Motivation	Model	Techniques	Action Plan
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Brain Imaging RSG - Problem Formulation

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7th February 2011





Motivation	Model	Techniques	Extension Topics	Action Plan
0000	0000000	000000000000000000000000000000000000	00000	00
Contents				



2 Model

3 Techniques

- Approximate Bayes Factors
- Kalman Filters
- Evaluation Metrics

4 Extension Topics





Motivation	Model	Techniques	Extension Topics	Action Plan
0000	0000000	000000000000000000000000000000000000	00000	
Contents				

Motivation

2 Model

3 Techniques

- Approximate Bayes Factors
- Kalman Filters
- Evaluation Metrics

4 Extension Topics

5 Action Plan



Motivation	Model	Techniques	Action Plan
●000	0000000	000000000000000000000000000000000000	00



Motivation	Model	Techniques	Action Plan
●000	0000000	000000000000000000000000000000000000	00

fMRI tries to assess "Brain Activity" indirectly, through measurements of the blood flow and oxygenation in the brain.

• MRI machine sends out a radio frequency pulse which generates a magnetic field.



Motivation	Model	Techniques	Extension Topics	Action Plan
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- MRI machine sends out a radio frequency pulse which generates a magnetic field.
- The energy of the field is enough to cause the spin of protons in blood Haemoglobin molecules to change.



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- MRI machine sends out a radio frequency pulse which generates a magnetic field.
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- Protons in oxygenated haemoglobin behave differently to deoxygenated haemoglobin.



Motivation	Model	Techniques	Extension Topics	Action Plan
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- MRI machine sends out a radio frequency pulse which generates a magnetic field.
- The energy of the field is enough to cause the spin of protons in blood Haemoglobin molecules to change.
- Protons in oxygenated haemoglobin behave differently to deoxygenated haemoglobin.
- When the pulse is turned off, the energy absorbed by the resonating protons is released.



Motivation	Model	Techniques	Extension Topics	Action Plan
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EEG directly monitors electrical activity in the brain.



Motivation	Model	Techniques	Action Plan
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• Numerous electrodes are placed on the scalp.



Motivation	Model	Techniques	Extension Topics	Action Plan
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- Numerous electrodes are placed on the scalp.
- Each electrode detects a change in electrical potential at that point on the scalp.



Motivation	Model	Techniques	Extension Topics	Action Plan
0000				

EEG directly monitors electrical activity in the brain.

- Numerous electrodes are placed on the scalp.
- Each electrode detects a change in electrical potential at that point on the scalp.
- Voltages between electrodes can then be used to chart the electrical activity inside the brain.



Motivation 00●0	Model 0000000	Extension Topics 00000	Action Plan 00
Limitations			



Motivation 00●0	Model 0000000	Extension Topics	Action Plan 00
Limitations			

• Spatial Resolution - EEG can't pinpoint the location of neural activity.



Motivation 00●0	Model 0000000	Techniques 000000000000000000000000000000000000	Extension Topics 00000	Action Plan 00
Limitations				

- 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"!

Motivation 00●0	Model 0000000	Techniques 000000000000000000000000000000000000	Extension Topics 00000	Action Plan
Limitations				

- 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.



Motivation	Model	Techniques	Extension Topics	Action Plan
000●	0000000	000000000000000000000000000000000000	00000	00
The Task				



Motivation 000●	Model 0000000	Extension Topics 00000	Action Plan 00
The Task			

• Create a time-indexed series of noisy images which mimic the motion of a signal



Motivation	Model	Extension Topics	Action Plan
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The Task			

- Create a time-indexed series of noisy images which mimic the motion of a signal
- Apply a technique to help remove the noise from these images



Motivation 000●	Model 0000000	Techniques 000000000000000000000000000000000000	Extension Topics 00000	Action Plan 00
The Task				

- Create a time-indexed series of noisy images which mimic the motion of a signal
- Apply a technique to help remove the noise from these images
- Apply a technique to track the motion of the signal through these images



Motivation 0000	Model 0000000	Techniques 000000000000000000000000000000000000	Extension Topics 00000	Action Plan 00
Contents				



2 Model

3 Techniques

- Approximate Bayes Factors
- Kalman Filters
- Evaluation Metrics

4 Extension Topics





Motivation 0000	Model ●oooooo	Techniques 000000000000000000000000000000000000	Extension Topics	Action Plan 00
Model				

Despite the technical difficulties with fMRI and EEG discussed previously, we seek to infer properties of the noisy signal.



