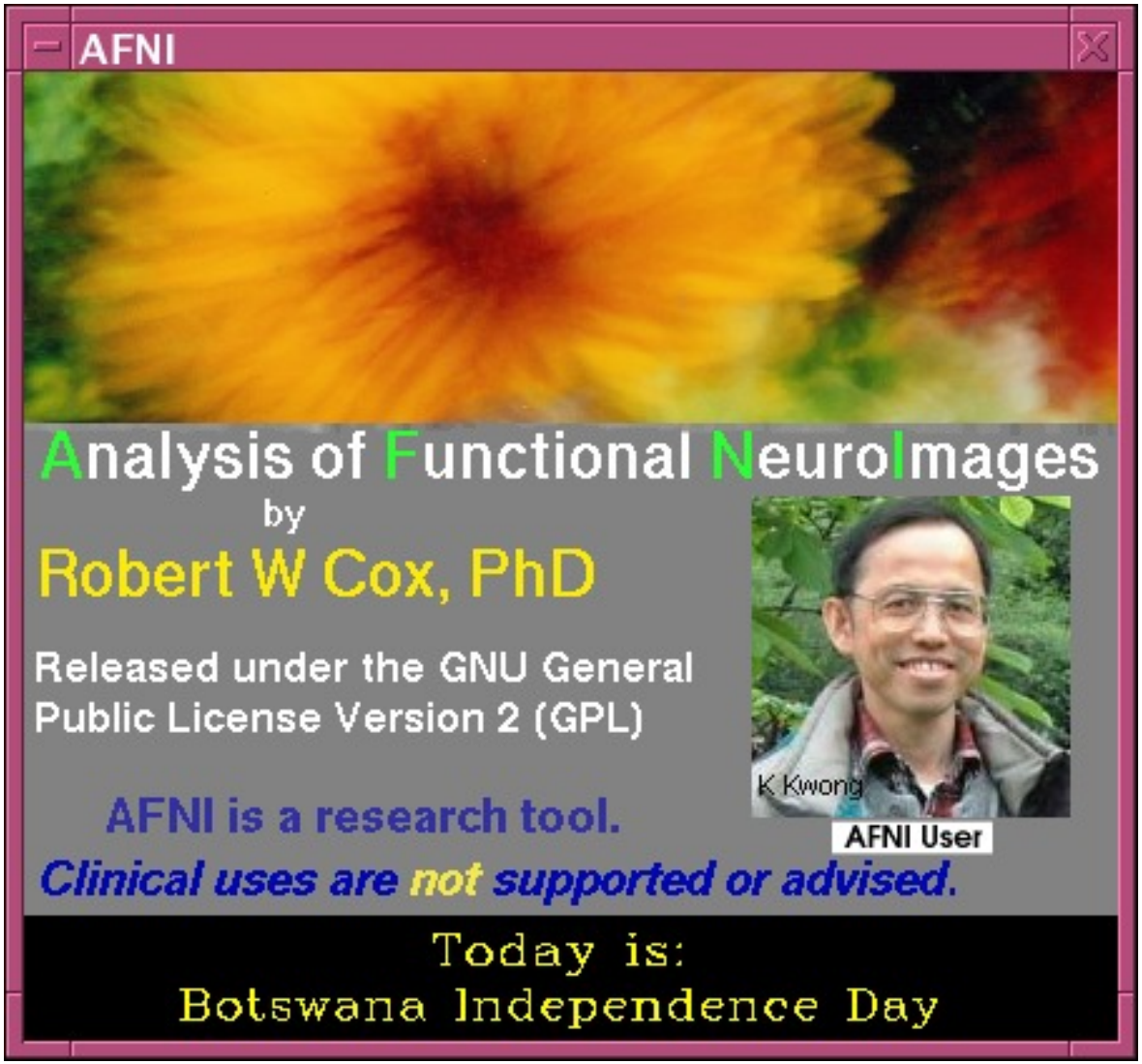
AFNI: Introduction and Concepts



http://afni.nimh.nih.gov/afni/

FMRI Data Analysis Principles

- Data analysis always takes place in the context of a mathematical and statistical model for the relationship between the observations (the numbers in the images) and the desired information (the location, timing, ..., of neural activity)
- Things that make FMRI data analysis intricate:
  - ⋆ The data↔activity/physiology relationship is complex with many facets, and is only partially understood
  - ⋆ Different experimental designs interact to varying degrees with different facets of the data↔activity/physiology relationship:
    - ↪ Block paradigms:
      Low frequency noise in FMRI data is often larger than high frequency noise
    - ↪ Event-related paradigms:
      Additivity of the BOLD response is open to question when the responses from closely spaced stimuli overlap;
      BOLD signal changes are smaller than for block paradigms
    - ↪ Pharmacologic challenges:
      Usually at very low frequencies (mHz or less);
      Mathematical model of response is not clear;
      Challenge itself may alter the hemodynamic response

  - ↪ Patient vs. Normal studies:
    Patients tend to move their heads more, making their data different from controls in a non-interesting way that can confound interesting differences (e.g., smaller areas of activation in patients may be due to poorer activation detectability due to larger/more frequent head movements)
  - ↪ Inventiveness of Neuroscientists and Psychologists:
    It seems that practically every time I turn around, they come up with a new experiment, or a new type of information about the activation that they want to extract from the data

