Sequential Monte Carlo Methods for Bayesian Model Selection in Positron Emission Tomography

Yan Zhou, John A.D. Aston and **Adam M. Johansen**

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Outline

Positron Emission Tomography (PET)

- Use compounds labeled with positron emission radionuclides as molecular tracers to image and measure biochemical process *in vivo*.
- One of the few methods available to neuroscientists to study *living* brains.
- Research into diseases where biochemical changes are known to be responsible symptomatic changes.
- For example, diagnostic procedure for cancer through fluorodeoxyglucose ($[^{18}F]$-FDG) tracers.

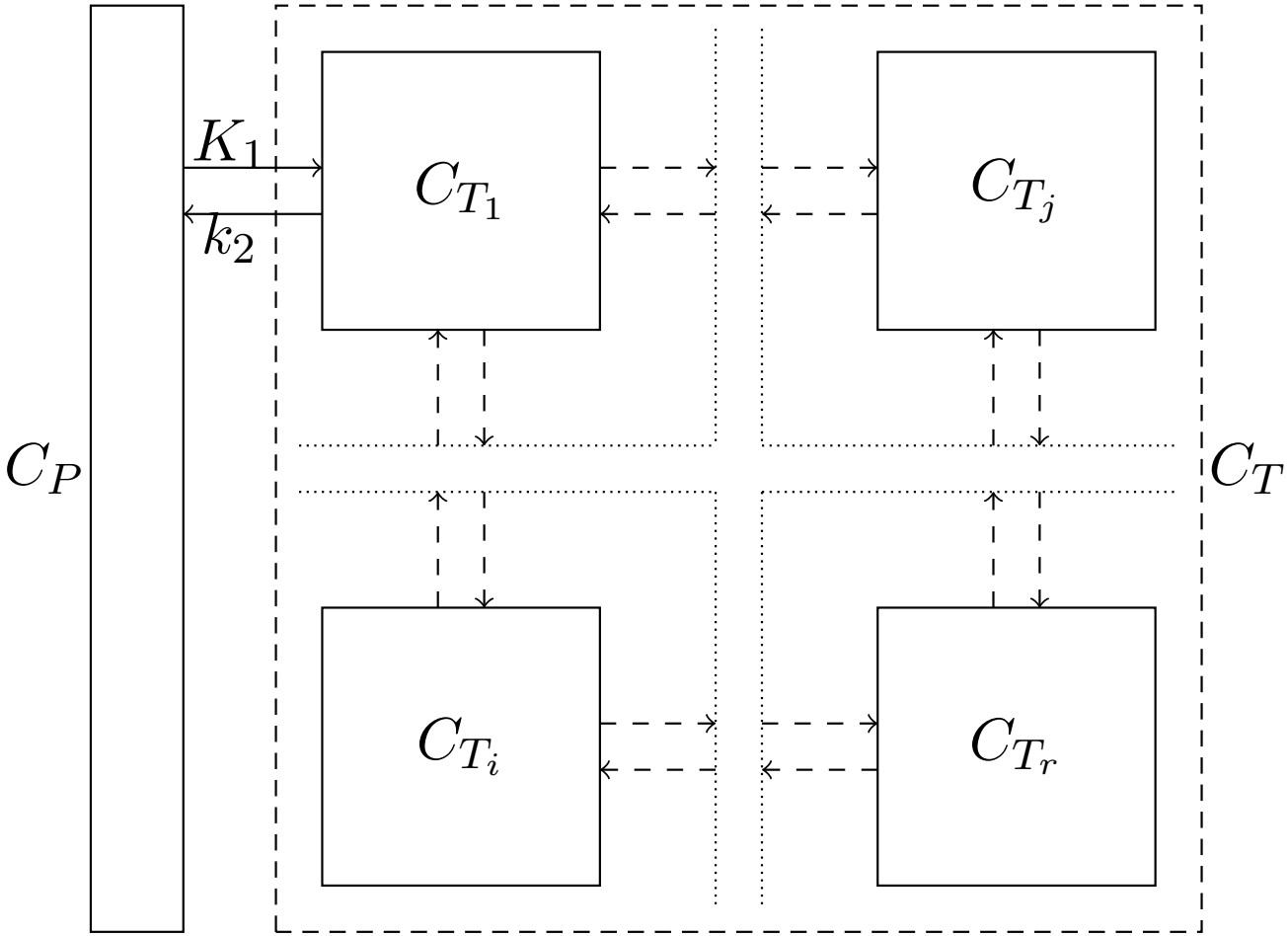
Linear Compartmental models

- Comprise a finite number of macroscopic subunits called *compartments*.
- Each is assumed to contain homogeneous and well-mixed material.
- Material flows from one compartment to another at a constant rate.
- In PET *total* concentration of material is measured.

