From CT to fMRI: Larry Shepp's Impact on Medical Imaging

Martin Lindquist
Department of Biostatistics
Johns Hopkins University

Introduction

- Larry Shepp worked extensively in the field of medical imaging for over 30 years.

- He made seminal contributions to the areas of computed tomography (CT), positron emission tomography (PET) and functional magnetic resonance imaging (fMRI).

- In this talk I will highlight some of these important contributions.

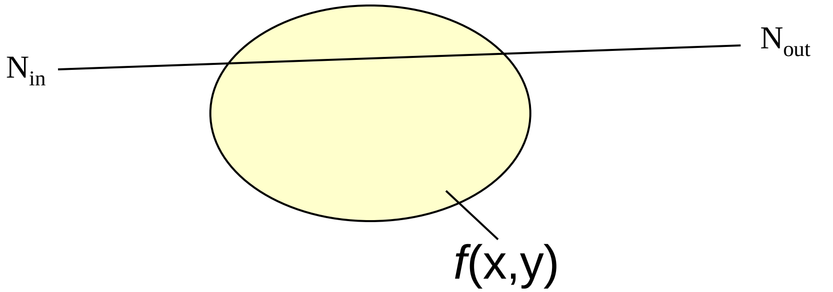
Computed tomography (CT)

CT Overview

- Consider a fixed plane through the body and let *f*(x,y) denote the density at point (x,y).

- Let *L* be any line through the plane.

- CT directs beams of x-rays into the body along *L* and measures how much of the intensity is attenuated.



CT Overview

- Beer's law states that the logarithm of the attenuation factor is given by

$$P_f(L) = \int_L f(x,y)\,ds$$

where s indicates length along *L*.

- Measuring the attenuation allows one to compute the line integral of *f* along *L*.
  - This mapping is known as the Radon transform.

CT Overview

- In CT the goal is to reconstruct $f(x,y)$ using a finite number of measurements $P_f(L)$.
- Hounsfield used an iterative algorithm to reconstruct the images.
  - Discretized $f(x,y)$ making it constant in each pixel.
  - Used iterative Gauss-Seidel method to solve problem.

CT Overview

- Shepp and Logan provided a direct algorithm for reconstruction of a density from its measured line integrals.

- Based on the observation that the 1-D Fourier transform of P_f is the same as that of the 2-D Fourier transform of *f* along the line *L*.
  - Possible to find *f* by Fourier inversion.

CT Overview

- This suggests an approximation of the form:

$$f(Q) = \sum C(Q, L) P_f(L)$$

where

$$C(Q, L) = \Phi\left(dist(Q, L)\right)$$

with Φ a function whose Fourier transform is roughly |t| for small |t|.

•Filtered back projection.