- As a result, FMRI data analysis is not now (nor likely to be soon) a stereotyped activity that can be packaged into a 'do everything' software package that solves all your problems for you
- Instead, the neuroscientist must understand the mathematical models of the signal and the noise in order to pick the tools to use, to know when the existing tools aren't adequate, and to prompt the development of new tools
  - ⋆ 'Tools' here means mathematical models, algorithms for extracting information from data using the models, and software that implements the algorithms
- A very solid grounding in statistics is the most important non-neuroscience/non-psychology skill that a successful FMRI investigator needs
  - ⋆ Otherwise you will use the wrong analysis tools, or misuse the correct tools

AFNI = Analysis of Functional NeuroImages

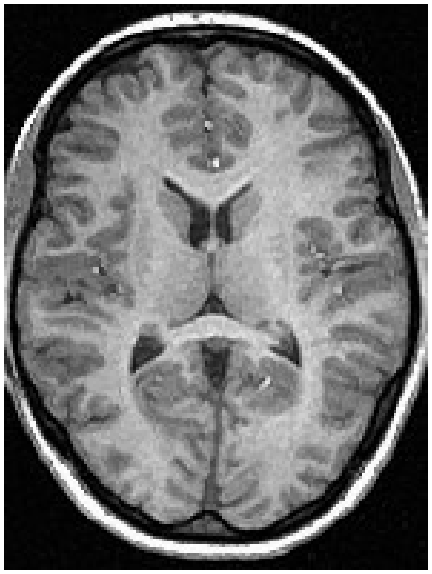
- Developed to provide an environment for FMRI data analyses, and a platform for development of new software to fit into this environment
- AFNI refers to both the program of that name and the entire package of auxiliary programs and plugins (more than 100 of them now; some trivial, some complex)
- Important principles I had in mind when creating AFNI (starting back in 1994):
  - ⋆ Allow user to stay close to data and to view it in many different ways
  - ⋆ Allow user to put pieces together in different ways to make customized analyses
  - ⋆ "Provide mechanism, not policy"
  - ⋆ Allow other programmers to add features that can interact/cooperate with the rest of the package
- Important principles I try to follow:
  - ⋆ Fix significant bugs as soon as possible $\Longrightarrow$ but I get to define 'significant'
  - ⋆ Nothing is secret or hidden $\Longrightarrow$ but maybe not well documented
  - ⋆ "Release early and often" $\Longrightarrow$ all users are beta-testers for life
  - ⋆ Help the user $\Longrightarrow$ until my patience runs thin