These models yield sytems of ODEs:

$$\dot{\boldsymbol{f}}(t) = \boldsymbol{A}\boldsymbol{f}(t) + \boldsymbol{b}(t)$$
$$\boldsymbol{f}(0) = \boldsymbol{\xi}$$

Plasma input PET compartmental models



N.B. We actually focus on *linear* compartmental models.

Plasma input PET compartmental models

System,

$$\dot{\boldsymbol{C}}_{\boldsymbol{T}}(t) = \boldsymbol{A}\boldsymbol{C}_{\boldsymbol{T}}(t) + \boldsymbol{b}C_P(t)$$
$$C_T(t) = \mathbf{1}^T\boldsymbol{C}_{\boldsymbol{T}}(t)$$
$$\boldsymbol{C}_{\boldsymbol{T}}(0) = \mathbf{0}$$

Solution,

$$C_T(t) = \int_0^t C_P(t-s)H_{TP}(s)\,\mathrm{d}s$$
$$H_{TP}(t) = \sum_{i=1}^{r} \phi_i \mathrm{e}^{-\theta_i t}$$

Parameter of interest,

$$V_D = \int_0^\infty H_{TP}(t)\,\mathrm{d}t = \sum_{i=1}^{r} \frac{\phi_i}{\theta_i}$$

