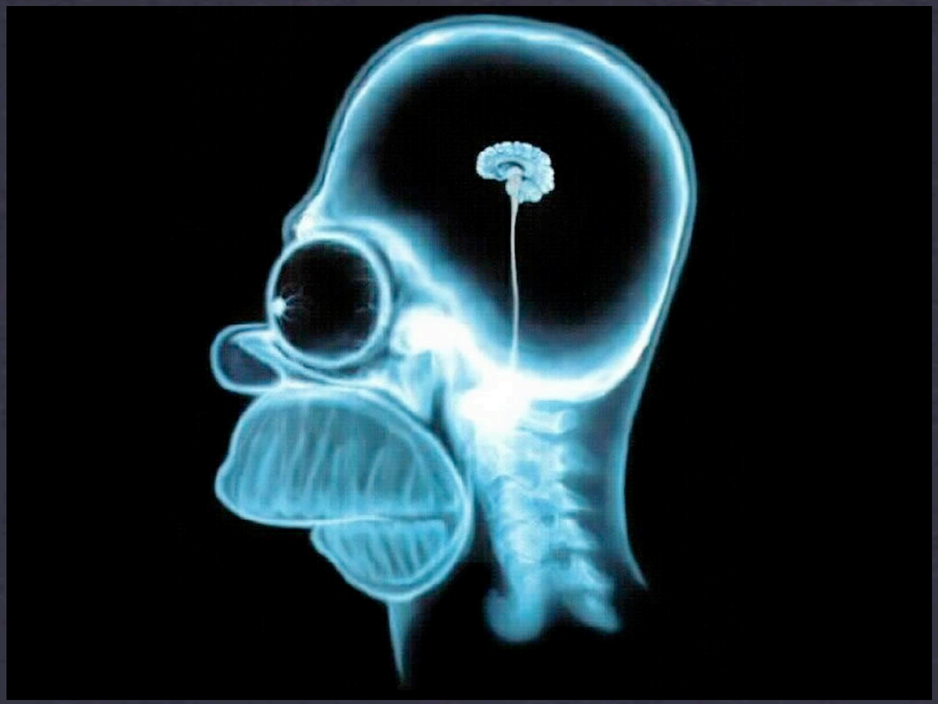


Using the Brain: Observation and interpretation

Matthew Sottile
Dept. of Computer Science/Neuroinformatics Center

Outline

- Goals of brain observation.
- Observation techniques.
- Analysis methods.
- Current questions and approaches.
- Where are we going?

Goals

- Observe the brain.
- Understand the connection of observation to activity.
  - Correlate an activity with some observed pattern in the brain.
- Acquire the ability to infer activity from observation.
  - Observe brain activity, infer functional actions.

Goals

* Matching observation to functional source:
    * This is the process of understanding what the brain looks like when it is doing something interesting.
* The end goal is to identify function solely from observation.
    * Start with an observation, and infer what the functional source was.
    * Basically, reading the mind.

Goals

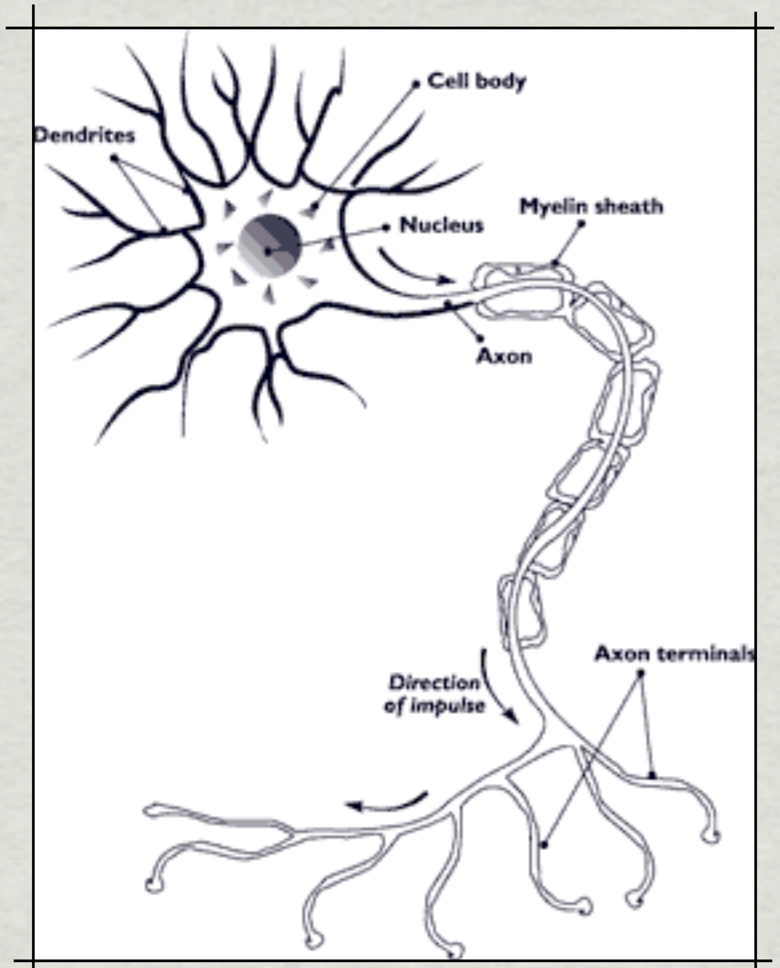
* Our goals are typically a bit more grounded than those of the text.
* Often we are interested in medical and behavioral applications.
* Example:
    * Detection of regions of the brain where seizures originate. Understanding the physical processes that cause what we observe as a seizure.

The Brain

- Before we dive into how we measure the brain, let's briefly discuss what it is we're actually measuring.
- How does the brain function?