A Few Fun Tools from the AFNI Package

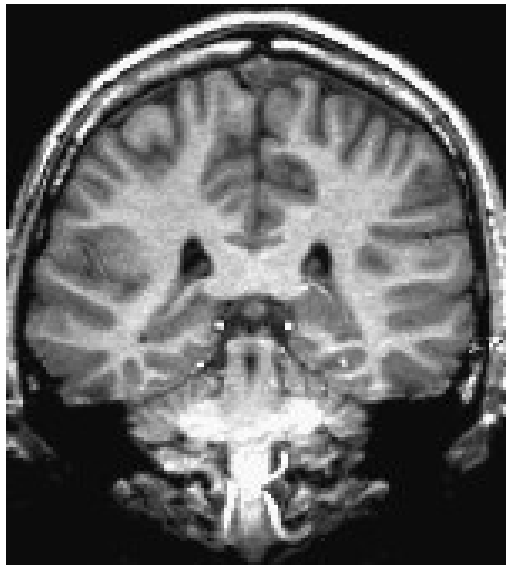
- Switch viewing/analysis between many different datasets
- Image display in axial, sagittal, and/or coronal views (with multi-image montages)
- Time series graphing of square regions linked to image viewers
  - ⋆ i.e., click on a pixel and see the graph of its data
- Linked image/graph viewing of multiple 3D datasets
  - ⋆ i.e., linked scrolling through multiple brains
- Computation of activation maps using correlation, linear and nonlinear regression
- Color overlay of activation maps onto higher-resolution anatomical images
  - ⋆ resampling of lower-resolution functionals is handled on the fly
- Display of volume rendered anatomy with activation maps embedded
- Interactive thresholding of functional overlays
- Transformation to Talairach coordinates
  - ⋆ followed by voxel-wise statistical analysis of inter-subject data (e.g., ANOVA)
- Manual selection of regions-of-interest (ROIs)
  - ⋆ followed by statistical analysis of ROI-averaged data

FMRI Background Concepts

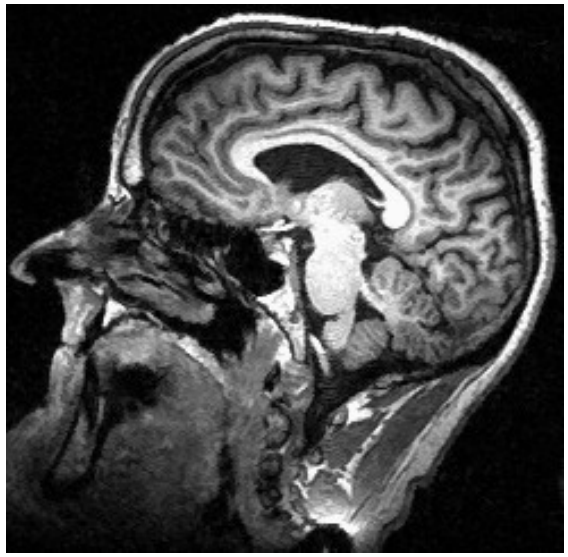
- Typical FMRI experiment produces at least two kinds of images:
- High-resolution T1-weighted anatomical (AKA structural) volumes
  - ⋆ Imaging methods are called SPGR by GE, MP-RAGE by Siemens, ...
  - ⋆ Takes 3–9 minutes to acquire one volume at about 1 mm^3 resolution



[Axial SPGR]



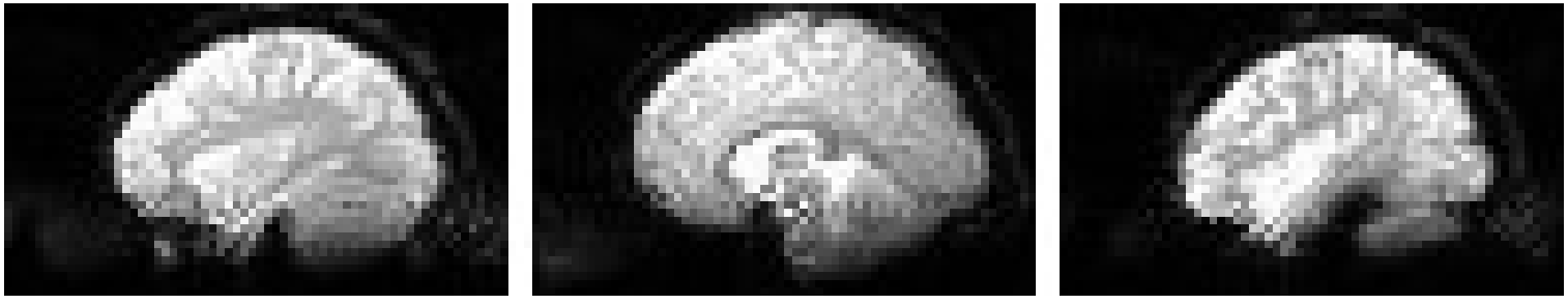
[Coronal SPGR]