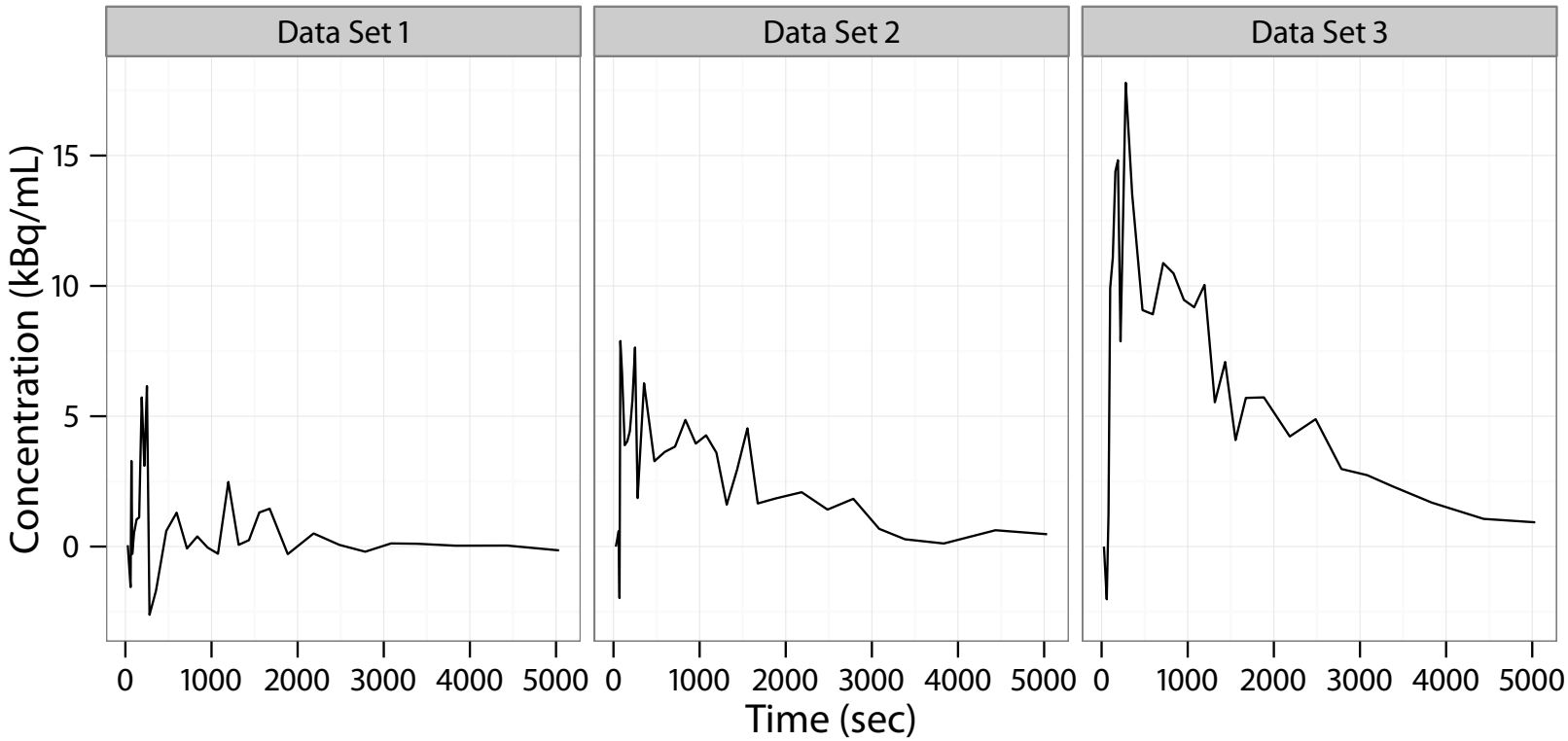
Bayesian model selection for PET

- Determine the number of tissue compartments.
- "Mass univariate analysis."
  - Each time course of $C_T(t)$ is analyzed individually.
  - Many: quarter of a million time series per PET scan.
- Data is measured at discrete times $t = t_1, \ldots, t_n$,

$$y_i = C(t_i) + \sqrt{\frac{C(t_i)}{t_i - t_{i-1}}}\varepsilon_i$$

where ε_i are (iid) errors.

Typical PET Time Courses



Robust modeling of the error structure

- Low signal to noise ratio.
- Standard approach (in likelihood-based procedures)
  - Use Normal distributions to model the error.
  - Employ weighted Non-negative Least Squares.
  - Assign (arbitrary) small weights to the most noisy data points.
- Bayesian modeling
  - No justifiable way to bound "weights" with normal errors.
  - Need more robust modeling of the error structure.
- Simple solution:

  Use three-parameter t distribution instead of Normal.

Biologically informative priors [Zhou et al., 2013a]

Starting point:

- Parameters $\phi_{1:r}$ and $\theta_{1:r}$ are functions of the rate constants.
- The matrix $\boldsymbol{A}$ of rate constants obey some simple rules.
- Rate constants are constrained by biophysical considerations.

Key observations: For $\theta_1 \leq \theta_2 \leq \cdots \leq \theta_r$: into the environment.

- In the linear plasma input model, there is one outflow, k_2, $\theta_1 \leq k_2$.
- There is also only one inflow K_1, $\sum_{i=1}^{r} \phi_i = K_1$.

Biophysical knowledge constrains possible values for $\phi_{1:r}$ and $\theta_{1:r}$.

Sequential Monte Carlo [Del Moral et al., 2006]

- Iteratively generate importance sampling proposal distributions for a sequence $\{\pi_t\}_{t=0}^T$.
- Use MCMC kernels to propose samples

1. Generate $\{X_0^{(i)}\}_{i=1}^N$ from π_0. Set $\{W_0^{(i)}\}_{i=1}^N$, the importance weights, to $1/N$.
2. For $t = 1, \ldots, T$,
   - 2.1 Resample if necessary.
   - 2.2 Generate $\{X_t^{(i)}\}_{i=1}^N$ from $K(x_{t-1}, x_t)$, a π_t-invariant Markov kernel.
   - 2.3 Set $W_t^{(i)} \propto W_{t-1}^{(i)} \tilde{w}_t^{(i)}$, where $\tilde{w}_t^{(i)} \propto \pi_t(X_t^{(i)})/\pi_{t-1}(X_t^{(i)})$.

Algorithm setting for Bayesian modeling

Sequence of distributions,

$$\pi_t(\varphi) \propto \pi_0(\varphi)[L(\varphi|y_{1:n})]^{\alpha(t/T)}$$

where φ is the parameter vector, π_0 is the prior and L is the likelihood function.
Markov kernels,

- Update $\phi_{1:r}$ with Normal random walks.
- Update $\theta_{1:r}$ with Normal random walks.
- Update λ, the scale parameter of the t distributed error, with a Normal random walk on $\log \lambda$.
- Update ν, the degree of freedoms of the t distributed error, with a Normal random walk on $\log \nu$.