Neurons

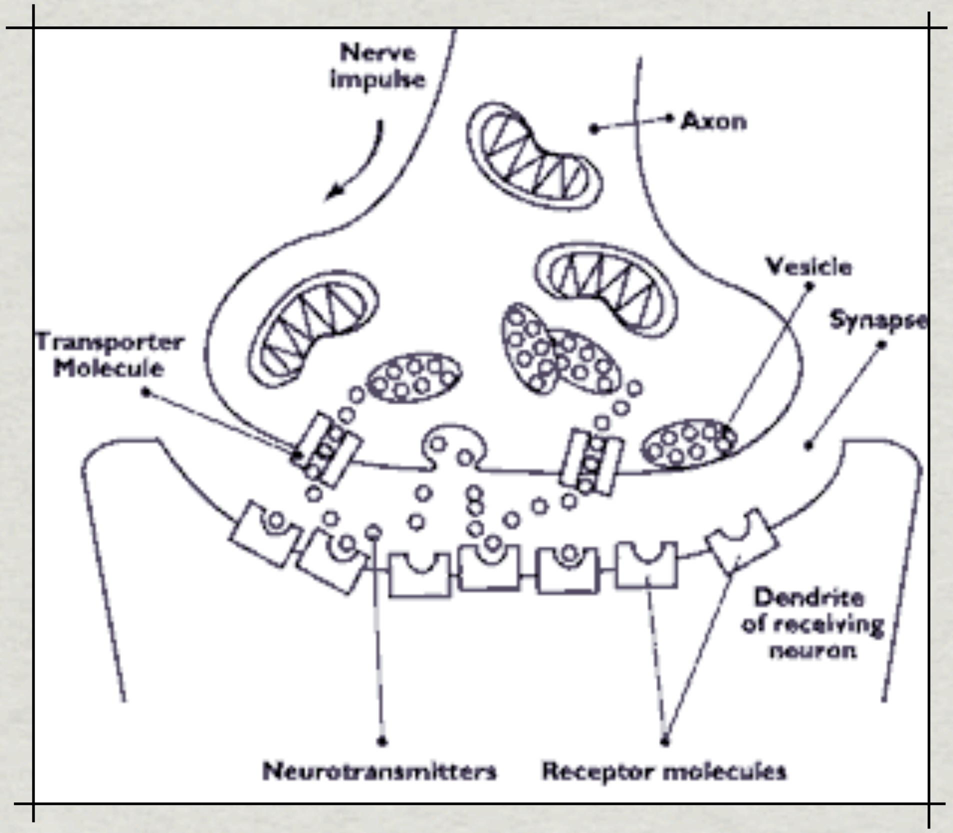
- The brain is a massive collection of cells known as **neurons**.
- These cells have an interesting structure: they have a small body, and long arms (**axons**) that reach out and connect to other neurons at their **dendrites**.
- The neurons accumulate up a concentration of chemicals, and when it reaches a certain point, an excitation wave can propagate down the axons causing stimulation of other neurons.



HTTP://WWW.DRUGABUSE.GOV/MOM/TG/MOMTG-INTROBG.HTML

Synapses

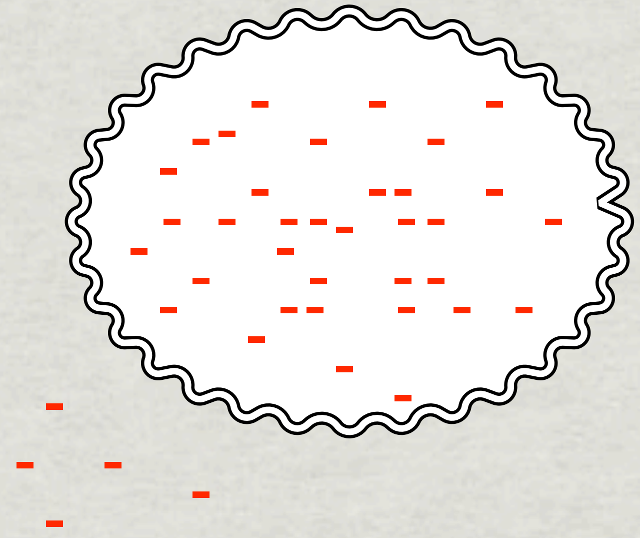
- The axons of neurons connect to the dendrites of other neurons at what are called **synapses**.
- This is where neurons stimulate each other by exchanging neurotransmitters. Axons stimulate dendrites.
- The exchange results in unequal distributions of charged particles on either side of a membrane.



HTTP://WWW.DRUGABUSE.GOV/MOM/TG/MOMTG-INTROBG.HTML

Electrical potential

- The propagation of signals between neurons is achieved by neurotransmitters flowing from the axon of one neuron to the dendrites of another.
- The unequal distribution of ions on either side of the cell membranes means that one side is slightly more negative than to the other.
- So we can observe electrical potentials due to this.
- This is where the notion of an "Electric Brain" comes from.



Observation

- Observation of the brain means measuring some property of it that changes in a meaningful way.
- **Blood flow and fluid properties** : Excited regions tend to have active blood flow.
- **Electrical properties** : Neuronal activity changes electrical properties of the brain.
- **Solid properties** : Materials in the brain and head have different physical properties.

Observation

- Many different types of observation can be made.
- They differ in:
  - Resolution (both in time and space).
  - Activities they can observe.
  - Perturbation of the individual from a normal state.

Observation

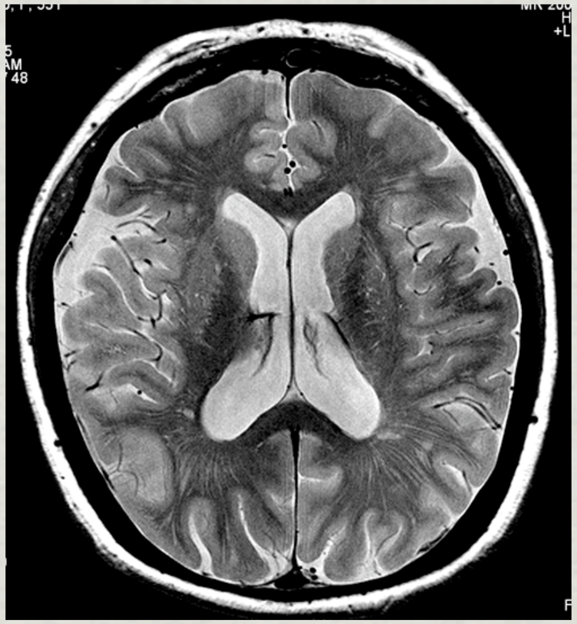
- The last point is important. Different observation techniques affect the individual differently.
- A purely passive method is ideal: you observe the brain in it's natural state.
- Less passive techniques add variables to what you are attempting to observe.
- For example, if a technique requires you to be very still while performing an activity, you will measure both the brain performing the activity ***and*** the conscious act of being still.