Contributions

1. Making explicit a direct algorithm for reconstruction of a density from its measured line integrals.

2. Providing a general framework for choosing convolution filters.

3. The use of a mathematical phantom.

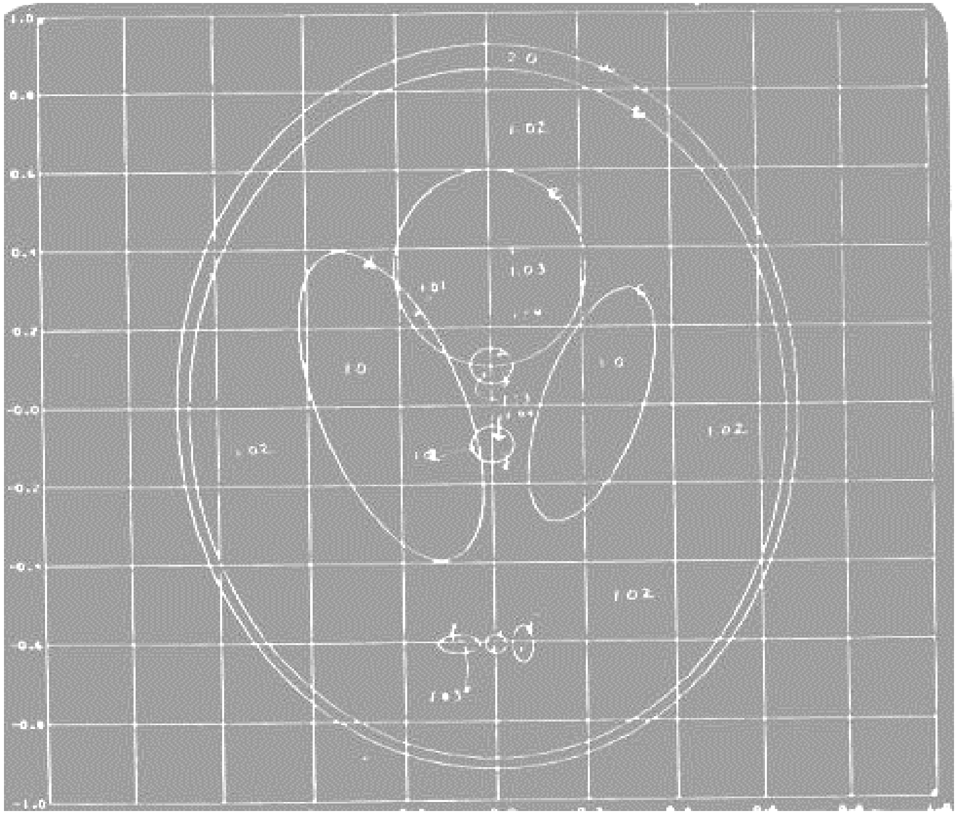
Mathematical Phantom

The Shepp-Logan head phantom

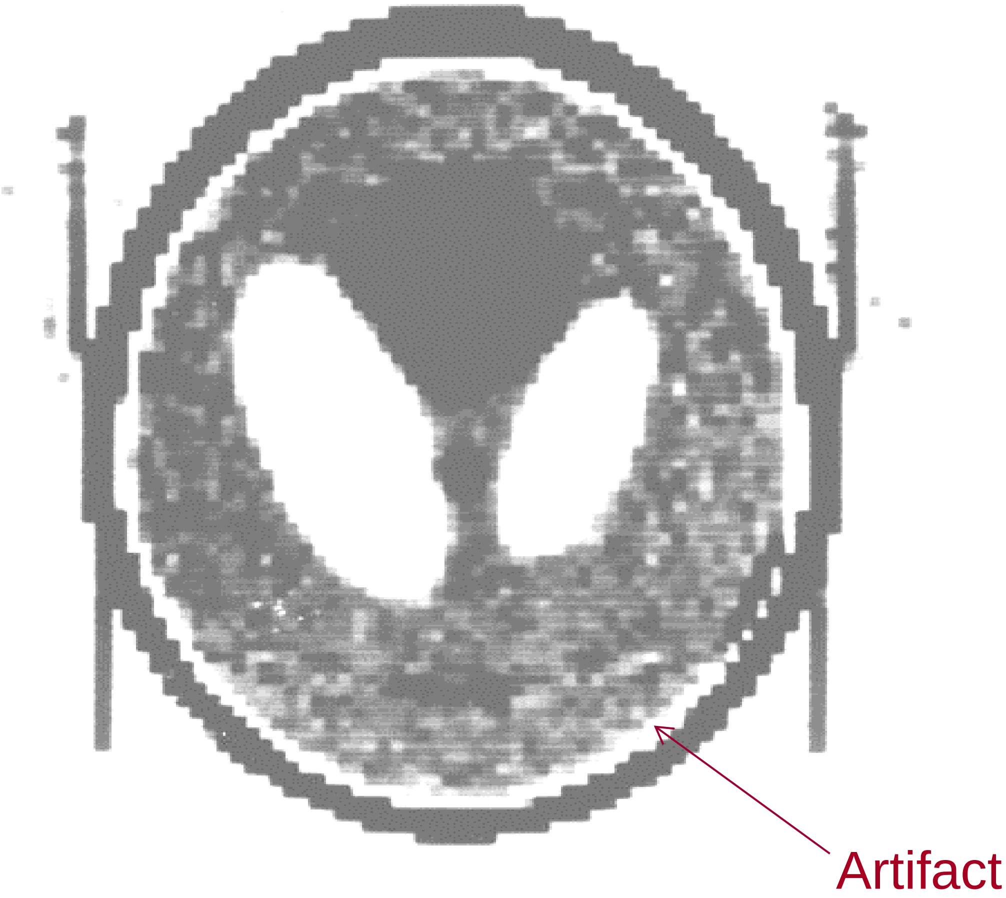
In Matlab:

```
>> Z = phantom(N);
```

We can calculate the line integrals in the phantom image exactly.



Reconstruction of phantom image using Hounsfield's original reconstruction method.



Reconstruction of phantom image using the Shepp-Logan approach.

Comments

- Today the use of a mathematical phantom seems almost trivial.

- However, it has had a profound effect on the manner in which algorithms are evaluated in the field to this day.

PET

PET Overview

- PET differs fundamentally from CT in the manner in which data is acquired.
- Glucose labeled with a positron emitting radioactive material is introduced into the body and the radioactive emissions are counted using a PET scanner.
- This makes it possible to estimate the location of each emission, allowing for the creation of an image of the brain's glucose consumption.

PET Overview

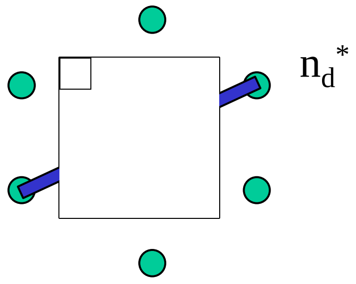
- Emissions occur according to a spatial point Poisson process with unknown intensity $\lambda(x)$.
  - Want to construct a map of this emission density.

- Early reconstruction models did not distinguish the physics of emission tomography from that of transmission tomography.
  - Used a filtered back projection type approach.

  - Shepp and Vardi framed the problem as one of statistical estimation from incomplete data.

PET Overview

- Divide the region into pixels B_b, b=1,….B, and assume there are N detectors.
- Emissions cause two photons to “fly off” in opposite directions along a line.
- There are N choose 2 possible tubes D_d that can detect the emission.



PET Overview

- The observed data is n_d^* which represents the number of emissions in tube d.

- Let $p_{b,d}$ be the probability that the line produced by an emission in B_b finds it way into tube D_d.

- Let the number of unobserved emissions in each pixel n(b) be independent Poisson variables with unknown mean $\lambda(b)$, the emission density.

- Use the EM-algorithm to estimate the MLE of $\lambda(b)$.

Comments

- The competing reconstruction algorithm was filtered back projection.
  - Larry didn’t feel this properly incorporated the physics of the problem.

- Interestingly, Shepp and Vardi discretized the problem and used an iterative algorithm, much like Hounsfield did with the original CT reconstruction.

