Brain Imaging RSG - Problem Formulation

Don Praveen Amarasinghe, Andrew Lam, Pravin Madhavan

Mathematics and Statistics Centre for Doctoral Training
University of Warwick

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- Protons in oxygenated haemoglobin behave differently to deoxygenated haemoglobin.
- When the pulse is turned off, the energy absorbed by the resonating protons is released.
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Electroencephalography (EEG)

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- Voltages between electrodes can then be used to chart the electrical activity inside the brain.
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- **Spatial Resolution** - EEG can’t pinpoint the location of neural activity.
- **Signal Noise** - In both fMRI and EEG, there are issues of noise introduced through the detection process. The signal can even “disappear”!
- **External validity** - There is a time delay issue with fMRI. There are also problems in establishing a control reading to begin with.
<table>
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<td>Create a time-indexed series of noisy images which mimic the motion of a signal.</td>
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- Filter the noise out from the image taken at first time-point.
Despite the technical difficulties with fMRI and EEG discussed previously, we seek to infer properties of the noisy signal. To do so, we look at sequence of brain images taken in time to trace brain activity associated with stimulus. Two main objectives:

- Filter the noise out from the image taken at first time-point.
- The denoised data can be used to evolve the observed signal in time.
Original data is composed of noisy surfaces defined on the square domain $[-1, 1] \times [-1, 1]$. 
Original data is composed of noisy surfaces defined on the square domain \([-1, 1] \times [-1, 1]\). Model considers 2D function with rotational symmetry, given by

\[
\phi(x, y) = \exp(-\beta((x - c_1)^2 + (y - c_2)^2))
\]

where \(\beta\) controls how spiked the signal is and \(c = (c_1, c_2)\) the location of the signal.
Figure: Plot of $\phi$ for $\beta = 20$ and $c = (0, 0)$
Add noise to the function by drawing independent samples from normal distribution with mean 0 and small variance and adding it to the function.
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**Figure:** Plot of noisy signal for $\beta = 20$ and $c = (0, 0)$
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c follows a path of the form

$$c_2 = c_1^3 + u.$$  

where $c_1$ moves from $-1$ to $1$ and $u \sim \text{Unif}([-0.1, 0.1])$. 
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**Why have we chosen such models for these expressions?**

- For \( \beta \), want to incorporate key limitation of medical scanners, namely the disappearance of signal for short period of time.
- For \( c \), want to capture the non-linear structure of the brain in order to characterise the signal more realistically.

Regions of the brain activated by a stimulus need not lie on a path with simple geometry. Whilst our models do not fully reflect the complexity of such structures, it captures some of the non-linearity.
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Suppose we have a null hypothesis $H_0: \theta \in \Theta_0 \subset \Theta$ which we want to test against an alternative hypothesis $H_1: \theta \in \Theta \setminus \Theta_0$ where $\Theta$ is the parameter space. The usual method of hypothesis testing involves a Likelihood Ratio Test Statistic, given by

$$ S_{LR}(X) = \sup_{\Theta_0} L(\theta; X) / \sup_{\Theta} L(\theta; X) $$

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$$P(H_k|X) = \frac{P(X|H_k)P(H_k)}{P(X|H_0)P(H_0) + P(X|H_1)P(H_1)}$$

with \( k = 0, 1 \).
We then get

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P(H_0 | X) = P(H_1 | X) = P(X | H_0) P(H_0) / P(X | H_1) P(H_1)
\]

where

\[
P(X | H_k) = \int P(X | \theta_k, H_k) \pi(\theta_k | H_k) d\theta_k
\]

with $\theta_k$ the parameter under $H_k$ with prior $\pi(\theta_k | H_k)$.
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\frac{P(H_0|X)}{P(H_1|X)} = \frac{P(X|H_0) P(H_0)}{P(X|H_1) P(H_1)}
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with \(\theta_k\) the parameter under \(H_k\) with prior \(\pi(\theta_k|H_k)\). The highlighted term is the Bayes factor.
Why *Approximate* Bayes Factors?

The problem...
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- Asymptotic Approximation
- Monte Carlo Methods
- MCMC & Metropolis-Hastings
Application - Image Segmentation

We would like to use approximate Bayes factors to determine boundaries in a noisy image. In this particular example, we are interested in determining the number of gray levels to be used in an image.

