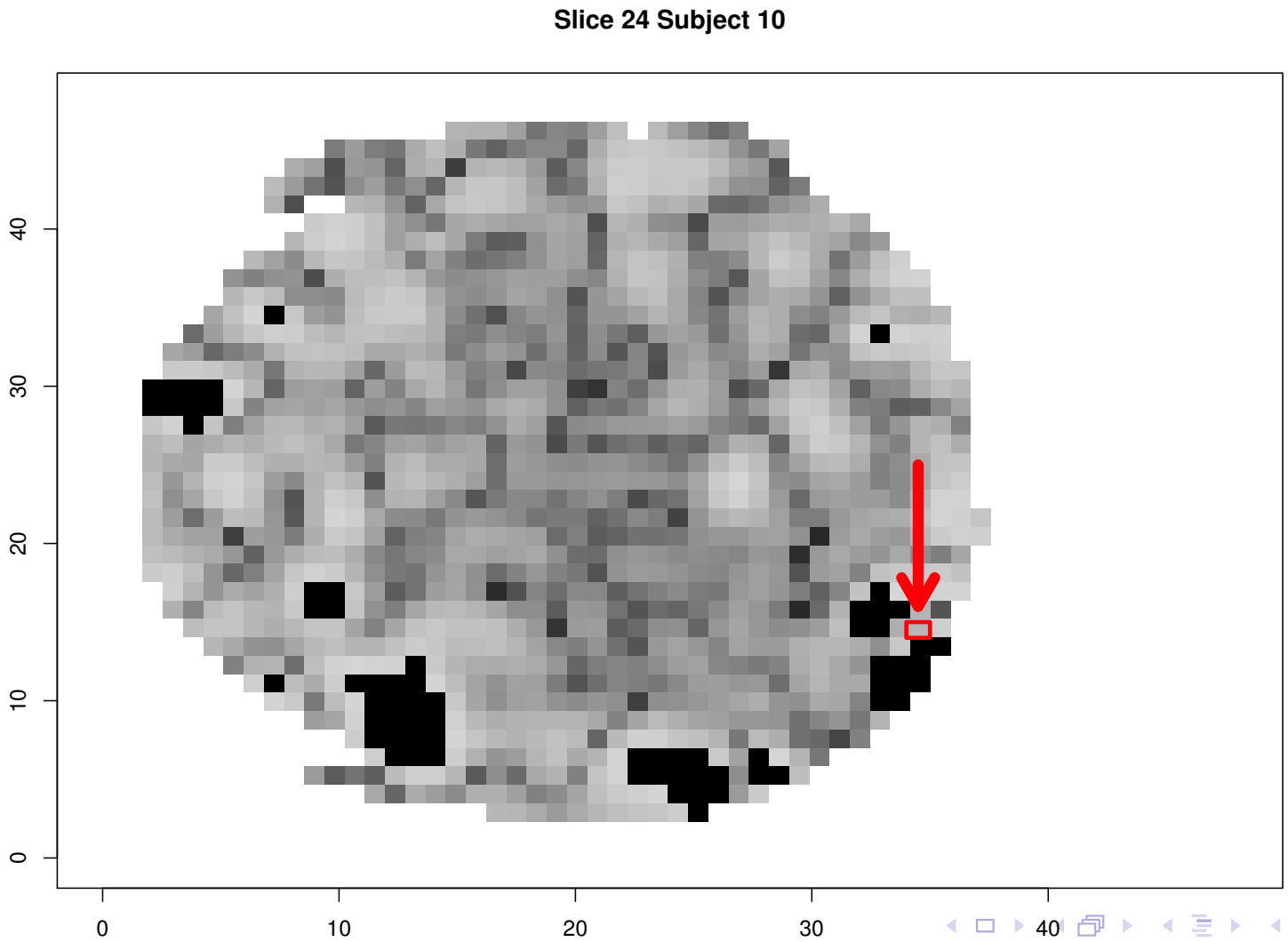