[Whole Head Sagittal SPGR]

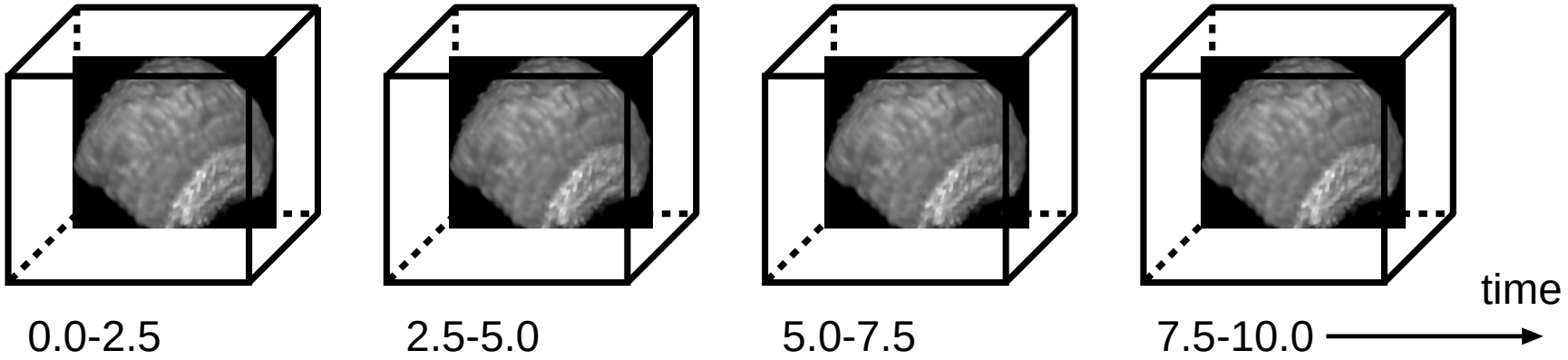
  - ⋆ FMRI purposes for such images:
    - ↪ Anatomical localization (recognizing where you are in the brain)
    - ↪ Recognition of gray and white matter regions by image intensity
    - ↪ Extraction of cortical surface (e.g., gray-white boundary)

- Low-resolution T2-, T2*-, or perfusion-weighted functional volumes
  - ⋆ Several similar imaging methods (pulse sequences) are in use:
    EPI (echo-planar imaging) and Spiral are the most common
  - ⋆ Takes $\approx$ 100 ms to acquire a single 2D slice
    (exact speed depends on pulse sequence and scanner hardware)



[Three Sagittal EPI Slices]

- ⋆ Speed of acquisition $\Longrightarrow$ can acquire $\approx$ 100 brain volumes in a few minutes