Observation

- What are some common techniques?
  - Magnetic Resonance Imaging (MRI)
  - Electroencephalography (EEG)
  - Magnetoencephalography (MEG)
  - Positron Emission Tomography (PET)
  - Computerized Tomography (CT)

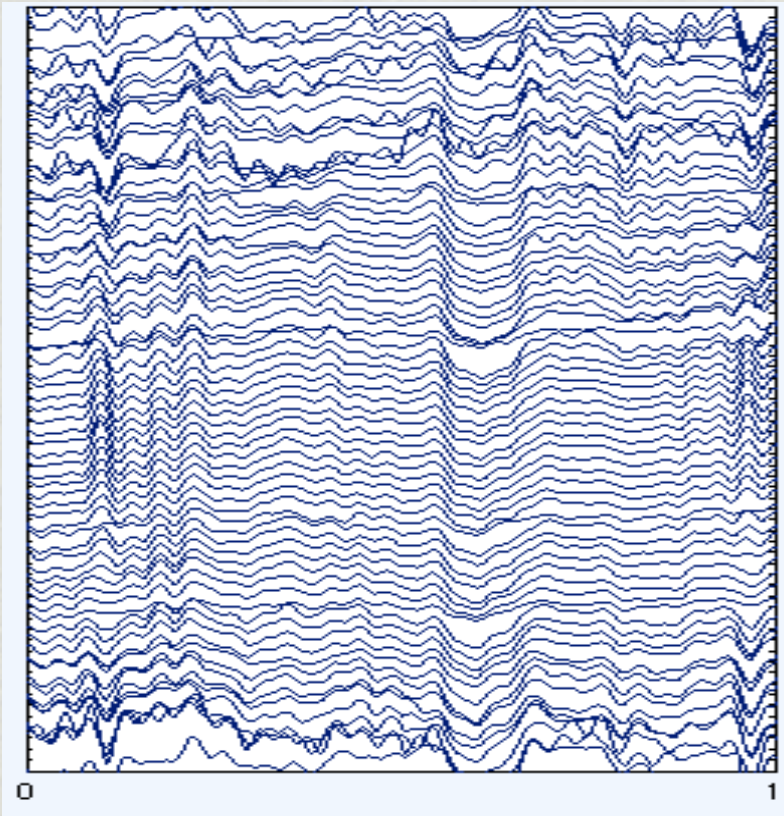
MRI

- Based on the use of powerful magnetic fields to cause atoms with a positive charge (such as hydrogen in water) to align with the field.
- A radio wave tuned to a frequency related to quantum states of the protons causes the atoms to resonate and absorb energy.
- When this energy is released by the atoms, a corresponding release of electromagnetic radiation occurs which can then be measured.



EEG

- Activity in the brain is based on movement of charged particles. Neurotransmitters are exchanged between neurons to let them talk to each other.
- The result is a changing electric field produced by the brain.
- EEG works by measuring the electrical potential due to this field on the surface of the head, much like a seismograph measures the surface movements due to the inner workings of the earth.



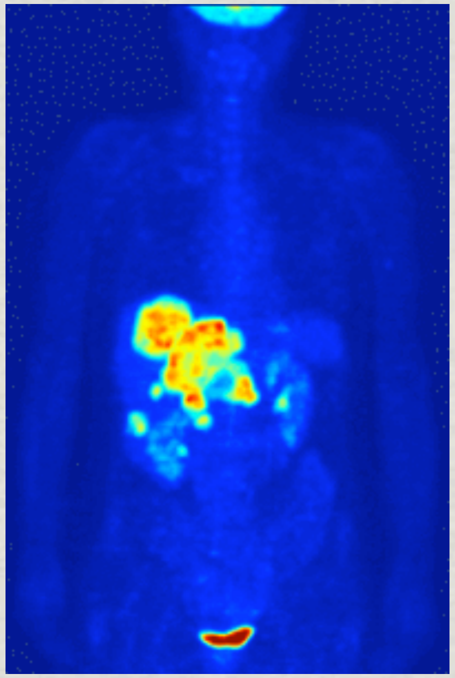
MEG

- MEG is very similar to EEG.
- In MEG, the magnetic fields induced by activity in the brain are observed instead of surface potentials.
- The benefit is that MEG is less affected by the conductive properties of the head, but MEG requires a more controlled environment to remove background magnetic disturbances.

IMAGE CREDIT: 4D NEUROIMAGING

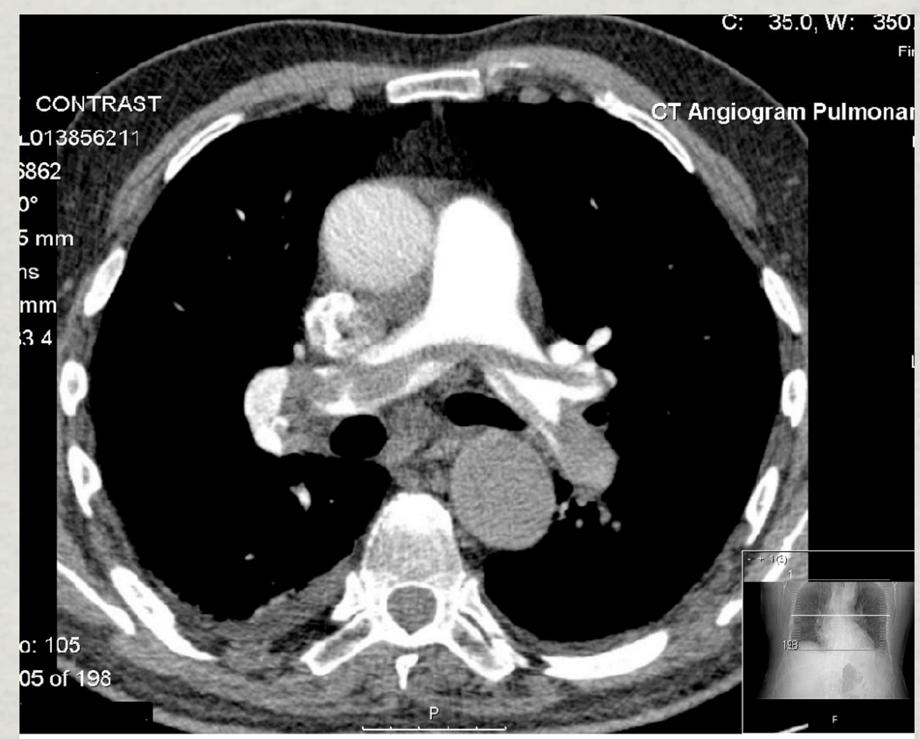
PET

- PET scanning requires the use of radioactive isotopes introduced into the body.
- These isotopes decay into positrons which in turn interact with electrons to create gamma photon pairs.
- These simultaneously measured photons allow the position of the isotope to be measured.
- Very useful in identifying static structure.



CT

- Computerized Tomography is based on taking many x-ray images from various angles around the individual.
- These are then combined into a single three dimensional picture.
- More views leads to better 3D reconstructions.
- The drawback is the exposure to ionizing x-ray radiation.