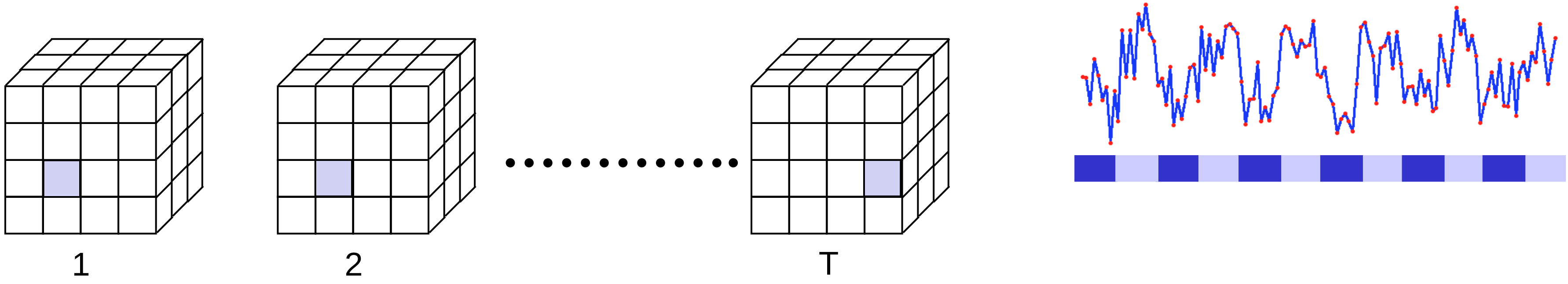
fMRI

fMRI Overview

- Functional magnetic resonance imaging (fMRI) is a non-invasive technique for studying brain activity.
- During the course of an fMRI experiment, a series of brain images are acquired while the subject performs a set of tasks.
- Changes in the measured signal between individual images are used to make inferences regarding task-related activations in the brain.

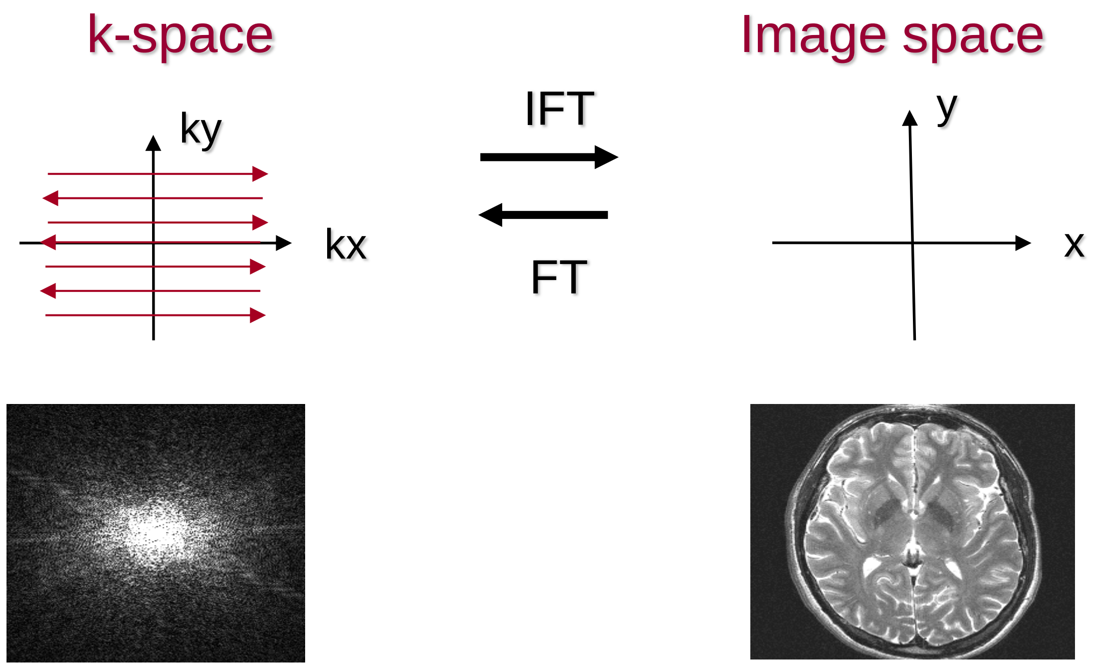
fMRI Overview

- Each image consists of ~100,000 brain voxels.
- Several hundred images are acquired, roughly one every 2*s*.



