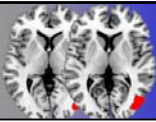


EMORY ROLLINS SCHOOL OF PUBLIC HEALTH
 CBIS Center for Biomedical Imaging Statistics




Bayesian Analysis

DuBois Bowman, Ph.D.
 Gordana Derado, M. S. Shuo Chen, M. S.

HBM 2008 Advanced fMRI Course Melbourne, Australia

EMORY ROLLINS SCHOOL OF PUBLIC HEALTH
 CBIS Center for Biomedical Imaging Statistics



Outline

I. Introduction to Bayesian Methods

- Bayesian concepts
 - Prior distribution
 - Data (Likelihood)
 - Posterior distribution
- Example: Normal-normal model
- Bayesian inference
 - Priors
 - Posterior summaries
- Estimation/Posterior sampling
- Bayesian learning

II. Implementation in fMRI Studies

- Two-stage modeling
- Priors
- Variational Bayes
- Spatial Bayesian Hierarchical Model

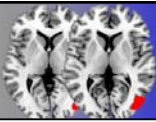
III. Data Example and Analyses

- Inhibitory control in cocaine addicts
- Two-stage modeling approaches
 - SPM: Classical/Classical
 - SPM: Classical/Bayesian
 - SPM: Bayesian/Bayesian
 - Classical/Spatial Bayesian hierarchical model

IV. Summary

HBM 2008 Melbourne, Australia 2

EMORY ROLLINS SCHOOL OF PUBLIC HEALTH
 CBIS Center for Biomedical Imaging Statistics




Bayesian Analysis:

I. Introduction to Bayesian Methods

HBM 2008 Advanced fMRI Course Melbourne, Australia

EMORY ROLLINS SCHOOL OF PUBLIC HEALTH
 CBIS Center for Biomedical Imaging Statistics



Perspectives

- Parameter of interest: θ
 - The population difference in BOLD activity between two tasks.
- Collect data from a sample
 - Regarded as realizations of *random* variables.

Bayesian


- Determine the distribution of the unknown *random* parameter θ , given the data.

Classical (Frequentist)

- Use the data to estimate the unknown *fixed* parameter θ .

HBM 2008 Melbourne, Australia 4

EMORY ROLLINS SCHOOL OF PUBLIC HEALTH
 CBIS Center for Biomedical Imaging Statistics




Notation

- Let θ represent the parameter of interest
 - Group (or population) mean BOLD response for a given experimental task or contrast
 - Assume Bayesian interpretation of θ here, unless otherwise noted
- Let \mathbf{Y} represent the data
 - Second level modeling: $\mathbf{Y} = [Y_1, \dots, Y_n]$.
 - E.g. contrasts of interest
 - Also applicable to first level modeling: $\mathbf{Y}_i = [Y_{i1}, \dots, Y_{iT}]$.

HBM 2008 Melbourne, Australia 5

EMORY ROLLINS SCHOOL OF PUBLIC HEALTH
 CBIS Center for Biomedical Imaging Statistics



Bayesian Inference

- Bayesian methods concern one's belief about θ .

[Current Belief (**Posterior**)] \propto

(Prior Belief) x **(Data)**

HBM 2008 Melbourne, Australia 6

Bayes Theorem

$$\Pr(\theta | y) = \frac{\Pr(\theta)\Pr(y | \theta)}{\Pr(y)}$$

Posterior : $\Pr(\theta | y)$ **Prior :** $\Pr(\theta)$
Marginal : $\Pr(y)$ **Data :** $\Pr(y | \theta)$

HBM 2008 Melbourne, Australia 7

Bayes Theorem

Case I: Assume θ has m possible states:

$$\Pr(y) = \sum_{i=1}^m \Pr(\theta_i)\Pr(y | \theta_i)$$

Case II: Assume θ is continuous:

$$\Pr(y) = \int_{\theta} \Pr(\theta)\Pr(y | \theta)d\theta$$

HBM 2008 Melbourne, Australia 8

Bayes Theorem

In either case,

$$\Pr(\theta | y) = \frac{\Pr(\theta)\Pr(y | \theta)}{\Pr(y)}$$

↓

Denominator is constant with respect to θ .