Motivation	Model	Techniques	Extension Topics	Action Plan
0000	●oooooo	000000000000000000000000000000000000	00000	00
Model				

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.



Motivation	Model	Techniques	Extension Topics	Action Plan
0000	●oooooo	000000000000000000000000000000000000	00000	00
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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:



Motivation	Model	Techniques	Extension Topics	Action Plan
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• Filter the noise out from the image taken at first time-point.

Motivation 0000	Model ●oooooo	Extension Topics 00000	Action Plan 00
Model			

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.



Motivation	Model	Techniques	Action Plan
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Original data is composed of noisy surfaces defined on the square domain $[-1,1]\times [-1,1].$



Motivation	Model	Techniques	Action Plan
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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

$$\phi(x, y) = \exp\left(-\beta((x - c_1)^2 + (y - c_2)^2)\right)$$

where β controls how spiked the signal is and $c = (c_1, c_2)$ the location of the signal.



Motivation	Model	Techniques	Extension Topics	Action Plan
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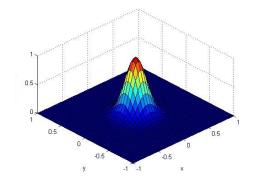


Figure: Plot of ϕ for $\beta = 20$ and c = (0, 0)



Motivation	Model	Techniques	Extension Topics	Action Plan
	0000000			

Add noise to the function by drawing independent samples from normal distribution with mean 0 and small variance and adding it to the function.



Motivation	Model	Techniques	Extension Topics	Action Plan
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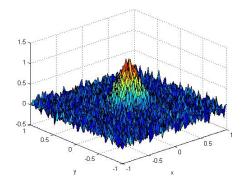


Figure: Plot of noisy signal for $\beta = 20$ and c = (0, 0)



Motivation	Model	Techniques	Action Plan
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Motivation	Model	Techniques	Action Plan
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We further improve the model by making β and c *noisy*. β is a binary process taking two distinct values:



Motivation	Model	Techniques	Action Plan
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- β is a binary process taking two distinct values:
 - One, with low probability, which drowns the signal in the noise for a short period of time.



Motivation	Model	Techniques	Extension Topics	Action Plan
0000	oooo●oo	000000000000000000000000000000000000	00000	00

- β is a binary process taking two distinct values:
 - One, with low probability, which drowns the signal in the noise for a short period of time.
 - The other, with high probability, in which the signal can be distinguished from the noise.



Motivation	Model	Techniques	Extension Topics	Action Plan
0000	oooo●oo	000000000000000000000000000000000000		00

- β is a binary process taking two distinct values:
 - One, with low probability, which drowns the signal in the noise for a short period of time.
 - The other, with high probability, in which the signal can be distinguished from the noise.

c follows a path of the form

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

where c_1 moves from -1 to 1 and $u \sim \text{Unif}([-0.1, 0.1])$.



Motivation	Model	Techniques	Extension Topics	Action Plan
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(signal.avi)



Motivation	Model	Techniques	Action Plan
0000	oooooo●	000000000000000000000000000000000000	00



Motivation 0000	Techniques 000000000000000000000000000000000000	Action Plan 00

 For β, want to incorporate key limitation of medical scanners, namely the disappearance of signal for short period of time.



Motivation	Model	Techniques	Action Plan
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- For β, 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.



Motivation	Model	Techniques	Action Plan
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- For β, 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.



Motivation	Model	Techniques	Action Plan
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- For β, 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.



Motivation 0000	Model 0000000	Techniques	Extension Topics	Action Plan 00
Contents				



4 Extension Topics

5 Action Plan



Motivation 0000	Model 0000000	Techniques •000000000000000000000000000000000000	Extension Topics 00000	Action Plan 00
Approximate Bayes Factors				
Contents				



4 Extension Topics





Motivation 0000	Model 0000000	Techniques o●ooooooooooooooooo	Extension Topics 00000	Action Plan 00
Approximate Bayes	Factors			
What are	e Baves Facto	ors?		



Motivation 0000	Model 0000000	Techniques 0●00000000000000000000000000000000000	Extension Topics 00000	Action Plan 00
Approximate Bayes Factors				
What are Ba	yes Factors	?		

Suppose we have a null hypothesis

 $\mathit{H}_{0}: \theta \in \Theta_{0} \subset \Theta$

which we want to test against an alternative hypothesis

 $H_1: \theta \in \Theta ackslash \Theta_0$

where Θ is the parameter space.