fMRI Overview

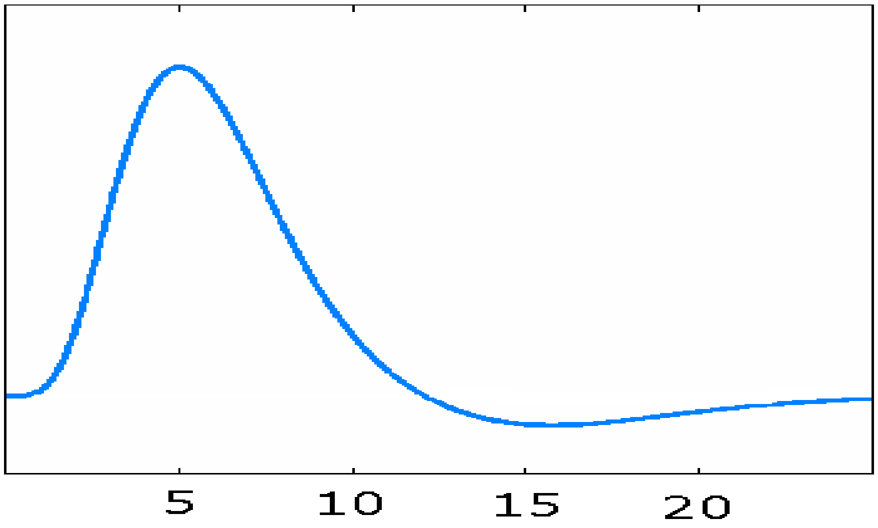
- The actual signal measurements are acquired in the frequency-domain (k-space), and then Fourier transformed into the spatial-domain.



BOLD fMRI

- The most common approach towards fMRI uses the Blood Oxygenation Level Dependent (BOLD) contrast.
  - It doesn't measure neuronal activity directly, instead it measures the metabolic demands of active neurons (ratio of oxygenated to deoxygenated hemoglobin in the blood).

- The hemodynamic response function (HRF) represents changes in the fMRI signal triggered by neuronal activity.



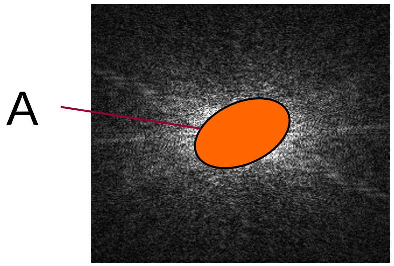
Fast fMRI

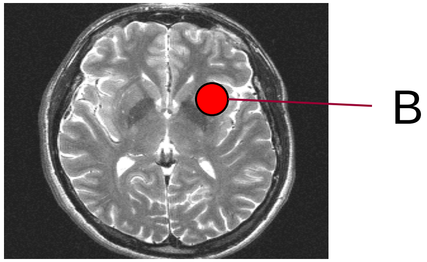
- Higher cognition involves mental processes on the order of tens of milliseconds.
  - A standard fMRI study has a temporal resolution of 2*s*.
  - There is a disconnect between the temporal resolution of neuronal activity and that of fMRI.

- How can the temporal resolution of fMRI be increased?
  - By sub-sampling k-space.
    - Leads to information loss.
  - Consider instead the problem of obtaining the total activity over a pre-defined region of the brain.

Fast fMRI

- Consider an arbitrarily shaped region B.





1. Find the k-space sub-region A, of fixed size a, that maximizes the information content in B.

2. Find the function with support on A whose IFT has maximal fraction of energy in B.

Fast fMRI

- Let us denote this function $\hat{f}(k)$.

- We can use it to compute the average activation over B using the formula:

$$I(B) = \int f(x) f^*(x)\,dx = \int \hat{f}(k)\hat{f}^*(k)\,dk$$

- Can limit sampling of k-space to the region A.
  - Sacrifice spatial resolution for temporal resolution.

Fast fMRI

- Shepp and Zhang found that the optimal $\hat{f}(k)$ for a given A and B can be obtained using an N-dimensional generalization of prolate spheroidal wave functions (Landau, Pollak and Slepian).