Figure: PET image of a dog's lung [Stanford & Raftery (2002)]
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Approximate Bayes Factors

We assume that the image has two “layers” (an actual image, and the observed image), giving rise to a Markov random field with the Potts Model. We have a number of hypotheses, each representing a model using a different number of shades of grey (segments). We use a Bayes factor approximation called the Penalised Pseudolikelihood Criterion, based upon maximum likelihood estimators, to compare favourability of these models (NB - Requires ICM first).

Start with the model which has one shade of grey. Calculate the PLIC for that model, then move on to the next model. Iterate. Look out for a local maximum.
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The result...
The result...

Figure: PET image of a dog’s lung after final segmentation [Stanford & Raftery (2002)]
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A common tool for tracking problems/noise reduction is the Kalman filter. Given an observation $X_t$ at time $t$, we want to infer on the state variable $θ_t$ of a system. The state variables are linked to the observations via a matrix $H$.

Measurements are typically noisy, so we include a noise term $n_t$. The Observation model is

$$X_t = Hθ_t + n_t.$$ 

The state vector is updated by a transition matrix $G$ with a noise process $w_t$,

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### Short summary

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- Denote the error $e_t = \theta_t - \hat{\theta}_t$ and its variance-covariance matrix $P_t$.
- Assume the prior estimate of $\hat{\theta}_t$ is $\hat{\theta}_{t|t-1}$. The update equation, combining the old estimate and measurement, is
  $$\hat{\theta}_t = \hat{\theta}_{t|t-1} + K_t(X_t - H\hat{\theta}_{t|t-1}),$$
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There is a similar update equation for $P_t$. 
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- EEG artifact removal
Applications

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- EEG spike enhancement
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- EEG artifact removal
- EEG spike enhancement
- Detecting activation regions
EEG artifact removal

Figure: EEG artifact removal [Morbidi et al. (2007)]
EEG spike enhancement

Figure: EEG spike enhancement [Oikonomou et al. (2006)]
Detecting activation regions

Figure: Incremental activation detection [Roche et al. (2004)]
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One key assumption needed to apply Kalman filters is that the noise is Gaussian. This may not necessarily be the case. If we apply the Kalman filter as if noise was Gaussian, how would this affect the outcome of our analysis?

We want to compare results that are derived from different models. We need some metric to evaluate this difference.

We can use the matrix norm. But we want our metric to take into account the inherent stochasticity of the denoised data matrices.
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As an example, we use the discussed mathematical and statistical tools to generate a number of signal trajectory paths at every timepoint. Then take the average of the computed paths and compare it with the true path.

Various statistical metrics that compare such paths can be found in [Needham & Boyle, 2003].
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Multiple signals

False positives arise from spatial delay or noise generated from the scanning process. There may also be spatial correlation among signals. Generate multimodal signal surfaces.
Multiple signals

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Multiple signals

- False positives arise from spatial delay or noise generated from the scanning process.
- There may also be spatial correlation among signals.
- Generate multimodal signal surfaces.
Delayed detection
Delayed detection

- Temporal bias arises from detection process.
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- What if a signal appears later in the time sequence?
Delayed detection

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Delayed detection

- Temporal bias arises from detection process.
- What if a signal appears later in the time sequence?
- Is this a delayed detection or just another false positive?
- How would one set a threshold to decide that? – based on how often this signal appears in the time sequence?
- Signals sometimes vanish from the trace – how would that change your threshold?
Difficulties and possible starting points

- Need to differentiate between the true signal and the false positives.
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- The signal surface resembles a random field – a starting point would be to look at Random Field Theory.
- Apply thresholds to these surfaces and use hypothesis testing to locate activation regions.
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Action Plan

- Generate noisy data – experiment with different parameter values to get a feel for how this toy model behaves. In addition, consider applying different noise distributions to your data. [1 day]
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- Read up on mathematical and statistical techniques which could be used to remove noise / track signals. [3 weeks]
Action Plan

- Generate noisy data – experiment with different parameter values to get a feel for how this toy model behaves. In addition, consider applying different noise distributions to your data. [1 day]
- Read up on mathematical and statistical techniques which could be used to remove noise / track signals. [3 weeks]
- Implement your chosen techniques – Test on dummy data before applying to the noisy data generated in the first step. [4 weeks]
Action Plan

- Compare your estimate the path of the signal with the actual data before noise was added to it. Furthermore, apply evaluation metrics to establish how sensitive your chosen techniques are to different noise distributions. [3 weeks]
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- Compare your estimate the path of the signal with the actual data before noise was added to it. Furthermore, apply evaluation metrics to establish how sensitive your chosen techniques are to different noise distributions. [3 weeks]

- If you have time, consider applying the work you have done to the extension problems.
References

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Thank you for listening!