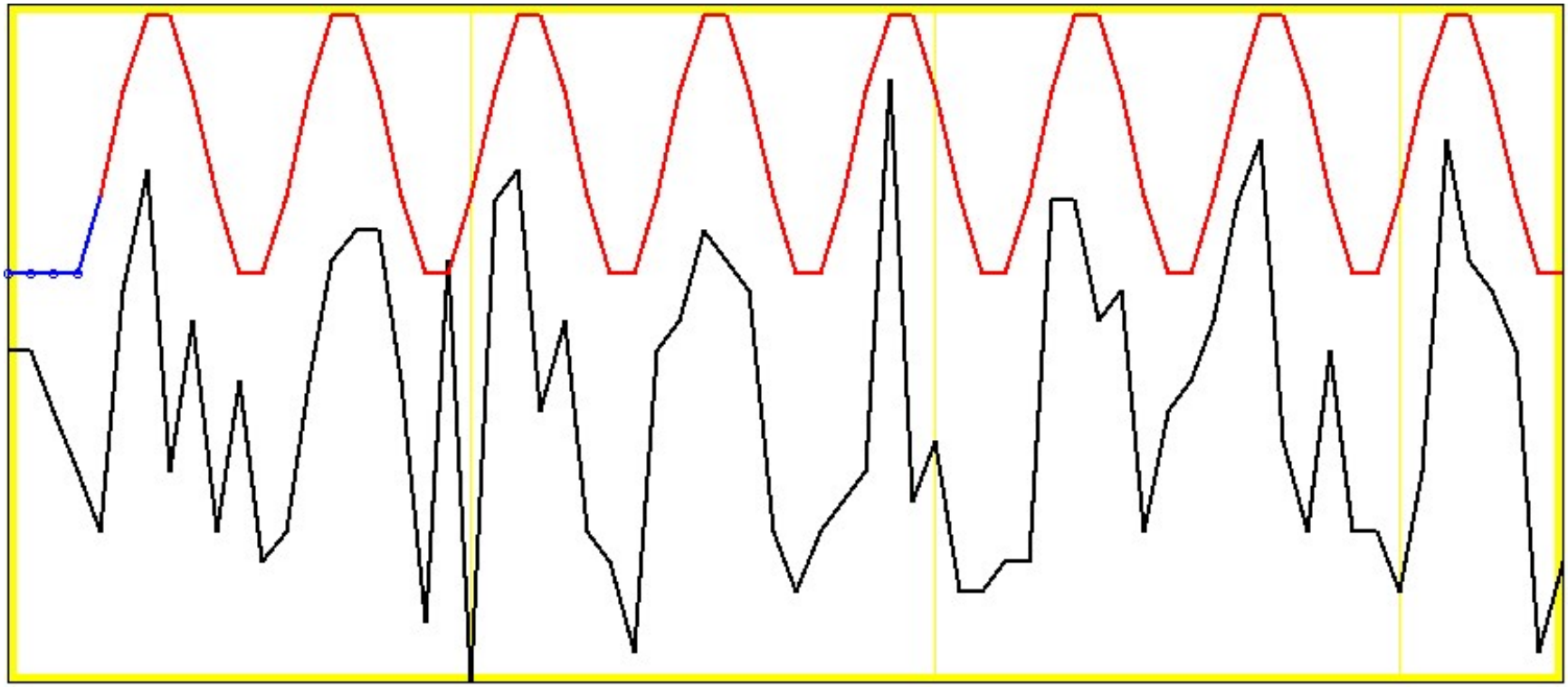
[Cartoon of 3D Brain Image Time Series, with TR=2.5 s]

⋆ Typical brain size (L-R) $\approx$ 140 mm $\Longrightarrow$ usually use 3-6 mm slice thickness

⋆ FMRI purposes for such images:

↪ MRI signal intensity depends on blood flow and oxygenation changes

↪ Blood flow and oxygenation fluctuate with neuronal metabolism on a 5–10 s timescale:

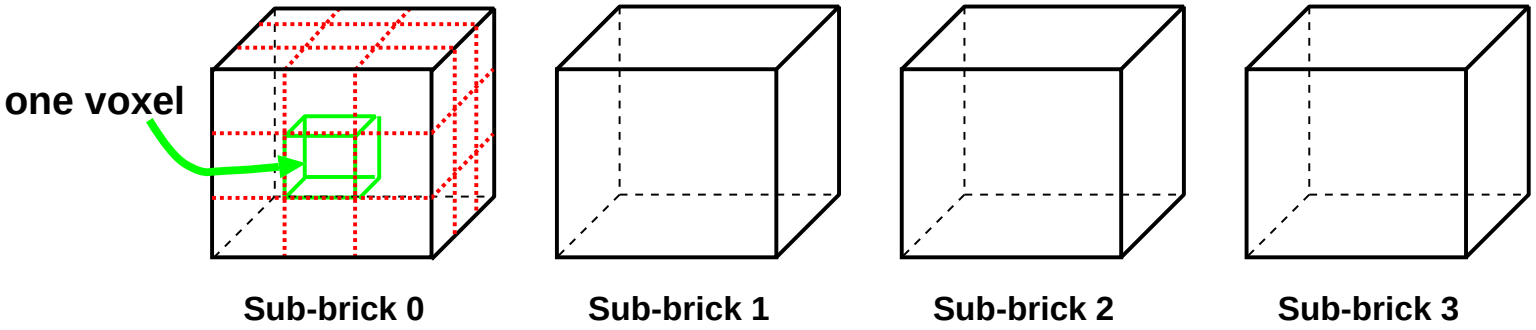


[Graph of Data Time Series from One Voxel, with Task Alternation Shown On Top]