- The optimal sampling region A, is defined as the one whose corresponding $\hat{f}(k)$ has a maximal fraction of its energy on B.
  - Heuristics suggest a flipped and scaled version of B.
  - Sampling A necessitates new acquisition algorithms.

Trajectory Design

- Defining trajectories for sampling k-space is a fun mathematical problem.

- Ideally, we want to develop a trajectory, *k(t)*, that transverses as large a portion of 3D k-space as possible in the allocated time.

- The trajectory must adhere to a number of constraints.

Machine constraints:

$$g(t) = \frac{1}{\gamma}\dot{k}(t) \leq G_0 \qquad\qquad s(t) = \frac{1}{\gamma}\ddot{k}(t) \leq S_0$$

Time constraint:

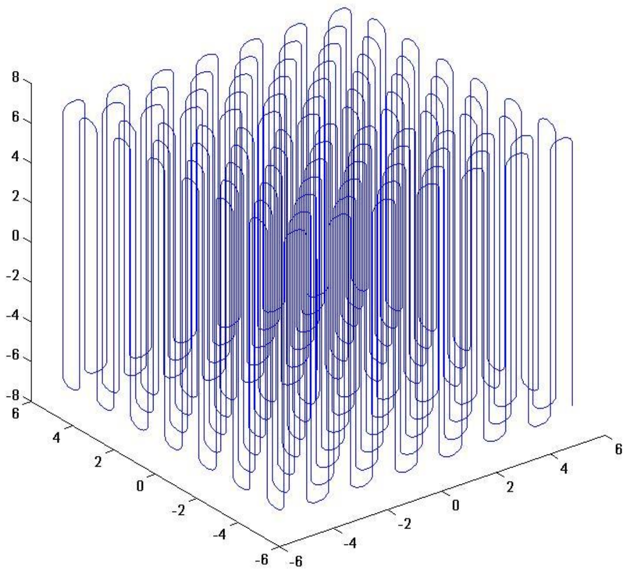
$$t \leq T_{\max}$$

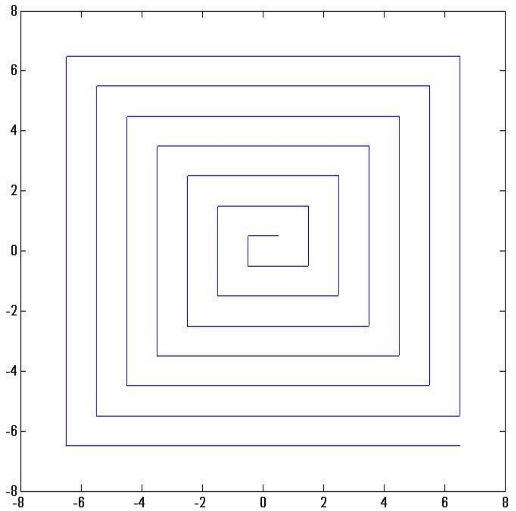
Reconstruction constraint:

The trajectory needs to visit every point in a 3D lattice, where the distance between the points is determined by the Nyquist criteria.

K-space Trajectory

- 3D trajectory samples 3D k-space every 100 *ms*.