Computational challenge

- Accuracy of estimator
- Heterogeneous structure
- Computational cost

Improve the accuracy of estimators [Zhou et al., 2013b]

- Increase the number of particles.
- Increase the number of intermediate distributions.
- Fast mixing Markov kernels.
  - Multiple MCMC passes each iteration.
  - Adaptive proposal scales for random walks.
- Better specification of intermediate distributions.
  - Place more distributions where π_t changes fast when $\alpha(t/T)$ increases.
  - Adaptive specification such that the discrepancy between π_t and π_{t-1} remain almost constant.

Improve the accuracy of estimators — adaptive specification of the sequence of distributions

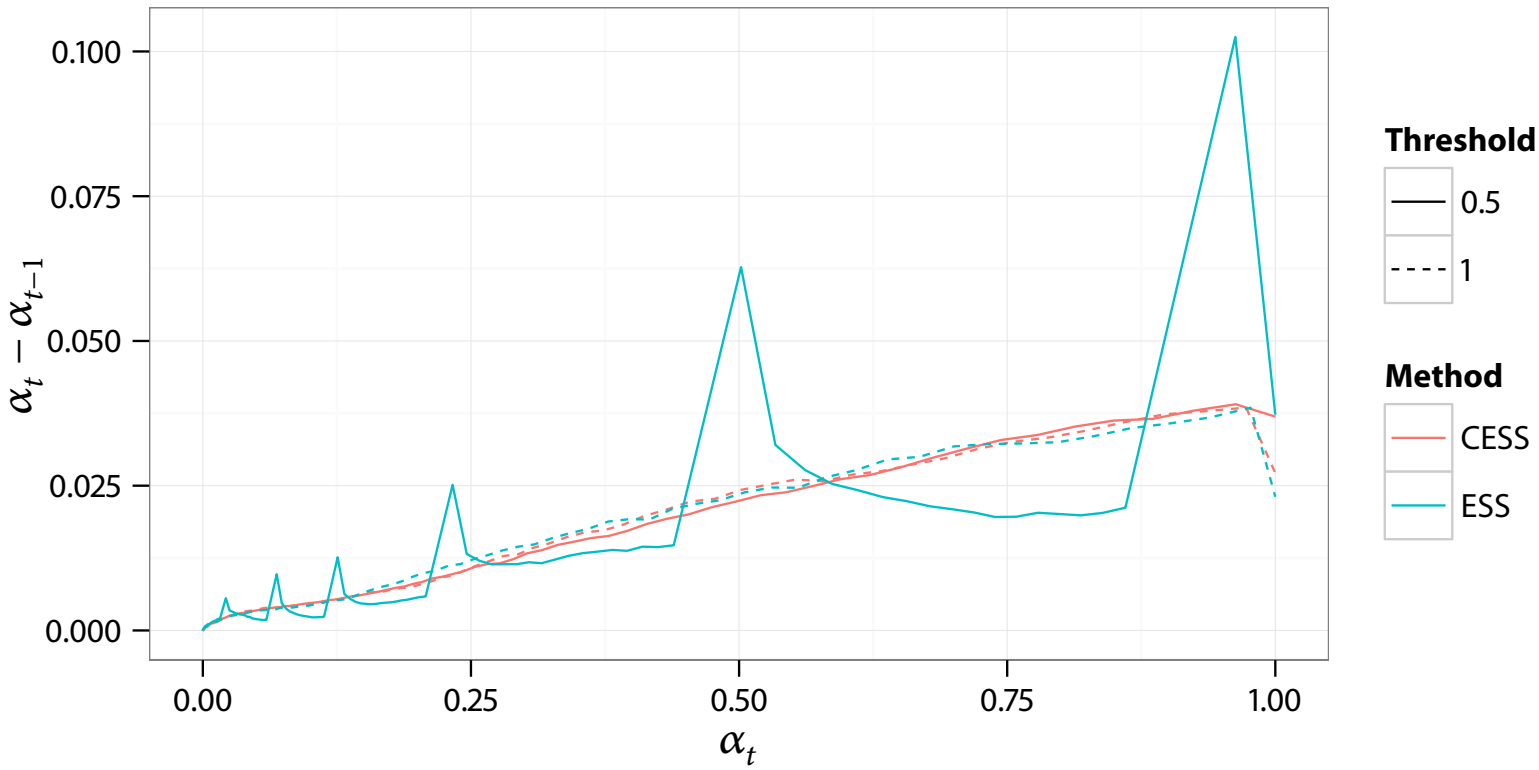


Figure : Variation of the distribution specification parameter $\alpha(t/T)$ when using adaptive algorithms.

