Your Name: Rohit Agarwal Your Entry Number: 2022ES11332

COL 786: Advanced Functional Brain Imaging

30/04/2025 Major Examination Maximum Marks: 140

Note: Write you answers in the space provided. You may use the blank sheet given at the end for rough work. But do not write your answers in the rough sheet. This paper has 16 sheets including two sheets for rough work at the end.

[25 Marks]

Q1. Answer the following questions in 4-5 sentences each.

(a) Explain the current scientific view about how the information processing happens in the brain

The current scientific perspective that the brain processes information by using network of neurons that talk to eachother using chemical and electrical messages. Memory, perception, and decision making are not confined to a single part of the brain instead they come from the dynamic exchanges between many brain areas. The brain processes information in two ways: in parallel & hierarchically. To make decisions it combines sensory input, internal states and knowledge about the environment. Synaptic plasticity changes the activity of neurons, which let the brain change & react based on experience

(b) Describe what are action potentials and how they are propagated

Action potentials are quick, short-lived changes in the electrical membrane potential of a neuron. They are the main way that messages get sent along axons. When the membrane depolarises more than a certain point (voltage-gated sodium channels open, letting a lot of Na+ ions in all at once). This depolarization causes wave-like depolarisation in nearby portions of the axon, sending the information down the axon. After the process, there is repolarisation through K^+ (potassium efflux) and a short refractory period. This makes sure that the signal only travel one way.

(c) Explain how the neuronal firing is related to the fMRI BOLD response.

The fMRI Bold response reaction indirectly shows neuronal activity by checking changes in blood oxygenation that happen when the body needs more energy. Neurons use more O_2 & glucose when they fire, which causes more blood to flow to that area of the brain to refill these supplies. This makes the amount of oxygenated heamoglobin go up and the amount of deoxygenated heamoglobin to go down. This changes the way fMRI can spot bold magnetic properties. The Bold signal on the other hand shows the combined reaction of the blood vessells over a number of seconds & is more closely related to local synaptic input.

(d) What is corpus callosum? Where is it located? Describe its main function.

The corpus callosum is a thick band of nerve fibres located deep in the longitudinal fissure of the brain, connecting the left & right cerebral hemispheres.

It facilitates the communication between homologous areas of the two hemispheres allowing integration of sensory, motor & cognitive information. It enables bilateral activity such as controlling movements that require both sides of the body. Damage to this can result in 'split-brain' effects

(e) What are mirror neurons? Give two distinct examples of situations when you expect the mirror neurons to be active?

Mirror neurons are a class of neurons in the frontal cortex (for actions as well as touch) that fire both when an individual performs an action & when they observe the same action performed by another. They were first discovered in the cortex of monkeys.

One example → When a boy watches someone hold a cricket bat & their brain emulates a similar motor representation as if they were performing the action

2nd example → During ~~em~~ emphatetic roles, when a friend of mine is facing some pain then the action to please ~~me~~ him or calm down as I am experiencing the same pain are the examples where I expect these neurons to be active.

[35 Marks]

Q2. **[For Data Science Stream]** Consider the General Linear Model for fMRI analysis as given by the following equation in the matrix-vector notations of the class. Here Y represents the fMRI BOLD signal of a voxel and ε represents iid Gaussian noise with zero mean, X represents the design matrix and β represents the unknown model parameters.

$$Y = X\beta + \varepsilon$$

Instead of finding an unbiased estimator, suppose we wish to find a median estimator of the model parameters β from the iid samples of the data (Y). A median estimator $\hat{\theta}$ of parameters θ has the property $\Pr[\hat{\theta} \leq \theta] = \Pr[\hat{\theta} \geq \theta] = 0.5$.

(a) Derive the expression for a median estimator for the model parameters β.
(b) Prove the correctness of your estimator.
(c) Will your estimator be still a median estimator if the distribution of noise is iid exponential with parameter λ;
(d) Will your estimator be still a median estimator if noise distribution is iid uniform in the range [-1, 1].