Technique comparison

Technique	Spatial resolution	Temporal resolution	Perturbation
MRI	mm	sec	restricted movement
EEG	cm/mm	ms	involuntary effects (eg: eye blinks)
MEG	cm	ms	involuntary effects, restricted movement
PET	mm	min (!)	radioactive tracer, long sampling period
CT	cm/mm	ms/sec	ionizing radiation, restricted movement

Technique comparison

Technique	Properties measured	Activities observed
MRI	Tissue and fluid composition	Blood flow, structural changes
EEG	Electrical potential	Activation of brain regions.
MEG	Induced magnetic fields	Activation of brain regions.
PET	Localized features	Location of static objects.
CT	Solid and tissue structure	Unknown

A point of reference

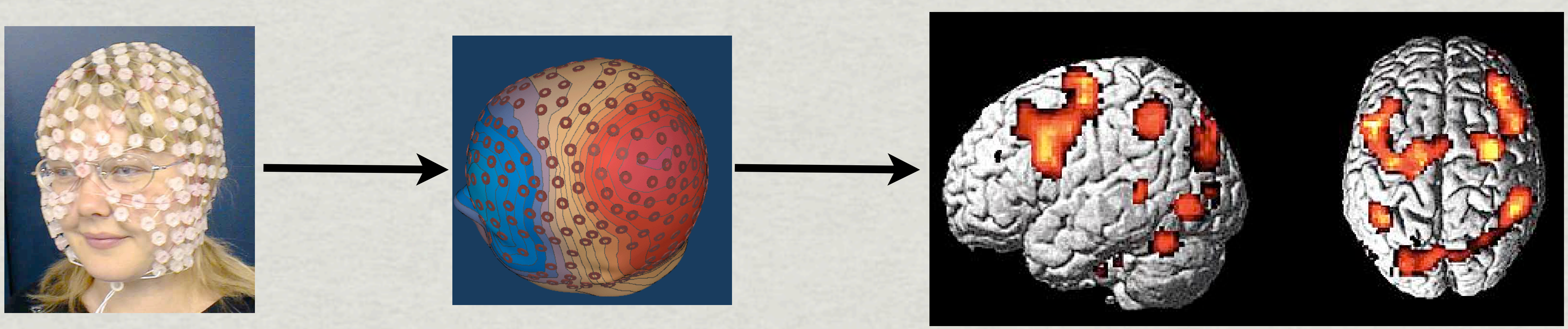
- How do these resolutions relate to the brain?
  - Neuron: 10-100 micrometer scale.
    - (1mm=1000um)
  - Activity is on the millisecond time scale.
    - This is good: we're getting close to this.

Our work

- Here at the NIC and EGI, we are interested in EEG.
- Why?
  - High temporal resolution.
  - Low perturbation on the individual.
  - Combined with techniques like MRI, we can get high spatial resolution too.

EEG

- So how do we use EEG to observe the brain?
- Recall that EEG is surface potential readings. We want an internal image or movie of the brain.



EEG

- This is an example of what EEG data tends to look like.

EEG

- Clearly the raw EEG data is not enough to give us a picture of the brain. This is OK though.
- There has been great success at using raw EEG to identify very interesting activities within the brain.
- The high temporal resolution makes it possible to observe very fast activities in the brain, meaning complex activities can be seen in detail.

EEG Example

- One example from the UO Brain Electrophysiology Lab was the use of EEG to observe the neural mechanisms employed by intelligence analysts looking for features in satellite imagery.
- People have used EEG to control a mouse cursor on the screen simply by thinking about it.
  - This is particularly exciting, especially with respect to aiding handicapped individuals.

EEG and Images

- Sometimes a 3D image is necessary though.
- In this case, we use what is known as a *source localization algorithm* to map the observations on the surface of the head back to the locations within the brain.
- This is actually quite a hard problem. I will go into detail on this shortly.