Motivation 0000	Model 0000000	Techniques ○●○○○○○○○○○○○○○○○	Extension Topics	Action Plan 00
Approximate Bayes Factors				
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which we want to test against an alternative hypothesis

$$H_1: \theta \in \Theta ackslash \Theta_0$$

where Θ is the parameter space.

The usual method of hypothesis testing involves a Likelihood Ratio Test Statistic, given by

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



Motivation	Model	Techniques	Extension Topics	Action Plan
		000000000000000000000000000000000000000		
Approximate Bayes Factors				

Under the Bayesian paradigm, we would like to modify this method to take into account our prior beliefs about the behaviour of the model. This gives rise to Bayes factors [Jeffreys (1935)].



Motivation	Model	Techniques	Extension Topics	Action Plan
		000000000000000000000000000000000000000		
Approximate Bayes Factors				

Under the Bayesian paradigm, we would like to modify this method to take into account our prior beliefs about the behaviour of the model. This gives rise to Bayes factors [Jeffreys (1935)]. Bayes' Theorem says

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

with k = 0, 1.



Motivation	Model	Techniques	Extension Topics	Action Plan
		000000000000000000000000000000000000000		
Approximate Bayes Factors				

We then get



Motivation	Model	Techniques	Extension Topics	Action Plan
		000000000000000000000000000000000000000		
Approximate Bayes Factors				

We then get

$$\frac{\mathbb{P}(H_0|\mathbf{X})}{\mathbb{P}(H_1|\mathbf{X})} = \frac{\mathbb{P}(\mathbf{X}|H_0)}{\mathbb{P}(\mathbf{X}|H_1)} \frac{\mathbb{P}(H_0)}{\mathbb{P}(H_1)}$$

where

$$\mathbb{P}(\mathbf{X}|H_k) = \int \mathbb{P}(\mathbf{X}| heta_k, H_k) \pi(heta_k|H_k) d heta_k$$

with θ_k the parameter under H_k with prior $\pi(\theta_k|H_k)$. The highlighted term is the Bayes factor.



Motivation 0000	Model 0000000	Techniques 000000000000000000000000000000000000	Extension Topics 00000	Action Plan 00
Approximate Bayes Fa	actors			
Why App	<i>roximate</i> Ba	yes Factors?		



Motivation 0000	Model 0000000	Techniques 000000000000000000000000000000000000	Extension Topics	Action Plan 00
Approximate Bayes Factors				
Why Approx	<i>imate</i> Baye	s Factors?		

$$\mathbb{P}(\mathbf{X}|H_k) = \int \mathbb{P}(\mathbf{X}| heta_k, H_k) \pi(heta_k|H_k) d heta_k$$

Unless we're lucky, we need to find ways of approximating this integral.



Motivation 0000	Model 0000000	Techniques 000000000000000000000000000000000000	Extension Topics	Action Plan 00
Approximate Bayes Factors				
Why Approx	<i>imate</i> Baye	s Factors?		

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Unless we're lucky, we need to find ways of approximating this integral. There are various methods of doing this [Kass & Raftery (1995)]:



Motivation 0000	Model 0000000	Techniques 000000000000000000000000000000000000	Extension Topics 00000	Action Plan
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Unless we're lucky, we need to find ways of approximating this integral. There are various methods of doing this [Kass & Raftery (1995)]:

- Asymptotic Approximation
- Monte Carlo Methods
- MCMC & Metropolis-Hastings



Motivation 0000	Model 0000000	Techniques 000000000000000000000000000000000000	Extension Topics 00000	Action Plan 00
Approximate Bayes Factors				
Application -	- Image Seg	gmentation		



Motivation 0000	Model 0000000	Techniques 00000●0000000000000000000000000000000	Extension Topics 00000	Action Plan 00
Approximate Bayes Factors				
Application -	- Image Se	gmentation		

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.



Motivation 0000	Model 0000000	Techniques 00000€0000000000000000000000000000000	Extension Topics 00000	Action Plan 00
Approximate Bayes Facto	ors			
Application	- Image S	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.

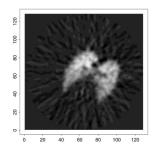


Figure: PET image of a dog's lung [Stanford & Raftery (2002)]



Motivation	Model	Techniques	Extension Topics	Action Plan
		000000000000000000000000000000000000000		
Approximate Bayes Factors				



Motivation	Model	Techniques	Extension Topics	Action Plan
		000000000000000000000000000000000000000		
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.