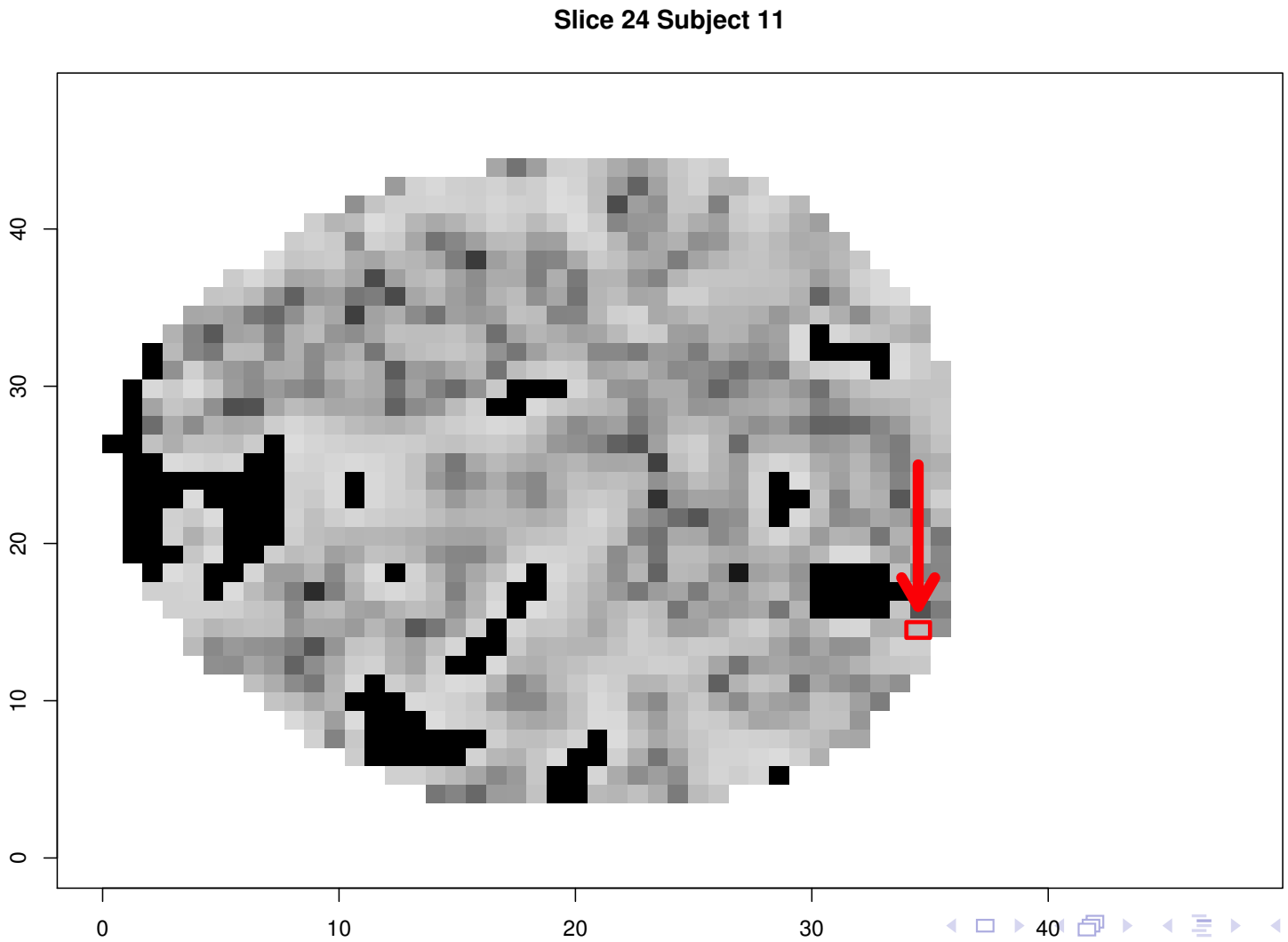