- For background information on FMRI physics, see (near bottom) `http://afni.nimh.nih.gov/afni/mrip/index.html`

Fundamental AFNI Concepts

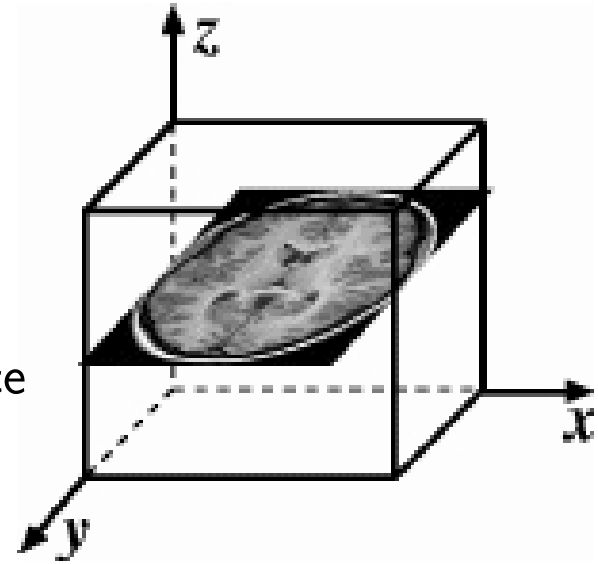
- AFNI is the name of both the original interactive program and the collection of batch (command line) programs that have grown up around it in the last 7 years.
- Basic unit of data in AFNI is the dataset:
  - ⋆ A collection of 1 or more 3D arrays (tables) of numbers
    - ↪ Each entry in the array is in a particular spatial location in a 3D grid (a voxel)
    - ↪ Image datasets: each array holds a collection of slices from the scanner; each number is the signal intensity reported by the scanner for that particular voxel
    - ↪ Derived datasets: each number is computed from one or more other datasets (e.g., each voxel value is the average intensity at that spatial location from a number of different image acquisitions)
  - ⋆ Each 3D array in a dataset is called a sub-brick; there is one number in each voxel in each sub-brick:



[Cartoon of a $\mathbf{3} \times \mathbf{3} \times \mathbf{3}$ AFNI Dataset with 4 Sub-Bricks]

- Different types of numbers can be stored in datasets: 8 bit bytes (grayscale photos); 16 bit shorts (MR images); 32 bit floats (calculated values)
- Besides the voxel values, a dataset also contains auxiliary information, including (some of which is optional):
  - ⋆ xyz-dimensions of each voxel (in mm)
  - ⋆ Orientation of dataset axes;
    for example, x-axis = R-L, y-axis = A-P, z-axis = I-S $\Longrightarrow$ Axial slices

    R=Right, L=Left,
    A=Anterior, P=Posterior,
    S=Superior, I=Inferior



  - ⋆ Location of dataset in scanner coordinates;
    in particular, the slice offset = z-coordinate of 1st slice
  - ⋆ Time/date of creation
  - ⋆ Time between sub-bricks (TR), for 3D+time datasets

  ↪ 3D+time datasets are the basic unit of FMRI data (one per imaging run)

  - ⋆ Type of data stored in each sub-brick (anatomical? functional? statistical?)
  - ⋆ Statistical parameters associated with each sub-brick;
    e.g., a t-statistic sub-brick has the degrees of freedom (a single number) stored

- Datasets are stored in 2 files:
  - ⋆ The `.BRIK` file holds all the numbers in all the sub-bricks:
    a $\mathbf{100 \times 100 \times 100}$ dataset would have $\mathbf{1,000,000}$ numbers per sub-brick
  - ⋆ The `.HEAD` file holds all the auxiliary information
- Datasets can be in one of 3 coordinate systems (also called views):
  - ⋆ Original or `+orig` view: The original (scanner) coordinate system
  - ⋆ AC-PC Aligned or `+acpc` view: Where the dataset is rotated so that the anterior commissure (AC) and posterior commissure (PC) are horizontal, the AC is at $(x, y, z) = (0, 0, 0)$, and the longitudinal (inter-hemispheric) fissure is vertical
  - ⋆ Talairach or `+tlrc` view: Where the dataset has been further squeezed/stretched to have its size conform to the Talairach-Tournoux atlas;
    coordinates in this view are often called Talairach or stereotaxic coordinates
- Dataset filenames consist of 3 parts:
  - ⋆ The user-selected prefix (almost anything)
  - ⋆ The view (one of `+orig`, `+acpc`, or `+tlrc`)
  - ⋆ The suffix (one of `.HEAD` or `.BRIK`)
  - ⋆ Example: files `ElvisPresley+tlrc.HEAD` and `ElvisPresley+tlrc.BRIK`