HBM 2008 Melbourne, Australia 9

Bayes Theorem

$$\Pr(\theta | y) \propto \Pr(\theta)\Pr(y | \theta)$$

Posterior : $\Pr(\theta | y) \rightarrow \pi(\theta | y)$
Prior : $\Pr(\theta) \rightarrow \pi(\theta)$
Data : $\Pr(y | \theta) \rightarrow p(y | \theta)$

HBM 2008 Melbourne, Australia 10

Bayesian Inference

$$\text{Posterior} \propto \text{Prior} \times \text{Data}$$

HBM 2008 Melbourne, Australia 11

Example: Normal-Normal Model

- Let: $\mathbf{Y} = [Y_1, \dots, Y_n]'$
- Data: $Y_i | \theta \sim \text{Normal}(\theta, \sigma^2), \quad i = 1, \dots, n$
- Prior: $\theta \sim \text{Normal}(\theta_0, \phi_0)$
- Posterior: $\theta | \mathbf{Y} \sim \text{Normal}(\theta_1, \phi_1)$

$$\phi_1^{-1} = \phi_0^{-1} + (\sigma^2/n)^{-1} \quad \text{and} \quad \theta_1 = \theta_0 \left(\frac{\phi_1}{\phi_0} \right) + \bar{Y} \left(\frac{\phi_1}{\sigma^2/n} \right)$$

HBM 2008 Melbourne, Australia 12

Example: Normal-Normal Model

- **Posterior:** $\theta | \mathbf{Y} \sim \text{Normal}(\theta_1, \phi_1)$

$$\phi_1 = \left[\phi_0^{-1} + (\sigma^2/n)^{-1} \right]^{-1} \quad \text{and} \quad \theta_1 = \theta_0 \left(\frac{\phi_1}{\phi_0} \right) + \bar{Y} \left(\frac{\phi_1}{\sigma^2/n} \right)$$

- Consider as a function of **prior uncertainty:**

$$\theta | \mathbf{Y} \rightarrow \text{Normal} \left(\bar{Y}, \frac{\sigma^2}{n} \right) \quad \text{as} \quad \phi_0 \rightarrow \infty$$

- Data will dominate when ϕ_0 is large compared to σ^2/n

HBM 2008 Melbourne, Australia 13

Prior Probabilities

- **Noninformative Prior:**
 - Conveys little knowledge about parameters
 - Also called diffuse or vague prior
- **Informative Prior :**
 - Precise knowledge about parameters
- **Conjugate Prior:**
 - Posterior distribution has the same parametric form as the prior
 - Convenient mathematical form and often justifiable scientifically

HBM 2008 Melbourne, Australia 14

Influence of Prior Beliefs

- Normal-Normal Model: $\theta | \mathbf{Y} \sim \text{Normal}(\theta_1, \phi_1)$

$$\theta \sim \text{Normal}(\theta_0, \phi_0), \quad \phi_0 = V(Y_v)$$

- Empirically-based prior

HBM 2008 Melbourne, Australia 15

Influence of Prior Beliefs

- Normal-Normal Model: $\theta | \mathbf{Y} \sim \text{Normal}(\theta_1, \phi_1)$

$$\theta \sim \text{Normal}(\theta_0, \phi_0), \quad \phi_0 = 10 \times V(Y_v)$$

- More weakly informative prior

HBM 2008 Melbourne, Australia 16

Influence of Prior Beliefs

- Normal-Normal Model: $\theta | \mathbf{Y} \sim \text{Normal}(\theta_1, \phi_1)$

$$\theta \sim \text{Normal}(\theta_0, \phi_0), \quad \phi_0 = 100 \times V(Y_v)$$

- Diffuse or Vague prior

HBM 2008 Melbourne, Australia 17

Caution about Prior Beliefs!!

- Normal-Normal Model: $\theta | \mathbf{Y} \sim \text{Normal}(\theta_1, \phi_1)$

$$\theta \sim \text{Normal}(\theta_0, \phi_0)$$

- U.S. Political Debate
- Biased Jurors

HBM 2008 Melbourne, Australia 18

Bayesian Inference

- After analysis, all information about a parameter θ is contained in the **posterior**
- Useful summaries
 - Posterior mean/median/mode
 - Posterior exceedance probabilities
 - Highest (posterior) density regions (HDR)
 - Credible intervals
 - Bayesian confidence intervals
 - Bayes factors (*not discussed here)

HBM 2008 Melbourne, Australia 19

Bayesian Inference

Posterior distribution

HBM 2008 Melbourne, Australia 20

Bayesian Inference

Posterior mean

HBM 2008 Melbourne, Australia 21

Bayesian Inference

Posterior Probability Maps (PPM)