Heterogeneous structure and algorithm tuning

We cannot tune the algorithm for each of 250,000 time series.

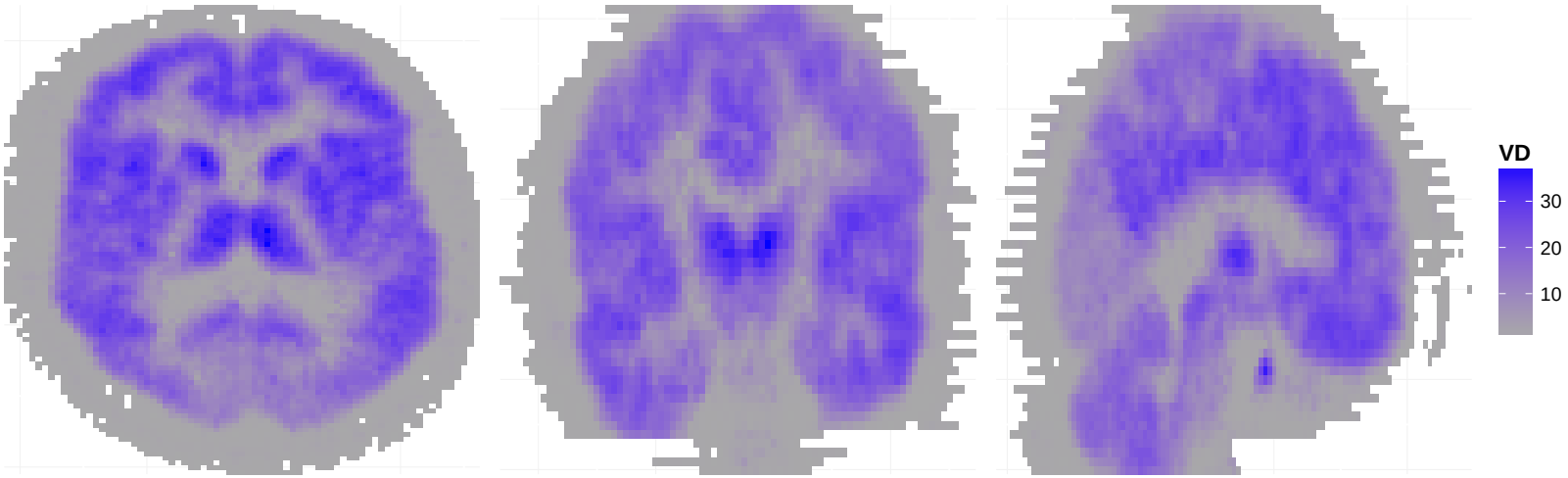


Figure : Estimates of V_D using selected model

- SMC is more robust compared than (our) MCMC.
- Adaptive strategies.