Partial Overlap Example



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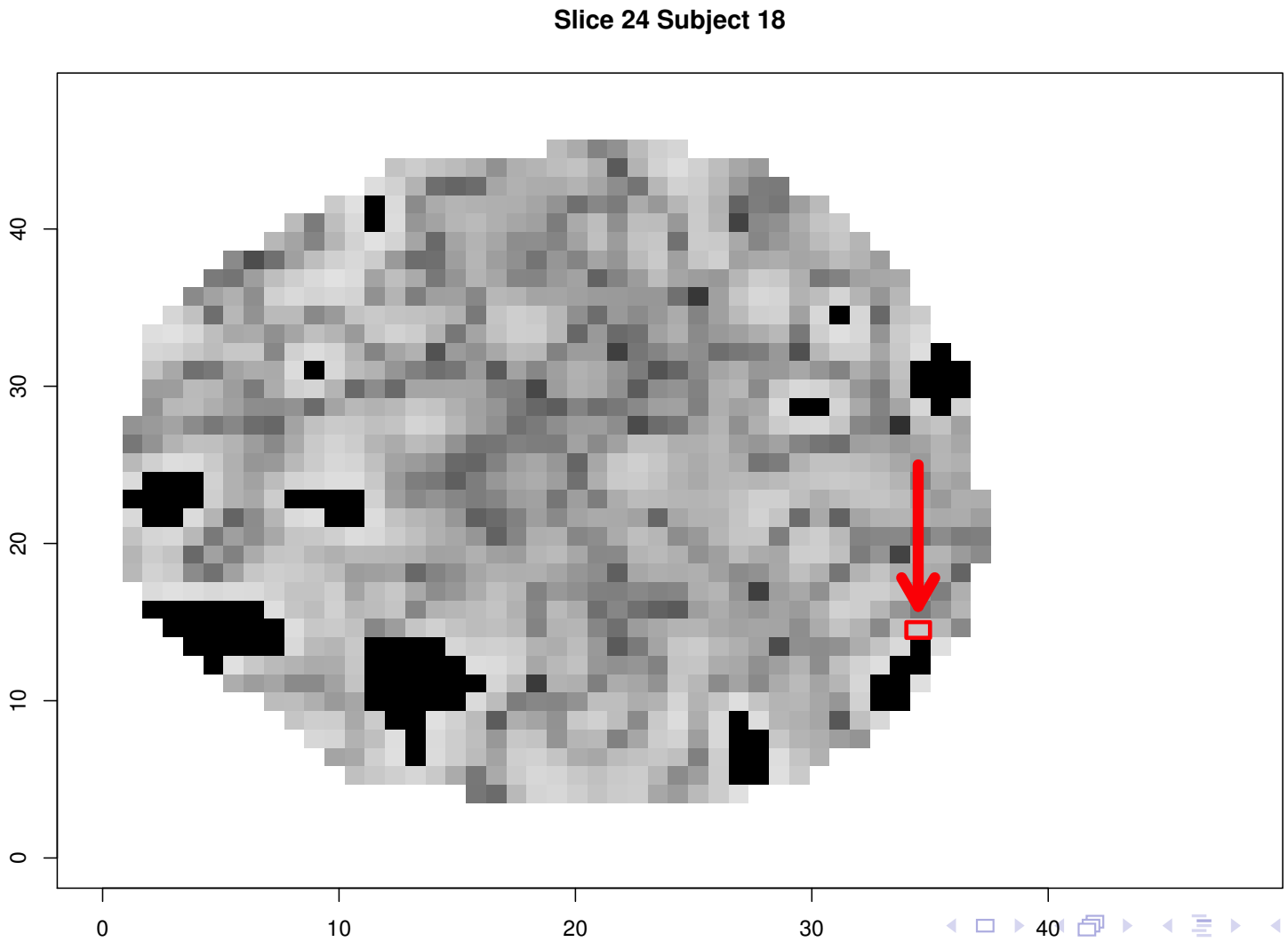