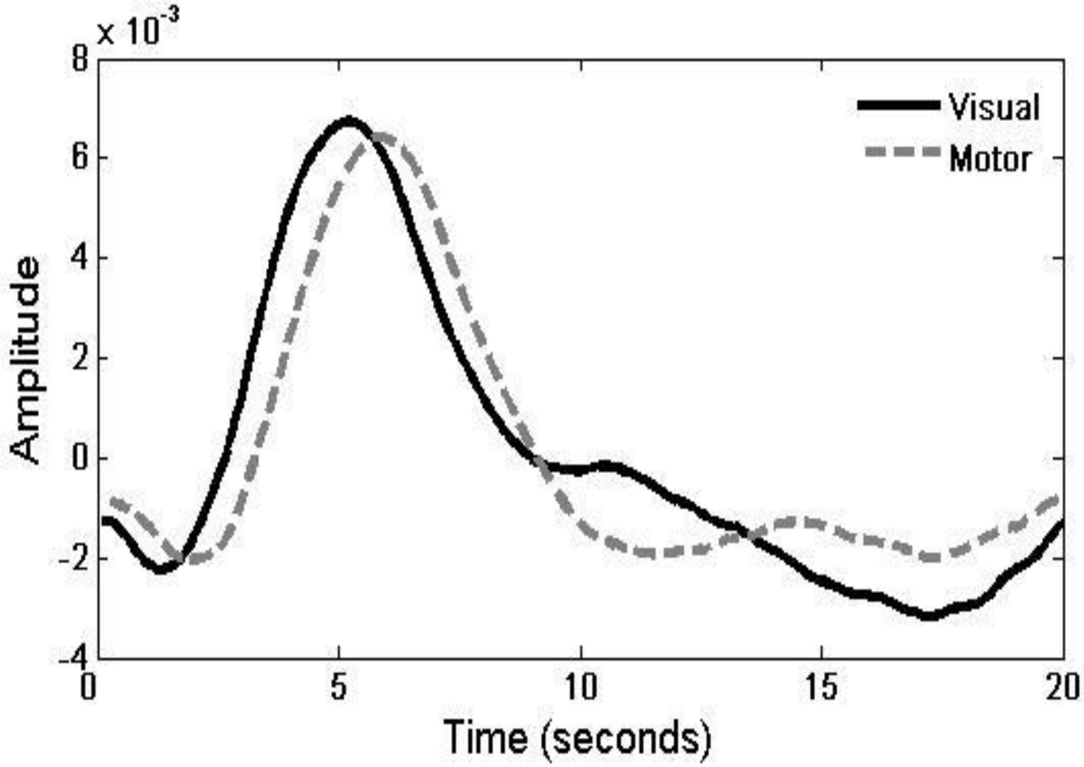


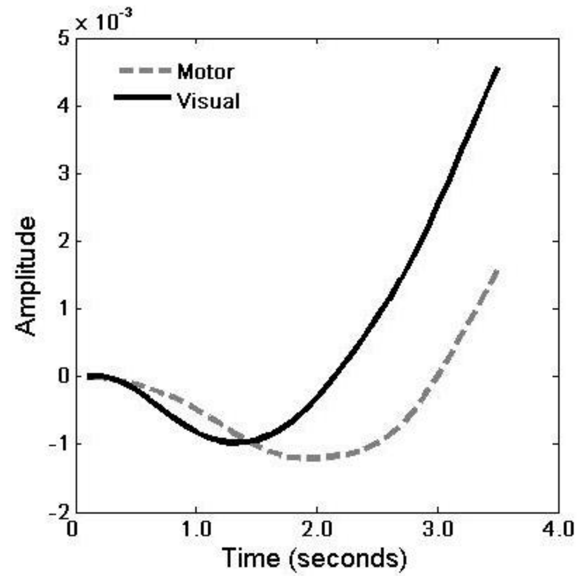


Experimental Design

- The experiment consisted of 15 cycles of a visual-motor stimuli.
- Each cycle lasted 20 seconds, during which 200 images (TR 100*ms*) were sampled.
- 500*ms* into each cycle a flashing checker board appeared on a computer screen.
- The subject was instructed to press a button in reaction to the checker board.