- Posterior (exceedance) probability:

$$\Pr[\theta > \gamma | Y]$$
 E.g. $\gamma = 0$

HBM 2008 Melbourne, Australia 22

Posterior Probability Maps

Threshold PPM's: $\Pr[\theta > \gamma | Y] > \alpha$

Two thresholds:

- probability α : (e.g. 90%)
- activation threshold γ : percentage of global mean signal (physiologically relevant size of effect)

HBM 2008 Melbourne, Australia 23

Posterior Sampling

- Joint posterior follows a known distribution, leading to direct sampling
- Markov Chain Monte Carlo (MCMC)
 - Gibbs sampler (known parametric forms for conditional posterior distributions, which collectively yield samples from the joint posterior distribution)
 - Metropolis-Hastings algorithm
- Variational Bayes Approximation
- Laplace Approximations

HBM 2008 Melbourne, Australia 24

Bayesian Learning

- Natural framework for *learning* and *updating*
- Study 1: $\pi_1(\theta | y_1) \propto \pi(\theta) \times p(y_1 | \theta)$
- Study 2: $\pi_2(\theta | y_2) \propto \pi_1(\theta | y_1) \times p(y_2 | \theta)$

HBM 2008 Melbourne, Australia 25

Bayesian Analysis:

II. Implementation in fMRI Studies

HBM 2008 Advanced fMRI Course Melbourne, Australia

Two-stage modeling

- Use conventional two-stage modeling, emulating a random effects analysis
 - **Stage 1:** Subject-specific analyses producing estimates of task-related activity (or contrasts)
 - **Stage 2:** Group-level estimates of task-related activity (or contrasts), using stage 1 estimates (contrasts) of regression coefficients as data
- Choice of Bayesian versus classical (frequentist) modeling at each of the two stages

HBM 2008 Melbourne, Australia 27

Estimation in SPM

Stage 2

	Classical	Bayesian
Classical	1	2, 4
Bayesian		3

Stage 1

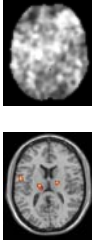
4. Classical/Spatial Bayesian hierarchical model (BHM) [†Not in SPM]

HBM 2008 Melbourne, Australia 28

Posterior Probability Maps

For fMRI applications,

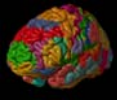
- It is useful to compute PPM's
 - Each voxel contains an exceedance probability, e.g. that the difference between two tasks is greater than zero.
 - Can display thresholded PPM's, e.g. with $p > 0.80$.



HBM 2008 Melbourne, Australia 29

Spatial Bayesian Hierarchical Model

- Use anatomical (or functional) parcellations (e.g. Brodmann)
 - # regions < # subjects per group
- Models **spatial correlations** in activity **within** and **between** regions
- Inferences:
 - Voxel-level
 - Regional
 - Task-related functional connectivity



HBM 2008 Melbourne, Australia 30

EMORY ROLLINS SCHOOL OF PUBLIC HEALTH CBIS Center for Biomedical Imaging Statistics

Bayesian Analysis:

III. Data Example and Analyses

HBM 2008 Advanced fMRI Course Melbourne, Australia

EMORY ROLLINS SCHOOL OF PUBLIC HEALTH CBIS Center for Biomedical Imaging Statistics

Data Example

- Inhibitory Control in Cocaine Addicts**
 - N=27 subjects: 12 patients (cocaine addicts) and 15 healthy controls (matched on several variables)
 - Two sessions: (170 scans per subject in each session)
 - Cocaine addicts: Pre and post-treatment (behavioral therapy)
 - Controls: Baseline and follow-up
 - fMRI Tasks: Stop signal task (Inhibitory control)**
 - Subjects were presented with visual cues and directed to respond to a "GO stimulus" (an uppercase alphabetical letter) by pressing a button as quickly as possible
 - A "STOP signal" – a brief auditory tone lasting 0.5 seconds – was presented randomly in 16% of the trials, and subjects were instructed to refrain from pushing the button if the GO stimulus was followed by a STOP signal
 - A successful performance required prepotent behaviors to be inhibited.
 - Objective:** (Post-treatment – Pre-treatment activity in addicts) > (Follow-up – baseline activity in controls)

HBM 2008 Melbourne, Australia 32

EMORY ROLLINS SCHOOL OF PUBLIC HEALTH CBIS Center for Biomedical Imaging Statistics