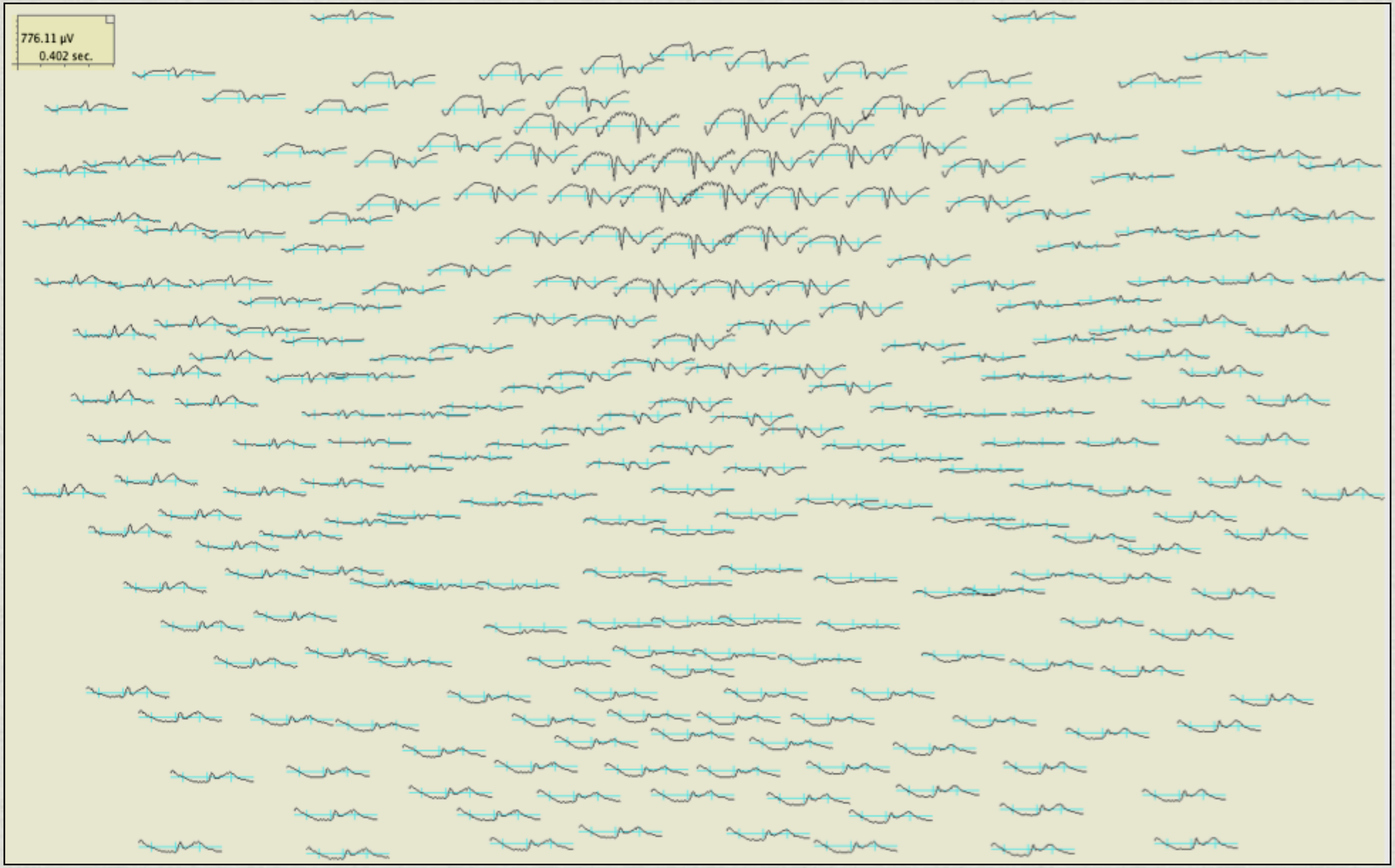
Analysis

- What are some of the questions we ask given raw EEG data?
  - How do we identify seizures or other important features in the data?
  - How do we identify features related to an activity performed by the subject?
  - How do we map surface measurements back to the sources inside the brain?

Analysis

- Here is what we are handed to perform our analysis:
  - 256 individual sequences of potential values measured at some regular sampling interval.
  - The sampling interval tends to be around 100-300Hz, so we have 100-300 samples per second.
  - In some cases, the measurements are taken all night long during sleep. 8 hours of sleep yields around 2,200,000,000 samples.

A snapshot of the head



Analysis

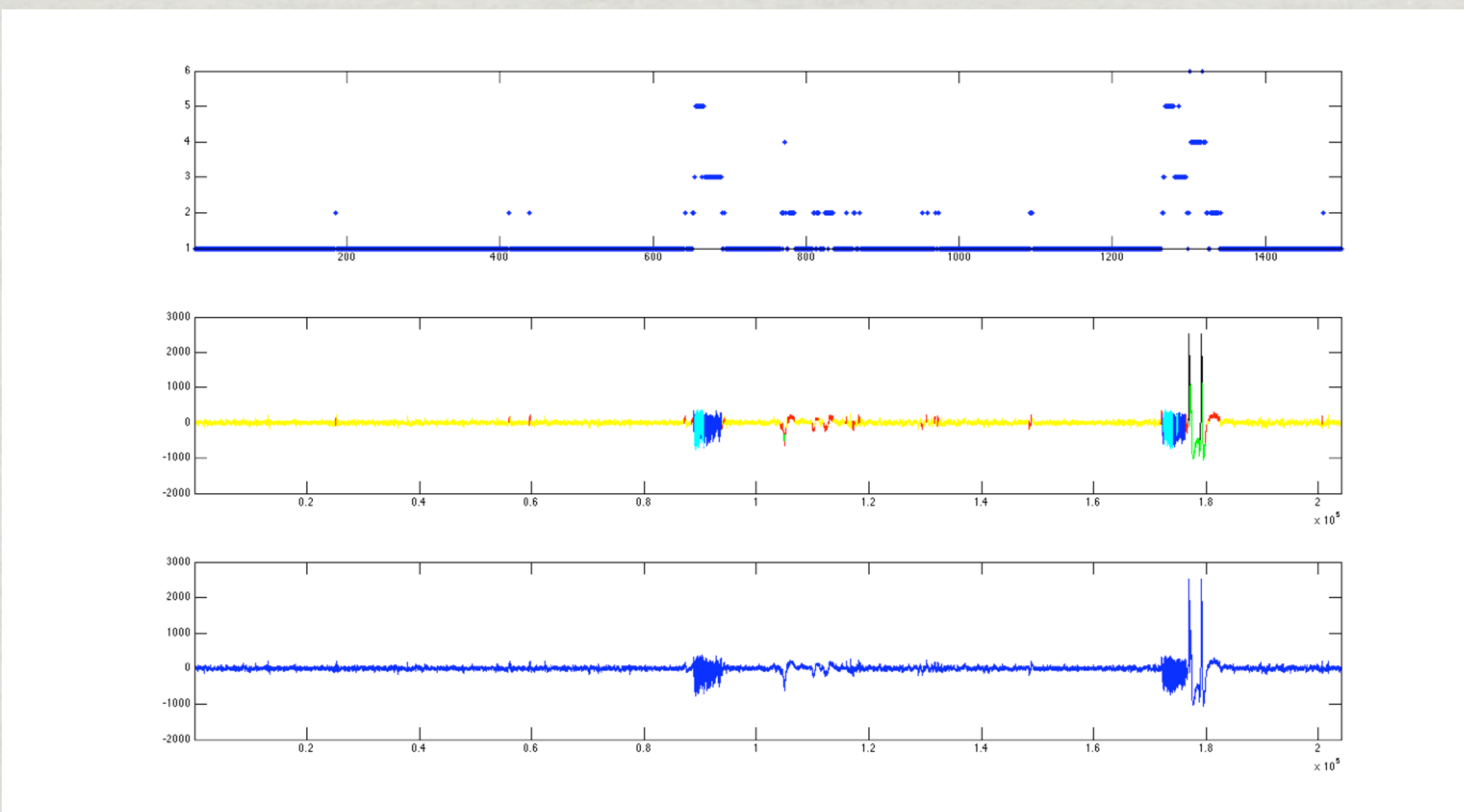
- That's quite a bit of data.
- What tools do we throw at the problem?
  - Statistical techniques.
  - Signal processing techniques.
  - Machine learning techniques.

Signal processing

- In signal processing, we try to identify features in the data by looking at it's periodic, or frequency, properties.
- The brain naturally has existing frequency characteristics related to basic function.
- Activation of specific areas causes changes in the frequency properties.
- Feature identification means finding the places in the signal where these frequency changes occur.

Seizure detection

- An example of this is detection of seizures. Here is some example data from a single channel.