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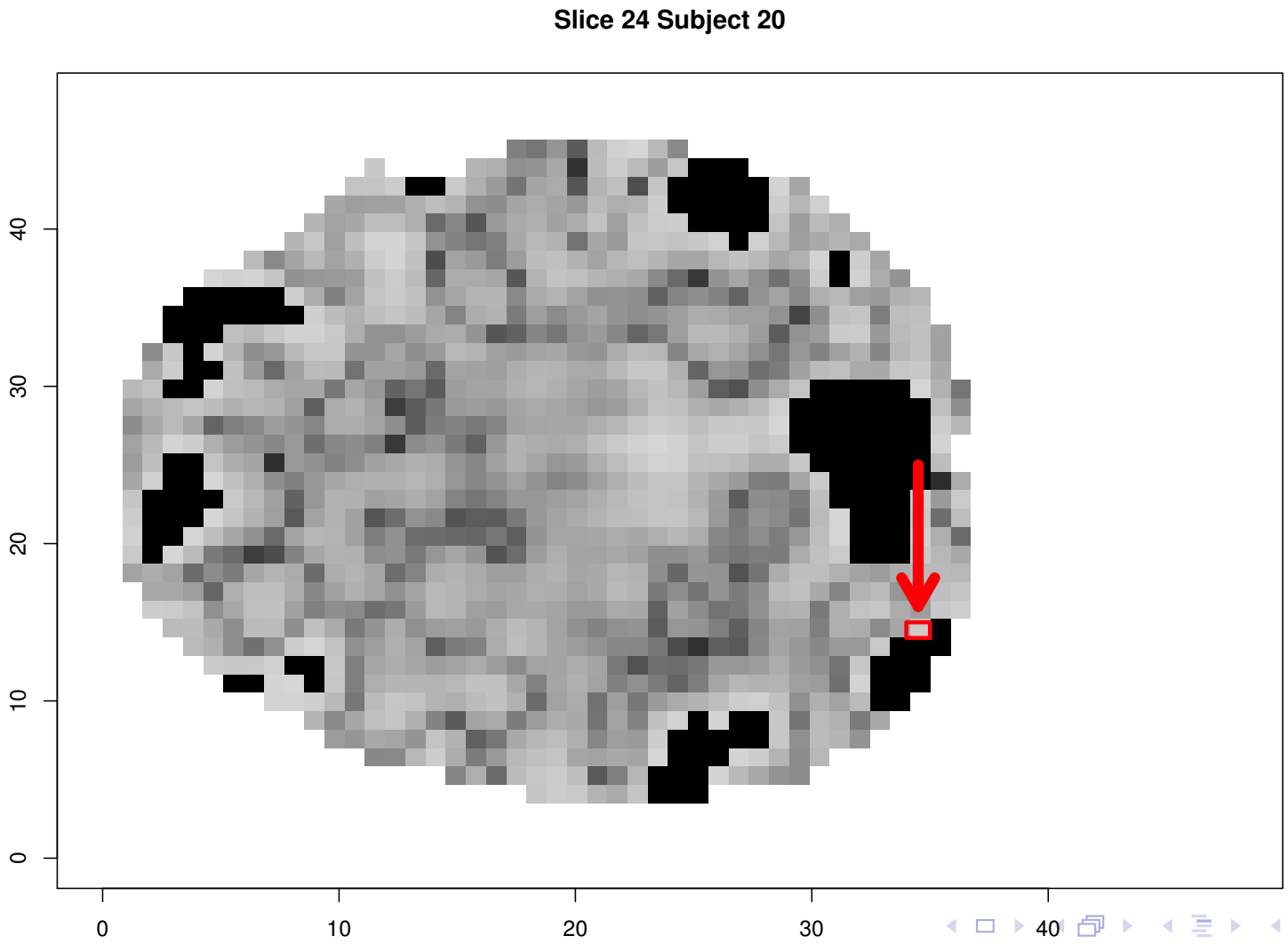
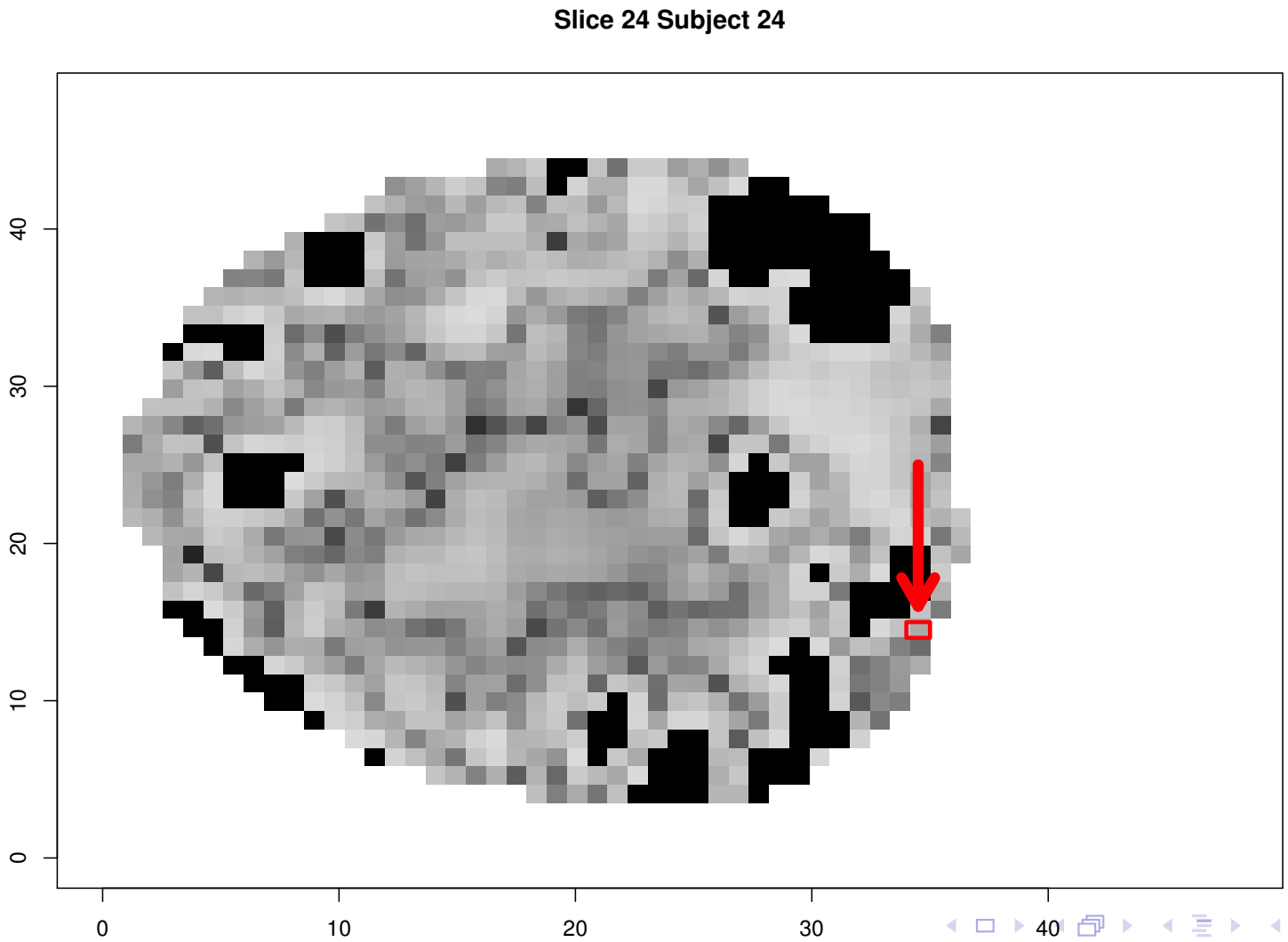