Motivation	Model	Techniques	Extension Topics	Action Plan
		000000000000000000000000000000000000000		
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).



Motivation	Model	Techniques	Extension Topics	Action Plan
Approximate Bayes Factors				00

- 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).



Motivation	Model	Techniques	Extension Topics	Action Plan
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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.



Motivation	Model	Techniques	Extension Topics	Action Plan
		000000000000000000000000000000000000000		
Approximate Bayes Factors				

The result...



Motivation	Model	Techniques	Extension Topics	Action Plan
		000000000000000000000000000000000000000		
Approximate Bayes Factors				

The result...

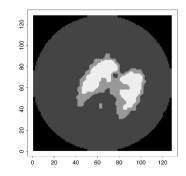


Figure: PET image of a dog's lung after final segmentation [Stanford & Raftery (2002)]



Motivation 0000	Model 0000000	Techniques ○○○○○○●○○○○○○○	Extension Topics 00000	Action Plan 00
Kalman Filters				
Contents				







Motivation 0000	Model 0000000	Techniques	Extension Topics 00000	Action Plan 00
Kalman Filters				
Short summa	ary			



Motivation 0000	Model 0000000	Techniques	Extension Topics 00000	Action Plan 00
Kalman Filters				
Short summ	ary			

• A common tool for tracking problems/noise reduction is the Kalman filter.



Motivation 0000	Model 0000000	Techniques ○○○○○○○●○○○○○○	Extension Topics 00000	Action Plan 00
Kalman Filters				
Short sumr	mary			

- 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.



Motivation 0000	Model 0000000	Techniques	Extension Topics	Action Plan 00
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Motivation 0000	Model 0000000	Techniques ○○○○○○○●○○○○○○	Extension Topics 00000	Action Plan 00
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$$X_t = H\theta_t + n_t.$$



Motivation 0000	Model 0000000	Techniques ○○○○○○○●○○○○○○	Extension Topics 00000	Action Plan 00
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- Measurements are typically noisy, so we include a noise term n_t .
- The Observation model is

$$X_t = H\theta_t + n_t.$$

• The state vector is updated by a transition matrix *G* with a noise process *w*_t,

$$\theta_t = G\theta_{t-1} + w_t.$$



Motivation 0000	Model 0000000	Techniques ○○○○○○○○○○○○○○○○	Extension Topics 00000	Action Plan
Kalman Filters				
Short summ	ary			

• We estimate θ_t with $\hat{\theta}_t$. Assume w_t and n_t are uncorrelated, with corresponding variance-covariance matrices Q and R.



Motivation 0000	Model 0000000	Techniques	Extension Topics 00000	Action Plan 00	
Kalman Filters					
Short summary					

- We estimate θ_t with $\hat{\theta}_t$. Assume w_t and n_t are uncorrelated, with corresponding variance-covariance matrices Q and R.
- The simplest update of our estimate $\hat{\theta}_t$ is

$$\hat{\theta}_{t+1} = G\hat{\theta}_t.$$



Motivation 0000	Model 0000000	Techniques ○○○○○○○○○●○○○○○○	Extension Topics 00000	Action Plan 00
Kalman Filters				
Short sum	imary			

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- The simplest update of our estimate $\hat{\theta}_t$ is

$$\hat{\theta}_{t+1} = G\hat{\theta}_t.$$

• Denote the error $e_t = \theta_t - \hat{\theta}_t$ and its variance-covariance matrix P_t .



Motivation 0000	Model 0000000	Techniques ○○○○○○○○○●○○○○○○	Extension Topics 00000	Action Plan 00
Kalman Filters				
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$$\hat{\theta}_{t+1} = G\hat{\theta}_t.$$

- 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

$$\hat{\theta}_t = \hat{\theta}_{t|t-1} + K_t(X_t - H\hat{\theta}_{t|t-1}),$$

where the Kalman gain K_t is derived while minimising the mean square error of the estimate.



Motivation 0000	Model 0000000	Techniques ○○○○○○○○○●○○○○○○	Extension Topics 00000	Action Plan 00
Kalman Filters				
Short sum	imary			

- We estimate θ_t with θ̂_t. Assume w_t and n_t are uncorrelated, with corresponding variance-covariance matrices Q and R.
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$$\hat{\theta}_{t+1} = G\hat{\theta}_t.$$

- 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

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where the Kalman gain K_t is derived while minimising the mean square error of the estimate.