FEATURE CLASSIFICATION

FEATURE IDENTIFICATION

RAW DATA

Seizure identification

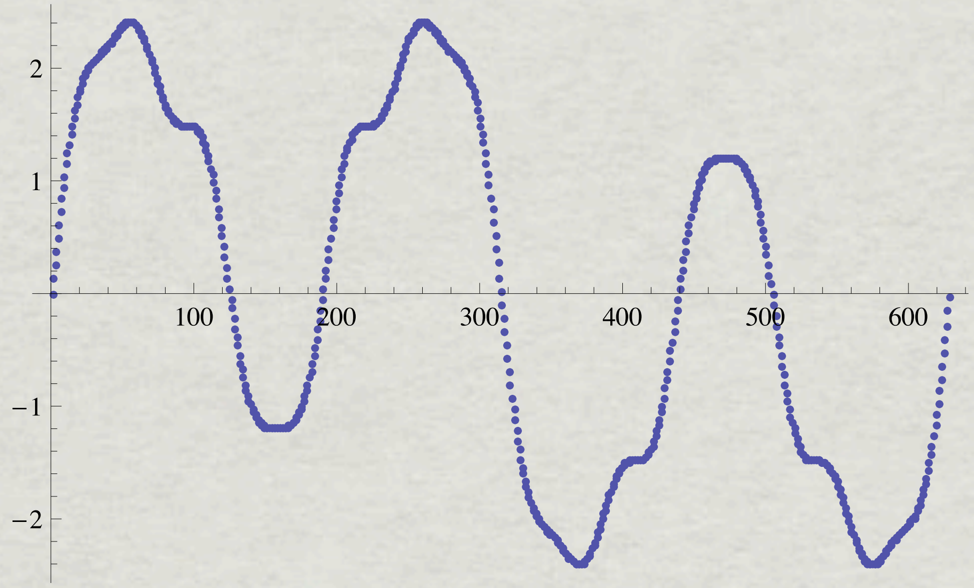
* What was that?
* The raw data is fed into an algorithm that looks at the signal properties over time, and attempts to determine when the signal has changed from one state to another.
* The basis of the algorithm is combining basic signal processing tools with machine learning techniques.

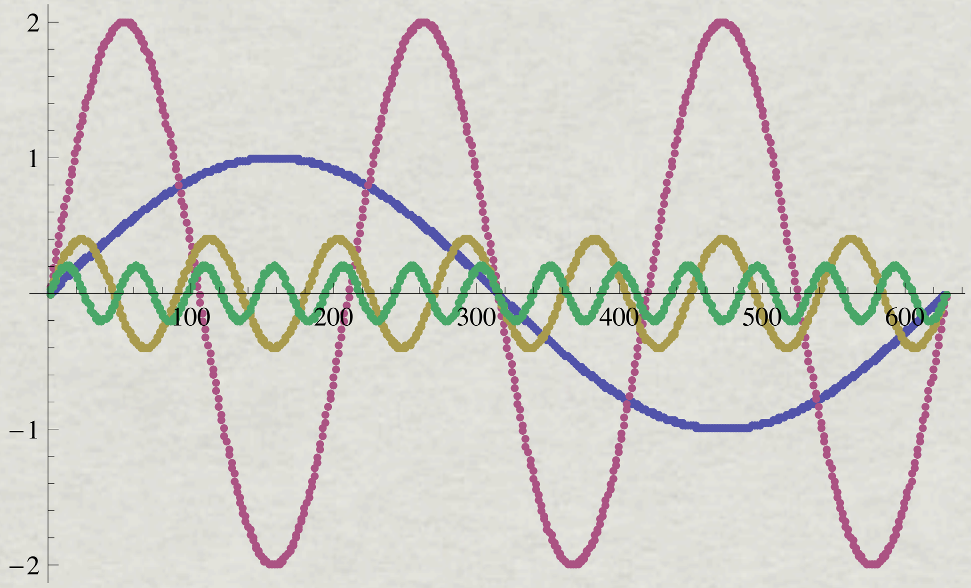
Signal processing

- Signal processing algorithms are a general class of algorithms used in many areas, not just EEG analysis.
- The basic algorithm we employ is one known as the Fast Fourier Transform. In a nutshell, given a signal, it breaks it into the simpler components that make it up.
- It's the basis of many technologies. FFTs are in cell phones, music players, graphics programs, games, etc...

FFT Concept

- The basic idea: break a signal into it's components.