SPM: Stage 1 Model Specification

Same for **classical** and **Bayesian**

HBM 2008 Melbourne, Australia 33

EMORY ROLLINS SCHOOL OF PUBLIC HEALTH CBIS Center for Biomedical Imaging Statistics

SPM: Stage 1 Design Matrix

Same for **classical** and **Bayesian**

HBM 2008 Melbourne, Australia 34

EMORY ROLLINS SCHOOL OF PUBLIC HEALTH CBIS Center for Biomedical Imaging Statistics

SPM: Stage 1 Classical Estimation

Same for **classical** and **Bayesian**

HBM 2008 Melbourne, Australia 35

EMORY ROLLINS SCHOOL OF PUBLIC HEALTH CBIS Center for Biomedical Imaging Statistics

SPM: Stage 1 Bayesian Estimation

Same for **classical** and **Bayesian**

HBM 2008 Melbourne, Australia 36

SPM: Stage 1 Results

Similar for **classical** and **Bayesian**

HBM 2008 Melbourne, Australia 37

SPM: Stage 2 Model Specification

Design:
Conditions: 2
25 d.f.
[27 images - 2 parameters]

Same for **classical** and **Bayesian**

HBM 2008 Melbourne, Australia 38

SPM: Stage 2 Classical Estimation

HBM 2008 Melbourne, Australia 39

SPM: Stage 2 Bayesian Estimation

HBM 2008 Melbourne, Australia 40

SPM: Stage 2 Results

Similar for **classical** and **Bayesian**

HBM 2008 Melbourne, Australia 41

Spatial Bayesian Hierarchical Model

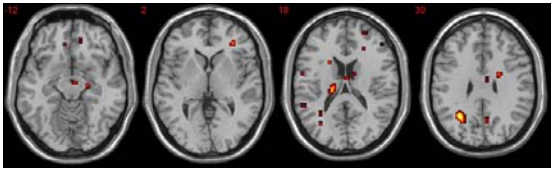
```

>> [clusts,post_sim1,post_sim2,pmean,pmedian,cont_pmean, ...
cov_pmed,glocs,cont_sim,bf,pp,misc]=stmod(7000,1000,0.2);
Outputs:
•Simulations from joint posterior distribution of all model parameters
•Posterior summaries of voxel, regional, and covariance parameters:
  E.g., posterior means, medians, probs., Bayes factors, etc.
•Information on prior distributions

Inputs: 1) Number of iterations or posterior samples drawn, 2) Number
of burn-in iterations (eventually discarded), 3) Prior covariance
weighting (percent reduction in covariances/100)
  
```

HBM 2008 Melbourne, Australia 42

Results: SPM

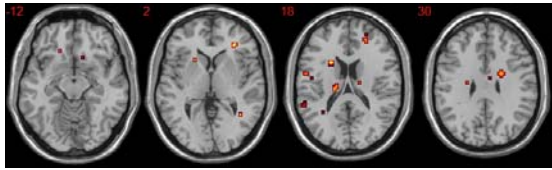


1. Classical/Classical

- Voxel-level t-statistic maps
- $p=0.005$ (uncorrected)