• There is a similar update equation for P_t .



Motivation 0000	Model 0000000	Techniques ○○○○○○○○○○○○○○○○	Extension Topics 00000	Action Plan
Kalman Filters				
Applications				



Motivation 0000	Model 0000000	Techniques	Extension Topics	Action Plan
Kalman Filters				
Applications				

• EEG artifact removal



Motivation 0000	Model 0000000	Techniques ○○○○○○○○○○●○○○○○	Extension Topics 00000	Action Plan
Kalman Filters				
Applications				

- EEG artifact removal
- EEG spike enhancement



Motivation 0000	Model 0000000	Techniques ○○○○○○○○○○○○○○○○	Extension Topics 00000	Action Plan 00
Kalman Filters				
Applications				

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



Motivation 0000	Model	Techniques	Extension Topics	Action Plan 00
Kalman Filters				

EEG artifact removal

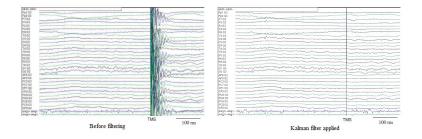


Figure: EEG artifact removal [Morbidi et al. (2007)]



Motivation 0000	Model 0000000	Techniques ○○○○○○○○○○○○○	Extension Topics 00000	Action Plan 00
Kalman Filters				
EEG spike	enhanceme	ent		

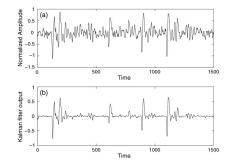
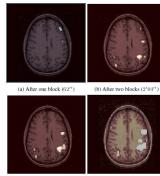


Figure: EEG spike enhancement [Oikonomou et al. (2006)]



Motivation 0000	Model 0000000	Techniques ○○○○○○○○○○○○○○○	Extension Topics 00000	Action Plan 00
Kalman Filters				
D				

Detecting activation regions



(c) Final result (3'08")

(d) SPM'99 result

Figure: Incremental activation detection [Roche et al. (2004)]



Motivation 0000	Model 0000000	Techniques ○○○○○○○○○○○○○○○○○	Extension Topics	Action Plan 00
Evaluation Metrics				
Contents				



2 Model

3 Techniques

- Approximate Bayes Factors
- Kalman Filters
- Evaluation Metrics

4 Extension Topics

5 Action Plan



Motivation 0000	Model 0000000	Techniques ○○○○○○○○○○○○○○○	Extension Topics 00000	Action Plan 00
Evaluation Metrics				
Evaluation	Metrics			



Motivation 0000	Model 0000000	Techniques ○○○○○○○○○○○○○○○	Extension Topics	Action Plan 00
Evaluation Metrics				
Evaluation N	Netrics			

• One key assumption needed to apply Kalman filters is that the noise is Gaussian. This may not necessarily be the case.



Motivation 0000	Model 0000000	Techniques ○○○○○○○○○○○○○○○	Extension Topics	Action Plan 00
Evaluation Metrics				
Evaluation N	Aetrics			

- 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?



Motivation 0000	Model 0000000	Techniques ○○○○○○○○○○○○○○○	Extension Topics 00000	Action Plan 00
Evaluation Metrics				
Evaluation	Metrics			

- 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.



Motivation 0000	Model 0000000	Techniques ००००००००००००००००	Extension Topics 00000	Action Plan
Evaluation Metrics				
Evaluation N	Metrics			

- 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.



Motivation	Model	Techniques	Extension Topics	Action Plan
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Evaluation Metrics				



Motivation	Model	Techniques	Extension Topics	Action Plan
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Evaluation Metrics				

• As an example, we use the discussed mathematical and statistical tools to generate a number of signal trajectory paths at every timepoint.



Motivation	Model	Techniques	Extension Topics	Action Plan
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Evaluation Metrics				

- 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.



Motivation	Model	Techniques	Extension Topics	Action Plan
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Evaluation Metrics				

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- Then take the average of the computed paths and compare it with the true path.



Figure: Example of a true path trajectory and the denoised $+ % \left({{{\rm{A}}} \right)_{\rm{A}} + {{\rm{A}}} \right)_{\rm{A}}$ averaged one



Motivation	Model	Techniques	Extension Topics	Action Plan
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Evaluation Metrics				

- 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.