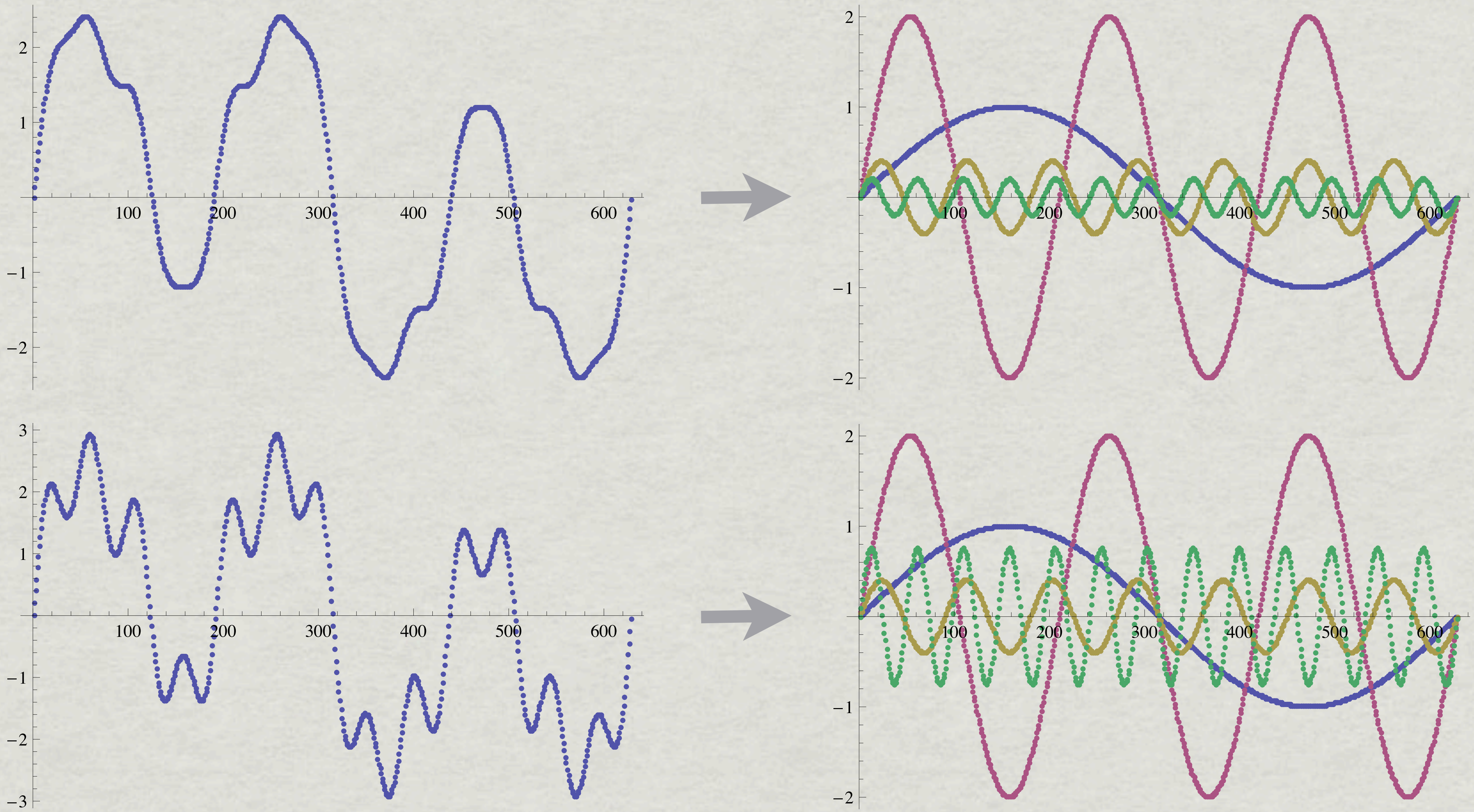


Finding features

- Once we have broken the signal into it's component parts, we want to find the features.
- This means we want to detect when some of the components change.
- How do we know when they have changed in a significant way?
- We use machine learning to make the decision when a component has changed in a significant way signaling the presence of a feature.

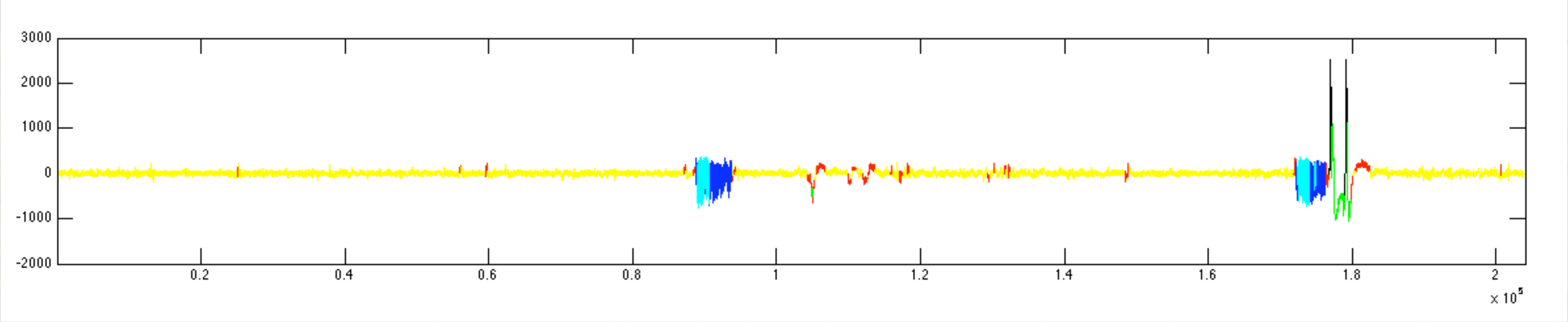
Component changes

- The change of a component is illustrated here:



Machine Learning

- The problem with this data is that there is no gold standard for what makes up a seizure. They differ between individuals.
- So, we let the computer identify what it believes to be the different classes of signal properties that are contained in the sequence.
- The technique used here is known as **clustering**. It is attempting to find the 6 most representative signal types found in the data.



Artifact removal

- As I mentioned earlier, one of the difficulties with EEG is the presence of artifacts that are not related to what you are observing.
- For example, when you blink your eyes, the potential characteristics of your scalp change leaving spikes and blips in the EEG data.
- This means you get spikes and blips in the EEG data that are not related to brain activity, but get mixed in with the brain data signals.
- If you want to observe the brain activity, you must clean the signal and remove these disruptive artifacts.

Source localization

* In some cases we want to not only identify features, but say something about where they originated in the brain.
* This requires mapping EEG data back to the 3D brain where activity occurs.

Source localization

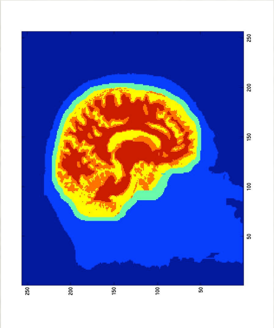
* This requires an intimate understanding of the head.
* An electrical signal originating in the brain has to move outwards through brain matter, fluids, bone and skin.
* The electrical properties of each of these materials is highly dependent on the individual. Your skull has different conductivity properties than my skull.

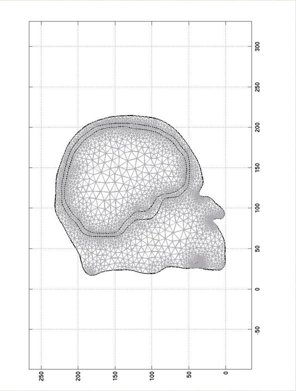
Source localization

- The process of performing this mapping back to the source from the surface is known as an **inverse problem**.
- Solving the inverse problem is mathematically hard.
- BUT, if we know something about the head, this constrains the number of possible sources a great deal. It allows us to eliminate guesses that are physically impossible.

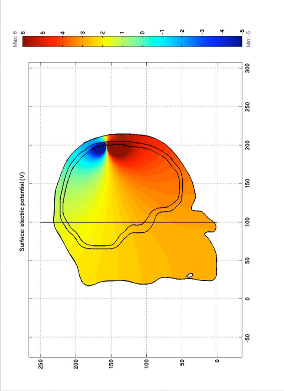
The problem

- So, we need a head model. This is a 3D picture of the structure of the head, in particular, the arrangement and electrical conductivity properties of the materials of the head.



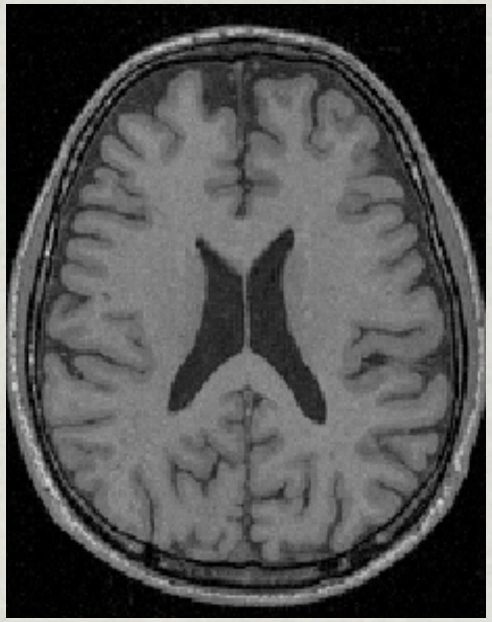


- You can't easily measure these conductivities and structures without invasive techniques.
- We use MRI data and physics models to build head models that can be used to estimate where sources came from.