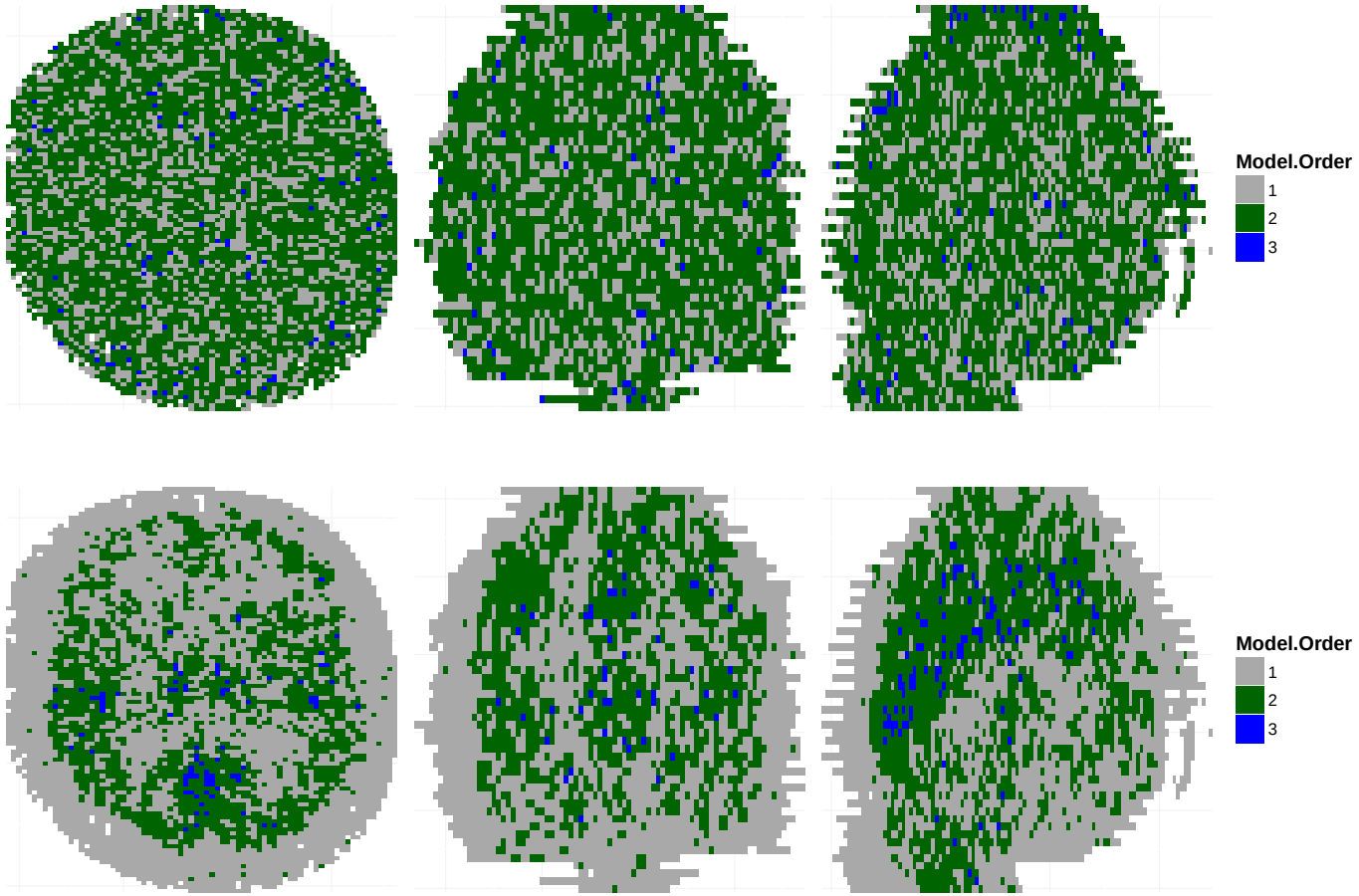
Computational cost and parallel computing

- SMC can be parallelized naturally in contrast to MCMC.
- SMC can be parallelized more efficient compared to other algorithms, such as population MCMC.
  - We can increase the number of particles freely.
  - Increase the number of distributions in population MCMC come with a cost – global mixing speed.
- Well suited for SIMD architectures, such as GPUs:
  - They perform best when each thread does *exactly* the same thing.

Results

- Bayesian model selection for simulated data performance considerably better than methods such as AIC and BIC.
  - Higher frequency of selecting the true model.
  - More accurate parameter estimates.
  - Biological informative priors improve the results further (but results are fairly insensitive to the prior).
- Bayesian model selection for real data shows more plausible structures than existing techniques.
  - Voxels with higher volume of distributions (V_D) are expected to have higher order models associated with them.

Results



Model selection results using AIC (above) / Bayes factor (below).

Conclusions

SMC is *not* "too computationally demanding" for neuroscience.

- Monte Carlo methods are feasible for large data problems.
- SMC can outperform MCMC even in time-limited settings such as this one.
- Many problems in neuroscience are amenable to similar solutions [Sorrentino et al., 2013, Nam et al., 2012]

Ongoing work on this problem seeks to replace the "mass univariate analysis" approach.

References

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