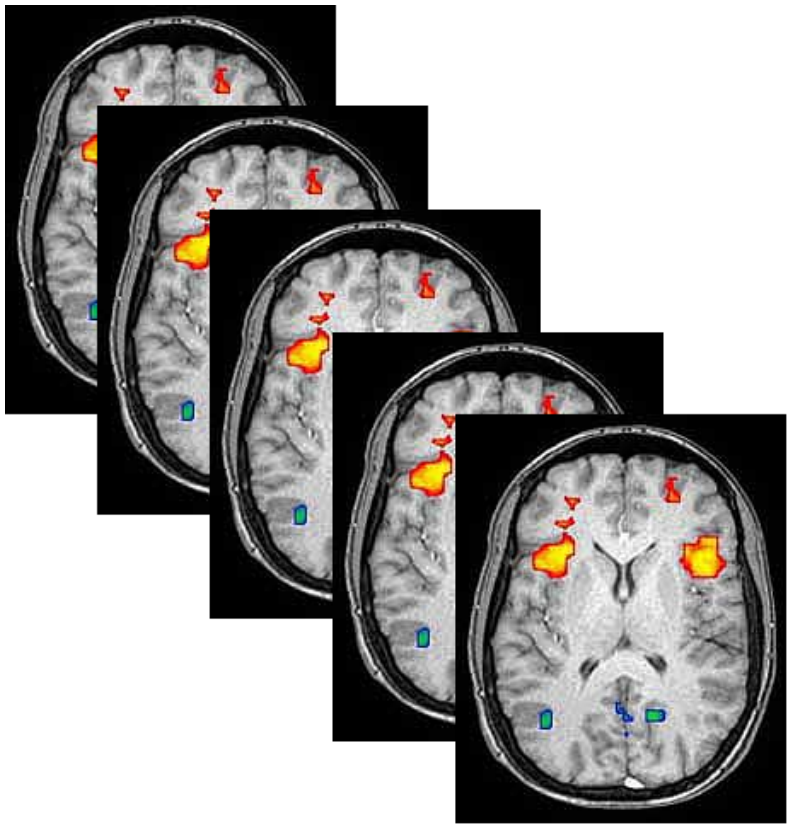