HBM 2008 Melbourne, Australia 43

Results: SPM

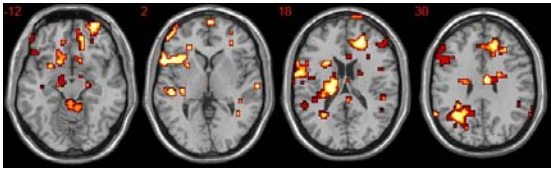


2. Classical/Bayesian

- Voxel-level PPM's
- Activation threshold (γ)=0
- $\alpha=0.85$

HBM 2008 Melbourne, Australia 44

Results: SPM

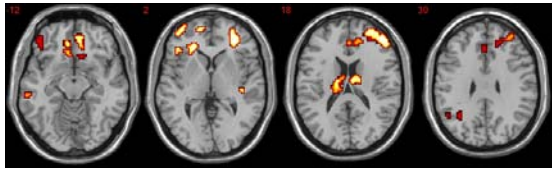


3. Bayesian/Bayesian

- Voxel-level PPM
- Activation threshold (γ)=0
- $\alpha=0.85$

HBM 2008 Melbourne, Australia 45

Results: Spatial BHM

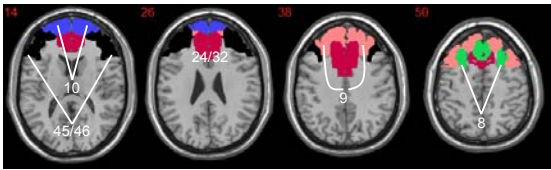


4. Classical/Spatial BHM

- Voxel-level PPM
- Likelihood of voxel-level activations
- $\alpha=0.85$

HBM 2008 Melbourne, Australia 46

Results: Spatial BHM



4. Classical/Spatial BHM

- Regional-level PPM
- Likelihood of regional-level activations
- $\alpha=0.50$

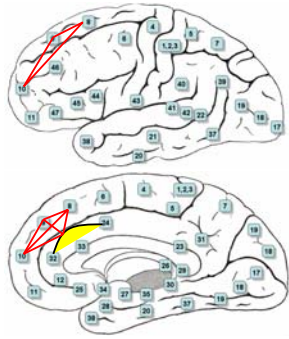
BA 10:	$p=0.50$ (Blue)
BA 45/46:	$p=0.52$ (Black)
BA 8:	$p=0.51$ (Green)
BA 9:	$p=0.55$ (Pink)
BA 24/32:	$p=0.53$ (Red)

HBM 2008 Melbourne, Australia 47

Results: Spatial BHM

Functional Connectivity

- Inter-regional task-related functional connections in cocaine addicts following treatment
- $FC > 0.3$
- BA 24/32: Anterior cingulate



HBM 2008 Melbourne, Australia 48

Results: Spatial BHM

Functional Connectivity

- Posterior probs. of FC **changes** (or differences)
 - Δ_s = Group difference in connectivity during session s
 - $\Pr(\Delta_{pre} > \Delta_{post}) > 0.9$
- BA 24/32: Anterior cingulate

HBM 2008 Melbourne, Australia 49

EMORY **CBIS**
ROLLINS SCHOOL OF PUBLIC HEALTH Center for Biomedical Imaging Statistics

Bayesian Analysis:

IV. Summary

HBM 2008 Advanced fMRI Course Melbourne, Australia

Summary: Strengths

Bayesian			Classical
SPM 2: C/B	SPM 3: B/B	4. C/SBHM	SPM 1: C/C
PPM's to quantify evidence (also Bayes Factors)			Conventional testing methodology
Flexible inferences from joint posterior distribution			
May circumvent (mitigate) multiple testing issues			
Fast computations		Fast computations	Fast computations
SPM	SPM	Regional inferences	SPM
		FC inferences	
	Local spatial corr.	Intra/inter-regional spatial corr.	
	No smoothing in pre-process.	No or minimal smoothing	

HBM 2008 Melbourne, Australia 51

Summary: Weaknesses

Bayesian			Classical
SPM 2: C/B	SPM 3: B/B	4. C/SBHM	SPM 1: C/C
Must specify prior distributions (somewhat subjectively)			
	Long computations		
		Personal implementation	
		Small sample constraint on no. of regions	
Unconventional thresholding methods	Unconventional thresholding methods		

HBM 2008 Melbourne, Australia 52

References

- Bowman, F. D., Caffo, B. A., Bassett, S., and Kilts, C. (2008). Bayesian Hierarchical Framework for Spatial Modeling of fMRI Data. *NeuroImage* 39, 146–156.
- Guillaume Flandin and William D. Penny (2007): Bayesian fMRI data analysis with sparse spatial basis function priors, *NeuroImage* 34(3), 1108-1125.
- Friston K.J., Glaser D.E., Henson R.N.A., Kiebel S., Phillips C., Ashburner J. (2002). Classical and Bayesian Inference in Neuroimaging: applications. *NeuroImage* 16(2): 484-512.
- Friston K, Penny W, Phillips C, Kiebel S, Hinton G, Ashburner J. (2002). Classical and Bayesian inference in neuroimaging: theory. *NeuroImage* 16(2): 465-483
- Penny, W., Kiebel, S., and Friston, K. (2003). Variational Bayesian inference for fMRI time series. *NeuroImage* 19, 727-741.
- Penny, W., Trujillo-Barreto, N.J., and Friston, K. (2005) Bayesian fMRI time series analysis with spatial priors. *NeuroImage* 24(2), 350-362.

Website: <http://www.sph.emory.edu/bios/CBIS>

HBM 2008 Melbourne, Australia 53