Q2. **[For Cognitive Science Stream]** (a) What is the relationship between attention, perception and awareness according to Jamie Ward (in the book Student's Guide to Cognitive Neuroscience). Give as much detail as possible, specifically describing different brain regions involved and experiments conducted to arrive at our current understanding (b) Describe the two different attention networks in the human brain. (c) Describe other theories of attention, perception and awareness if any. (d) Briefly summarize different theories of attention.

[Answer for part (a)]

We are given the General Linear Model (GLM) for fMRI analyses.

unknown parameters

$$Y = X\beta + \epsilon$$

iid Gaussian noise $\epsilon \sim N(0, \sigma^2 I)$

vector of observed BOLD signals

Design matrix

A median estimator that satisfies

$$P_r[\hat{\theta} \leq \theta] = P_r[\hat{\theta} \geq \theta] = 0.5$$

$$\hat{\beta}_{LS} = \arg\min_{\beta} \sum (Y - XB)^2$$

but for a median estimator $\rightarrow$ minimize the sum of absolute residuals.

Least Absolute Deviations or (L_1-norm regression)

$$\hat{\beta}_{median} = \arg\min_{\beta} \sum |Y - XB|$$

(median is the minimizer of the sum of absolute deviations) while mean minimizes squared deviation.

$$\hat{\beta}_{median} = \arg\min_{\beta} ||Y - XB||_1$$

[Answer for part (b)]

<u>Proof Intuition</u> We want $\hat{\beta}$ such that

$$\Pr[Y - X\hat{\beta} \leq 0] = 0.5$$

which means for each residual $r_i = Y_i - X_i\beta_i$, half the residuals are +ve, half are negative → estimator makes the residuals centered at 0 (median 0)

In statistics, minimizing sum of absolute residuals guarantees that the median residual is zero.

Thus, $\hat{\beta}_{median}$ satisfies:

- 50% residuals below zero
- 50% residuals above zero.

which is exactly the condition

$$\Pr[\hat{\beta} \leq \beta] = 0.5$$

Therefore minimizing L_1-norm yields median estimator.

<u>Proof:</u>

for a scalar z the sample median of n observations $z_1, z_2, \ldots z_n$ is the value m that minimizes $m = \arg\min_z \sum_{i=1}^{n} |z_i - z|$

for GLM $Y = X\beta + \epsilon$

$$r_i(\beta) = Y_i - X_i\beta$$

$$Q(\beta) = \sum_{i=1}^{n} |r_i(\beta)| = \sum_{i=1}^{n} |Y_i - X_i\beta|$$

our estimator $\hat{\beta}_{median} = \arg\min_\beta Q(\beta)$

the function $f(z) = |z|$ is not differentiable at $z=0$ but we can have subgradients

$$\frac{d}{dz}|z| = \begin{cases} +1 & z > 0 \\ -1 & z < 0 \\ [-1,+1], & z = 0 \end{cases}$$

$$\nabla Q(\beta) = -\sum_{i: r_i(\beta)<0} X_i + \sum_{i: r_i(\beta)>0} X_{i4} + \sum_{i: r_i(\beta)=0} \alpha_i X_i$$

$\alpha_i \in [-1,+1]$

at a minimizer $\hat{\beta}_{median}$ $0 \in \nabla Q(\hat{\beta}_{median})$

This condition holds when +ve & -ve contribution balances.

$$[\{i : r_i(\beta_{median}) > 0\}] = [\{i : r_i(\beta_{median}) < 0\}] = 0.5$$

where $r_i(\beta_{median}) = Y_i - X_i\beta_{median}$

$$P[Y_i - X_i\beta_{median} \geq 0] = 0.5$$

$$\Pr[\beta_{median} \leq \beta] = 0.5 \rightarrow \underline{Q.E.D}$$

[Answer for part (c)]

$\varepsilon_i \sim e^{\lambda}$

$f_\varepsilon(x) = \lambda e^{-\lambda x} \quad \forall\, x \geq 0$

(right skewed & not symmetric)
mean & median are not equal

$\mu = 1/\lambda$ (mean)

$m = \frac{\ln 2}{\lambda}$ (median)

the median estimator

from minimizing $\sum |Y_i - X_i\beta|$

works because under symmetric noise

→ 50% of noise above true value

→ 50% of noise below true value.