MRI

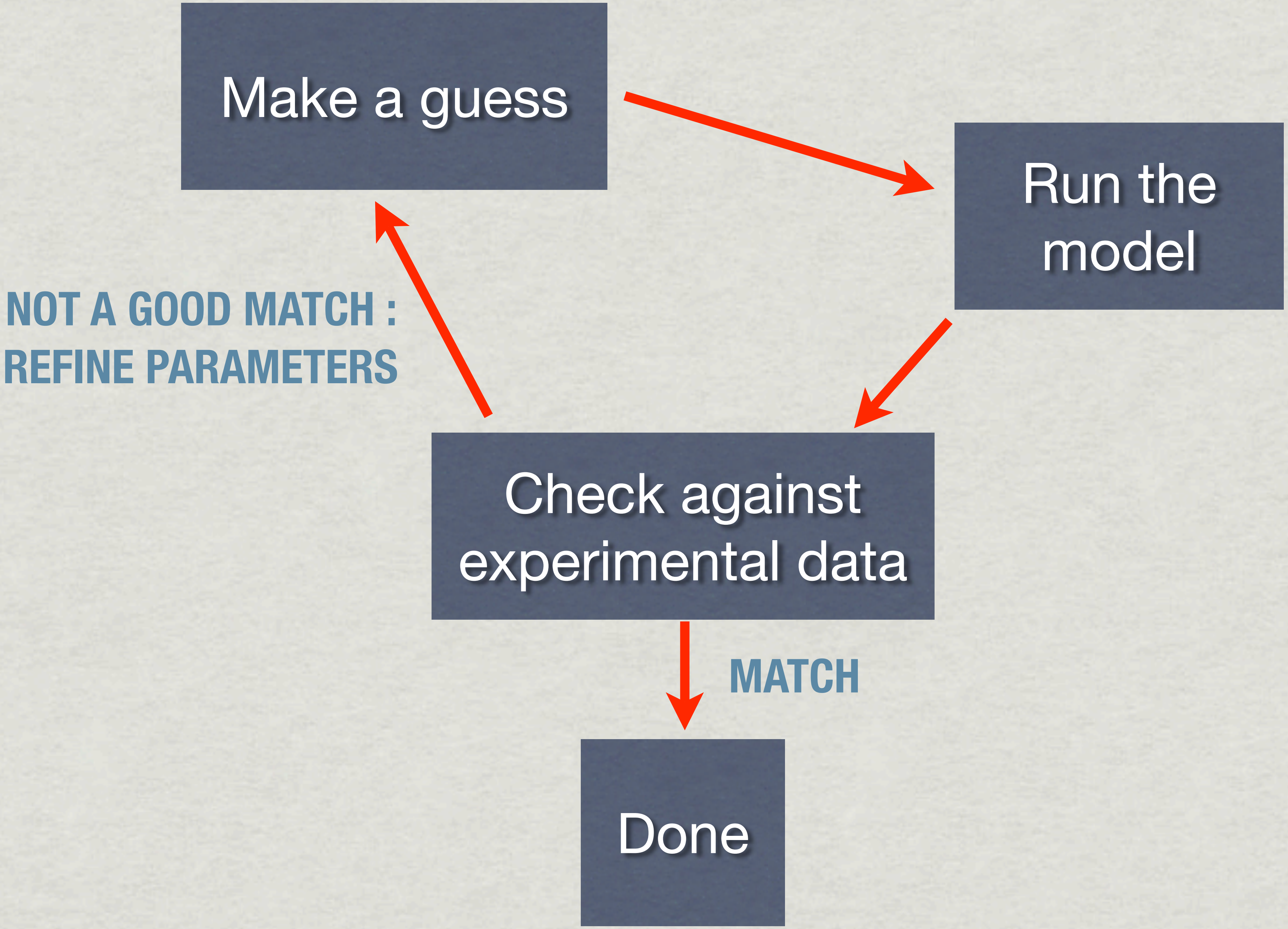
- We can start with MRI data to estimate the structure of the head.
- The process is known as **segmentation**, and was the subject of a recent UO PhD student's work.
- Segmentation takes an MRI image, and separates it into the different material classes (brain, skull, fluid, etc...)
- This forms the basis of the model. It provides a structural template from which we can start guessing the conductivity properties of the head.



Making a head

* This is a fairly challenging problem from a computational point of view.
* The method we use is known as an **optimization algorithm**.
* An optimization algorithm essentially makes educated guesses about the solution (in this case, the conductivity of the materials in the head), and tests how well it has done.
* This is then used to refine the guess and try again.

Optimization



Optimization

- How do we guide this?
- We start by injecting current into the head and measuring the potential observed all around the head as a result.
- A physics model then uses the guess for the composition of the head to see if the guess yields the same result that was observed experimentally for a given current injection.
- The head model is modified repeatedly until the physics model replicates what was experimentally measured.

Computational challenges

- There are many computational challenges to both of these problems:
  - Signal processing.
  - Head modeling and EEG source localization.

Massive amount of data

* There is a huge amount of data here. It is not unheard of to see multi-gigabyte files representing a single sitting.
* Algorithms tend to require clusters and other high performance computers simply to store the data in memory.

Many guesses

* When optimization is occurring to identify a good head model, there are many runs over and over of the physics model.
* The physics model itself is complex, and can run quickly on high performance computers.
* If we want to run more than one instance of the model to try multiple head guesses at the same time, we need even more computers.

Combinations

- In some analysis, the computation has many parameters related to the algorithm.
- For example, in signal processing, one may not know in advance how many components there are to a signal or how many different types of features may occur.
- To try all different possible combinations of parameters requires many, many computations.

Challenges in the present

* This poses some significant challenges to applying these techniques.
* One candidate area for EEG is to aid in traumatic brain injury patients.
* Time is critical here. We can't wait for a computer to take a day to generate a head model.
* An active area of research is how to build analysis and computational tools that can run very fast, employing high end computing tools like supercomputers and novel processors.

State of the art

- So where are we?
- Right now, we can build head models to understand the internal function of the brain.
- The models take a while to compute, and the quality (spatial resolution) leaves much to be desired.
- In signal processing, we can identify features, but tools require a great deal of hands on intervention. We cannot, at the present, detect and identify arbitrary activities in the brain.

Where are we going?

- We’re getting there.
- Computers are getting faster.
- Measurement techniques are improving as hardware improves.
- Mathematical advances are leading to algorithms that give more robust, reliable results.

Questions?