Partial Overlap Example



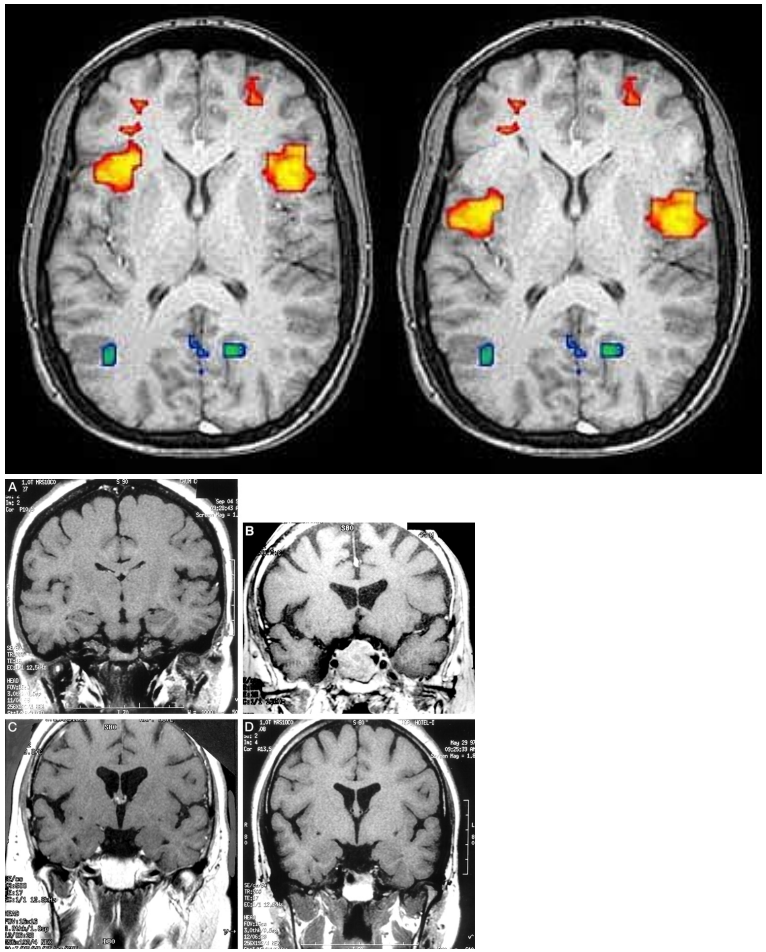
Group Studies

- Anatomical registration (a.k.a. normalization, warping)
- Subject random effect for out-of-sample inference.



Group Studies' Difficulties

- Brain plasticity
- Anatomically distinct brains



Remedies

- Force spatial similarity:
  - Smooth + standard random-effects analysis. [Friston et al., 2000]

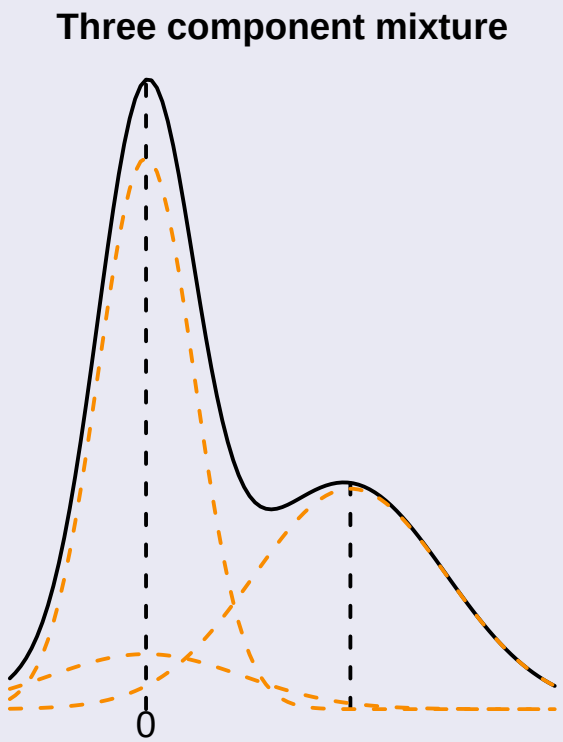
Solutions

- Allow spatial dissimilarities:
  1. Count active subjects.
  2. Full/Partial Conjunction Hypothesis :
     - Test for activity of **at least** u of n subjects. [Heller and Benjamini, 2008]
     - More power than counting rejections. ☺
     - A study group statement. ☹
  3. Mixture Random Effect
     - Allow active and non-active subjects at the same location.
     - A population statement (out of sample inference). ☺