Which balances positive & negative residuals equally.

But under exponential noise all noise values ε_i are ≥ 0

→ one sided → asymmetric distribution

$\Pr[\varepsilon_i \geq 0] = 1$ and there are no negative residuals possible.

→ The sum of absolute deviations will be minimized at a boundary (β_{min}) not at true β_{median}

$$Q(\beta) = \sum_{i=1}^{n} |Y_i - X_i\beta|$$

$$Y_i = X_i\beta + \varepsilon_i \quad \text{exponential} \quad \varepsilon_i \geq 0$$

with $\varepsilon_i \geq 0$ most residuals will be biased upwards pulling the estimate lower to compensate

→ ∴ Minimising the absolute deviation doesnot guarantee the median anymore under an asymmetric error distribution

$\boxed{\text{NO}}$, the $\hat{\beta}_{median}$ will not remain a median estimator under exponential noise.

[Answer for part (d)]

$\epsilon_i \sim U(-1, +1)$

$f_\epsilon(x) = \frac{1}{2}$ for $x \in [-1, +1]$

$= 0$ elsewhere.

This is a symmetric distribution around 0

Median $= 0$

mean $= 0$

$\rightarrow$ $\therefore$ mean & median are identical for uniform distribution centered at zero.

Since $U[-1, +1]$ is symmetric, same no. of +ve & -ve errors equally likely

$P[\epsilon_i \geq 0] = 0.5$ $\quad P[\epsilon_i \leq 0] = 0.5$

$\therefore$ minimizing $\sum |y_i - x_i \beta|$ still guarantees

$P_r[\hat{\beta}_{median} \leq \beta] = 0.5$ & $P_r[\hat{\beta}_{median} \geq \beta] = 0.5$

$\boxed{\text{Yes}}$, the β_{median} is a valid median estimator under iid uniform $[-1, +1]$ noise.

[25 Marks]

Q3. **[For Data Science Stream]** Answer the following questions.

(a) What is multiple comparison problem in fMRI data analysis?

(b) Explain the details of the Bonferroni correction and false discovery rate (FDR) correction.

(c) When will you prefer applying Bonferroni correction and when the false discovery rate correction method while analysing the fMRI data.

Q3. **[For Cognitive Science Stream]** (a) Describe the role of parietal lobe in processing of attention. (b) Describe as many curious phenomena pertaining to attention and parietal lobes as possible according to Jamie Ward's book chapter on attention (c) Why do actors who prefer to remain hidden enter the stage from its right?

(a) The multiple comparison problem is a statistical issue in the fmri data analysis. In fMRI studies, researchers typically analyze brain activity by dividing the brain into thousands of small volume elements → the voxels. Statistical test are then performed on each voxel to determine whether it shows significant activation in response to a stimulus or task.

The issue arises because

1. A typical fMRI scan might contain 100,000+ voxel
2. each voxel is tested independently for statistical significance
3. Using the standard significance threshold ($\alpha < 0.05$) means we would expect 5% of inactive voxels to falsely appear significant. (i.e.) around 5000 voxels). Which is unacceptable — a massive false positive problem

(b) Bonferroni correction → Divide α by no of test

$$\alpha' = \frac{\alpha}{N}$$

threshold for rejecting null hypothesis = $t_{1-\alpha}, 1-\frac{\alpha}{2N}$

Pr(false discovery of voxel 1) $= \alpha/N$

Pr(false discovery of voxel i) $= \alpha/N$

Pr (at least one false discovery) = 1 − Pr (No false discovery)

$$\Rightarrow 1 - \left(1 - \frac{\alpha}{N}\right)^N$$

(Binomial expansion)

$$\Rightarrow \alpha - \frac{N(N-1)}{2}\frac{\alpha^2}{N^2} + \ldots$$

α − (+ve number)

∴ Pr (at least one false discovery) $\leq \alpha$

Ground truth \ Result of hypothesis	Pos	Non-Pos
Pos	TP β	TN $1-\beta$
Non-Pos	FP α	FN $1-\alpha$

FDR (False Detective Rate) correction.

$$FDR = \frac{FP}{FP + TP}$$

FP → false positive
TP → True positives.