  - ⋆ When creating a dataset with an AFNI program, you specify the prefix — the program does the rest

- The `to3d` program is used to read in image files and create an AFNI dataset
  - ⋆ Can read following formats you're likely to get from reconstruction software: GE `I.`; Siemens `.ima`; ANALYZE `.hdr/.img`; DICOM part 10
  - ⋆ Also can read some non-MRI image files: JPEG `.jpg`; GIF `.gif`; PPM `.ppm`
    ↪ Can make AFNI datasets out of images from digital cameras
  - ⋆ Also can read 'naked' image files: just numbers with no header information

- AFNI and its associated programs can also read 3D and 4D datasets stored in several other formats (without conversion to the AFNI format)
  - ⋆ MINC format — `.mnc` files ..... [from MNI]
  - ⋆ ANALYZE 7.5 format — `.hdr/.img` file pairs ..... [very common]
  - ⋆ NIFTI-1 format — `.nii` files ..... [new format]
  - ⋆ CTF SAM format — `.svl` files ..... [MEG data analysis]
  - ⋆ Columns of ASCII numbers — `.1D` files ..... [very simple format]

- AFNI programs (mostly) write datasets out in the AFNI format
  - ⋆ Converter programs exist to translate AFNI datasets to MINC and ANALYZE formats.
  - ⋆ In the future, AFNI programs will be able to write NIFTI-1 datasets directly.

- Datasets are stored in directories called sessions
  - ⋆ All the datasets in the same session, with the same view, are presumed to be aligned in xyz-coordinates — voxels with the same value of (x, y, z) are presumed to correspond to the same brain location
  - ⋆ In the interactive AFNI program, you can overlay one dataset on top of another, even if their orientations and voxel sizes differ — this is how low-resolution functional data is combined with high-resolution anatomical data to produce cool looking images
  - ⋆ Typical AFNI contents of a session directory are all the data derived from a single scanning session for one subject:
    - ↪ Anatomical dataset (1 sub-brick)
    - ↪ 10–20 3D+time datasets from EPI functional runs (100? sub-bricks each)
    - ↪ Statistical datasets derived from the 3D+time datasets, showing functional activation (we hope)
    - ↪ Datasets transformed from `+orig` coordinates to `+tlrc` coordinates — for comparison and integration with datasets from other subjects
- AFNI will load all the datasets in all the directories specified on its command line
  - ⋆ Might be 100s or 1000s of datasets
  - ⋆ Current limit: max of 1024 datasets per session
  - ⋆ Current limit: max of 80 sessions per AFNI run

Installing AFNI on Your Computer

- AFNI runs on Unix systems: Linux, Sun, SGI, Mac OS X
  - ⋆ Can run on Windows, but only using the Cygwin Unix emulator
- Best way to install: have a computer that somebody else manages for you, and get him/her to do this task
- Second best way: if you are at the NIH, then I can auto-install AFNI upgrades onto your system, if you give me an account there
- Third best way: install a pre-compiled binary package from the AFNI distribution computer using program wget;
  - ⋆ The following command installs the Linux binaries:

```
wget -nv -m -np -nH -P /usr/local/abin --cut-dirs=3 \
     http://afni.nimh.nih.gov/AFNI/bin/linux_glibc22/
```

  - ⋆ See `http://afni.nimh.nih.gov/afni/afni_wget.shtml` for more details
- Fourth best way: download the source code and compile it
- AFNI Web site: `http://afni.nimh.nih.gov/afni`
  - ⋆ Documentation, FAQ list, Installation instructions, Humor, ...
- AFNI is updated fairly frequently (monthly or so)