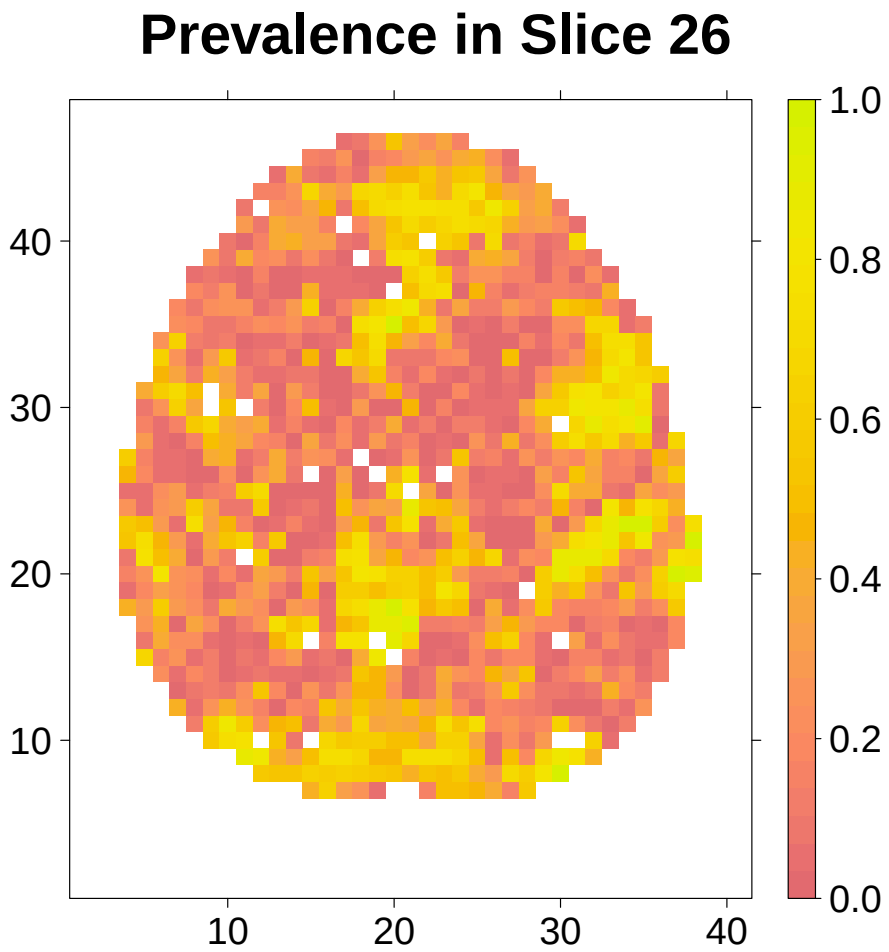
Mixed Random Effect

- Flexible under ill-registration. ☺
- Already suggested for **outliers**. ☺ [Woolrich, 2008]
- "Prevalence" interpretation. ☺

Distribution of effects over subjects at a given location.



Results



Why Bother?

- Power
- Interpretability

Under the Hood - Estimation

- Constrained parameter space
$$\left(p_3 \leq g\left(\mu_3, ...\right) : g\left(\mu_3, ...\right) \underset{\mu_3 \to 0}{\to} 0 \right):$$
  - Motivation:
    1. "Prevalence" interpretation of p_3.
    2. Identifiability under H_1.
  - Implementation:
    1. Unconstrained estimation.
    2. If constraint binding $\to$
       Force equality constraint
- Spatial structure:
  estimate $\to$ smooth initial values $\to$ re-estimate

Under the Hood - Estimation

- ML Estimation:
  - Six parameters.
  - Locations $\approx$ 30,000 (voxels). Subjects= 67.
  - EM.
  - Customized solver to deal with non-convex, non-rectangular constraints.
  - Initialization: Moment estimation inapplicable. ☹
  - Speed: ~ 6 min; Linux, 1 x Intel® Core™ i5, 8GB RAM ☺

Under the Hood- Initialization

1. Hybrid (grid+moment+likelihood):
   1. Partition the parameter: $\theta = (\theta_1, \theta_2)$
   2. Define a grid of values of θ_1
   3. Given each value of θ_1, solve the moment equations for θ_2.
   4. Compute the likelihood over all values of (θ_1, θ_2) and keep the maximum.
2. Random.
3. Arbitrary.

Under the Hood- Inference

- Inference:
  - No exact analytical results.
  - No asymptotic GLR results: Wald regularity conditions are not met. [Garel, 2007]
  - Bootstrap:
    - Many replications ☹
    - Many locations ☹
    - Easily parallelizable ☺

Under the Hood- R Packages

- tractor.base
- abind
- lattice
- colorspace
- snow

Upcoming

- Accelerate estimation [.C("likelihood")]
- Analytical results (hopefully)

Summary

- Mass univariate approach.
- Finite mixture random effects replacing "vanilla" random effects.
- Estimation: ML using EM + initialization + constraints.
- Inference: Parallelized bootstrap.

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Thank you for your time.

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