FDR < q → a target value

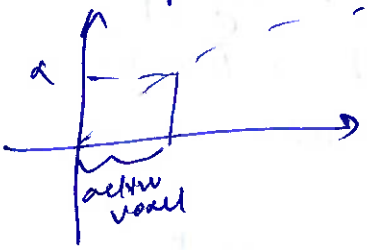
$$\frac{\hat{\beta}_i}{\hat{\sigma}_i} \sim t_{T-K}$$

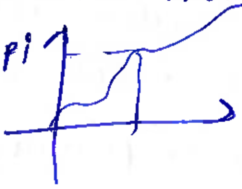
Reject α if $\frac{\beta}{\alpha_i} > t_{1-\alpha/2}$

$$\frac{\alpha_{min}}{2} > 1 - F_T\left(\frac{\hat{\beta}}{\alpha}\right)$$

$$\alpha > 2\left(1 - F_T\left(\frac{\hat{\beta}}{\alpha}\right)\right) = p_i$$

suppose the p values in increase order of p_i's





$p_1 \leq p_2 \leq \ldots p_N$

$$P(i) \leq \frac{i q}{N}$$

q → target FDR
N → total voxel
i → largest index i

$E(FDR) \leq q$

(c) Bonferroni

- Small number of tests
- Confirmatory study
- Need very low F.P
- Clinical

FDR

Large no. of tests (voxel-wise)

Exploratory study

To Retain sensitivity

Cognitive neuroscience research

[25 Marks]

Q4. Answer the following questions about default mode networks.

(a) What are default mode networks (DMN)?

→ The default mode networks (DMN) refers to a specific set of brain regions that show higher activity than brain is at rest (not engaged in any external task) and reduced activity during goal-directed tasks

It was discovered when researchers noticed that some brain ~~activity~~ regions consistently showed deactivation during cognitive tasks compared to resting base line → meaning they were more active during rest or passive states.

→ It is active when we are day-dreaming, mind-wandering, thinking about ourself, imagining the future, recalling the past or considering other's perspective.

(b) What was the defining characteristic of default mode networks at the time of its discovery?

→ At the time of its discovery the key characteristics of DMN were →

(i) Task-negative behaviour

- DMN showed decrease activation during a variety of attention demanding cognitive tasks.
- Brain regions were consistently deactivated ~~need~~ relative to baseline in fMRI studies

(ii) consistent spatial pattern

The same set of regions appeared across multiple researchers and participants irrespective of specific task

(iii) DMN showed high resting cerebral blood flow (CBF)

(iv) · Functional connectivity at rest

(c) Which areas of the human brain comprise its default mode networks? List all the areas that are known to comprise the DMN now.

Originally the DMN includes

- Medial Prefrontal cortex (mPFC)
- Posterior Cingulate cortex (PCC)
- Inferior parietal lobule / Angular gyrus

Now the DMN includes / known are →

- Medial Temporal Lobe
- Lateral Temporal cortex
- Retrosplenial cortex
- Ventral medial prefrontal cortex
- Dorsal medial prefrontal cortex
- Anterior medial prefronal cortex
- Sub cortical nodes

(d) What is presently known about the functions of DMN? Describe specific functions of specific DMN areas whenever possible.

(1) self-referencing processing → Medial prefrontal cortex.

- Thinking about oneself – traits, emotions; introspection.
- Social cognition – considering other people's mental state

(2) Autobiographical memory → medial temporal lobe

- Recalling personal past events
- Mental time travel – imagining future scenarios

(3) Mind-wandering (DMN)

- Areas activated during periods of unguided, spontaneous thoughts
- Correlates with creative thinking

(4) Conceptual processing → Angular Gyrus

- Integration of semantic information across modalities
- Abstract meaning.

(5) Mental simulation → PCC

- Simulating hypothetical scenarios
- planning the future.

[30 Marks]

Q5. Answer the following questions about Functional Connectivity Analysis

(a) Describe in detail different steps involved in carrying out the functional connectivity analysis of fMRI data.

Functional connectivity Analysis → • To capture interactions among brain region

• How to measure & characterize these interactions?