Figure: Example of a true path trajectory and the denoised $+ % \left({{{\rm{A}}} \right)_{\rm{A}} + {{\rm{A}}} \right)_{\rm{A}}$ averaged one

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



Motivation 0000	Model 0000000	Techniques 000000000000000000000000000000000000	Extension Topics	Action Plan 00
Contents				



2 Model

3 Techniques

- Approximate Bayes Factors
- Kalman Filters
- Evaluation Metrics

4 Extension Topics





Motivation	Model	Techniques	Extension Topics	Action Plan
0000	0000000	000000000000000000000000000000000000	•0000	00
Multiple sig	nals			



Motivation	Model	Techniques	Extension Topics	Action Plan
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Multiple s	ignals			

• False positives arise from spatial delay or noise generated from the scanning process.



Motivation	Model	Techniques	Extension Topics	Action Plan
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Multiple sig	gnals			

- False positives arise from spatial delay or noise generated from the scanning process.
- There may also be spatial correlation among signals.



Motivation 0000	Model 0000000	Techniques 000000000000000000000000000000000000	Extension Topics •0000	Action Plan 00
Multiple si	gnals			

- 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.



Motivation	Model	Techniques	Action Plan
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(ClusterSignal.avi)



Motivation 0000	Model 0000000	Techniques 000000000000000000000000000000000000	Extension Topics 00●00	Action Plan 00
Delayed de	etection			



Motivation 0000	Model 0000000	Techniques 000000000000000000000000000000000000	Extension Topics	Action Plan 00
Delayed o	letection			
Delayed				

• Temporal bias arises from detection process.



Motivation	Model	Techniques	Extension Topics	Action Plan
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Delayed d	etection			

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



Motivation 0000	Model 0000000	Techniques 000000000000000000000000000000000000	Extension Topics 00000	Action Plan 00
Delayed	detection			
Delayed o	letection			

- 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?



Motivation	Model	Techniques	Extension Topics	Action Plan
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Delayed det	ection			

- 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?



Motivation 0000	Model ooooooo	Techniques 000000000000000000000000000000000000	Extension Topics 00●00	Action Plan 00
Delayed c	letection			

- 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?



	Model	Techniques	Extension Topics	Action Plan
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Delayed dete	ction			

- 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?



Motivation	Model	Techniques	Action Plan
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(DelaySignal.avi)



Motivation	Model	Techniques	Extension Topics	Action Plan
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• Need to differentiate between the true signal and the false positives.



Motivation	Model	Techniques	Extension Topics	Action Plan
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- Need to differentiate between the true signal and the false positives.
- Taking into account the correlation between signals.



Motivation	Model	Techniques	Extension Topics	Action Plan
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- Need to differentiate between the true signal and the false positives.
- Taking into account the correlation between signals.
- The signal surface resembles a random field a starting point would be to look at Random Field Theory.



Motivation	Model	Techniques	Action Plan
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- Need to differentiate between the true signal and the false positives.
- Taking into account the correlation between signals.
- 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.



Motivation 0000	Model 0000000	Techniques 000000000000000000000000000000000000	Extension Topics 00000	Action Plan
C				
Contents				



2 Model

3 Techniques

- Approximate Bayes Factors
- Kalman Filters
- Evaluation Metrics

4 Extension Topics





Motivation	Model	Techniques	Extension Topics	Action Plan
0000	0000000	000000000000000000000000000000000000	00000	●0
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]



Motivation	Model	Techniques	Extension Topics	Action Plan
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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]
- Read up on mathematical and statistical techniques which could be used to remove noise / track signals. [3 weeks]



Motivation 0000	Model 0000000	Techniques 000000000000000000000000000000000000	Extension Topics 00000	Action Plan ●0
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]



Motivation 0000	Model 0000000	Techniques 000000000000000000000000000000000000	Extension Topics	Action Plan 0●
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]



Motivation 0000	Model 0000000	Techniques 000000000000000000000000000000000000	Extension Topics	Action Plan ⊙●
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]
- If you have time, consider applying the work you have done to the extension problems.

Motivation 0000	Model 0000000	Techniques 000000000000000000000000000000000000	Extension Topics 00000	Action Plan
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Motivation 0000	Model 0000000	Techniques 000000000000000000000000000000000000	Extension Topics 00000	Action Plan 00
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Motivation	Model	Extension Topics	Action Plan
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Motivation 0000	Model 0000000	Techniques 000000000000000000000000000000000000	Extension Topics 00000	Action Plan 00
References				

 [Needham & Boyle (2003)] – Performance Evaluation Metrics and Statistics for Positional Tracker Evaluation – Computer Vision Systems, 2003

Thank you for listening!