Comparing HRFs



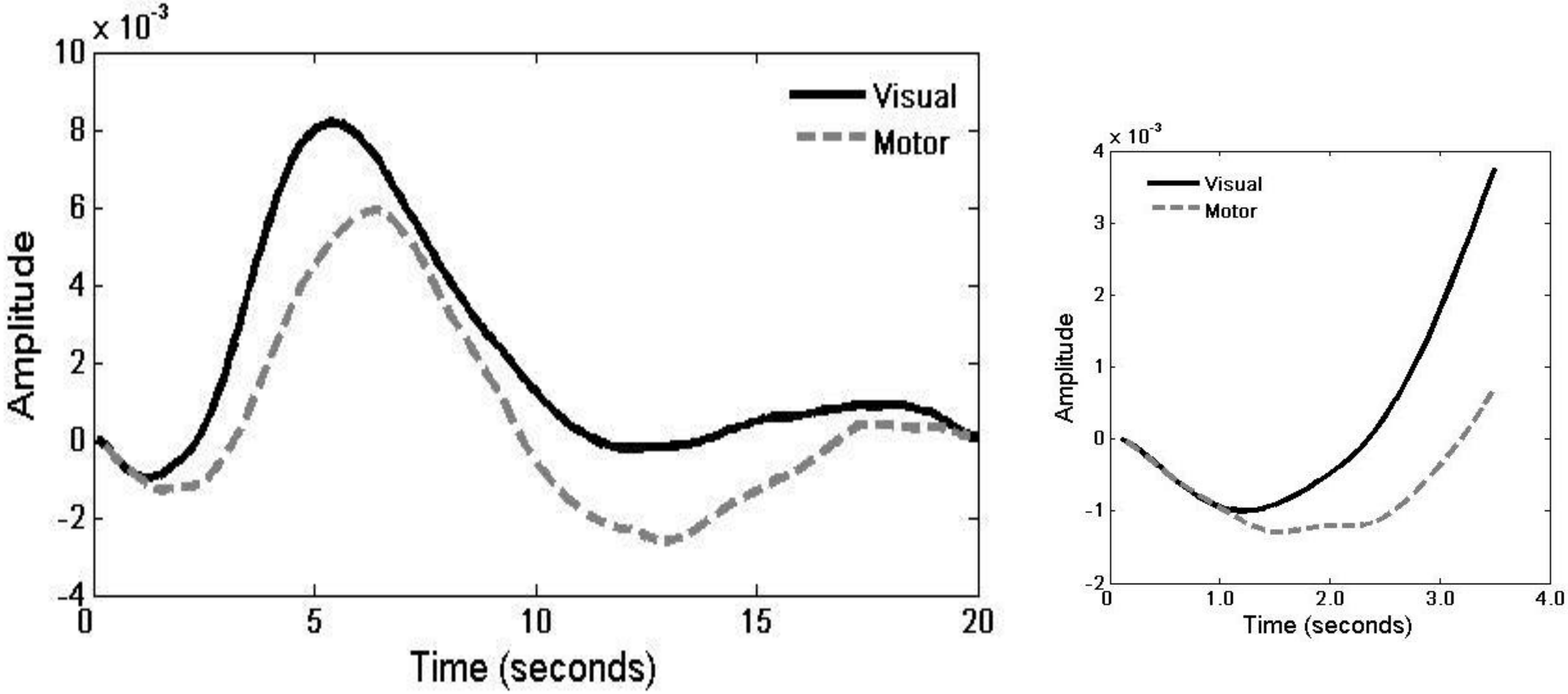


The signal in the visual cortex proceeds the signal in the motor cortex throughout the length of the HRF.

Experimental Design

- The experiment consisted of 15 runs of a auditory-visual-motor stimuli.
- Each cycle lasted 20 *s*, during which 200 images (TR 100 *ms*) were sampled.
- 500 ms into each cycle, the subject's auditory cortex was stimulated by a tone.
- They pressed a button in reaction to the tone, which in turn generated a flashing checkerboard.

Comparing HRFs



Both the onset and time-to-peak appears in the visual cortex prior to the motor cortex - confounding.

Comments

- Researchers were generally unwilling to sacrifice spatial resolution for temporal resolution.
- A decade later obtaining high temporal resolution fMRI is all the rage.
- Both mathematical (e.g. compressive sensing) and engineering (e.g., parallel imaging, multi-band) developments have helped drive these developments.

Thank You