→ It is defined as the temporal correlation between spatially defined brain regions. A measure of correlation of fMRI time series across two different brain regions. The correlation means that activity in one brain region is also accompanied by activity in other brain region. ~~As~~ -ve Correlation means the activity in one brain region is accompanied by a reduction in activity in the other region

→ Action methods output a map

→ N voxels in a brain → size of the map N

→ connectivity output a graph

→ A edge (i, j) is present in the graph if region i is functionally connected to region j.

→ N voxels in the brain → size of output N × N

Pipeline of functional Connectivity →

• Process and register data

• Define ROIs → • All voxels • Anatomical region (Broadman Areas) • functional region • combination

• Extract time series (TS) → • Peak voxel • Average of ROI • Average of cluster • PCA/ICA

• Remove covariates / noise → • Intensity normalisation • Motion • Experimental condition • Global signal • white matter signal • Grey matter signal • CSF signal

• Find functional connection

Parametric Tests • Functional connectivity statistics → • correlation • Delayed corr • coherence • Mutual information

Non parametric tests • Visualize & interpret result

(b) Suppose you carry out a seed based resting state functional connectivity analysis for a seed in medial pre-frontal cortex (MPFC). What brain areas do you expect to be functionally connected in Group-level resting state functional connectivity analysis? Give suitable reasons for your answer.

The expected regions that would be ~~[illegible]~~ functionally connected would be

(i) PCC, Posterior cingulate cortex

(ii) Inferior parietal lobule (Bilateral - supports semantic integration)

(iii) Medial temporal lobe

A seed in mPFC will reveal a canonical DMN connectivity pattern at rest → reflecting synchronised low frequency BOLD fluctuations among these regions. This pattern represents brain system engaged in internally focused cognition distinct from externally directed attention networks.

(c) Explain the impact of different types of noises in resting state functional connectivity analysis (RSFC). Explain specifically how different types of noise may impact the results of RSFC analysis.

Spontaneous, low-frequency fluctuations in the fMRI bold that exhibit specific networks of the human brain in the absence of overt task

Different noises → Physiological Noise, subject motion, MR related artefacts

Physiological Noise:

→ Cardiac Noise
→ creates signal fluctuations
→ can artificially inflate connectivity betw^n regions with spatial proximity

→ Respiratory Noise
→ ~~Can~~ Creates signal fluctuations
→ can create spurious correlations across the brain, particularly in regions susceptible to respiratory artifacts

Subject motion:

• Bulk head movement
→ Creates signal disruptions,
→ Systematically biases connectivity measurements by reducing long distance correlations

MR related artefacts:

• Thermal Noise
→ Adds white noise across all frequencies
→ Reduces statistical power but typically doesn't creat structured correlations

(d) Explain the differences in following different analysis methods (i) Resting-state functional connections analysis (RSFC) (ii) Inter-subject correlation (ISC) analysis (iii) Inter-subject functional connectivity analysis (ISFC). Explain the experimental paradigm needed and how different types of fMRI noise may impact the results for these analyses.

	RSFC	ISC	ISFC
Defn →	Measures temporal correlations of BOLD signals b/w diff brain regions during rest	Measures similarity of brain activity patterns across different subjects	Measures consistency of functional connectivity patterns across subjects during stimulus presentation
Mathematical →	Pearson correlation	correlation of voxel/region time series between different subject	Correlation between one region in subject A with another region in subject B.
Output →	Subject specific connectivity matrices showing region to region correlation strength	voxel-wise or region wise maps showing degree of synchronization	connectivity matrices representing shared network response to stimuli
Experimental Paradigm →	• Subject lies with eyes open or closed	→ All subjects view identical stimulus	• Same as ISC
	• Typically 5-15 minutes	• 10+ minutes	• same as ISC
	• Relax, don't fall asleep, do not think about anything in particular	• watch / listen attentively	• same as ISC + need for an anatomical alignment
	• minimal visual / auditory stimulation	• Identical stimulus presentation.	• Same as ISC
Noise: Cardiac	High impact	Moderate impact	High impact
Respiration	High impact	Moderate impact	High impact
Thermal noise	Moderate impact	Low impact	Low impact

Sheet for rough work

Sheet for rough work