functional Magnetic Resonance Imaging – Methods

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3/4

Next ~~3~~ 2 lectures

1. Spatial and temporal properties of fMRI
   (+ linearity, convolution)
2. Signal and Noise
   (+ Fourier domain, convolution)
3. Preprocessing of fMRI data
   (+ common software tools, registration)
4. Statistics + experimental design
   (+ linear regression, GLM,
   multiple comparisons)

Matlab

```
>> demo % opens demo window
>> help stats % statistics toolbox
>> help images % image proc toolbox
>> why % Provides succinct answers to
   almost any question.
```

Recap: *last lecture*

Data: indexing

- multi-dimensional (n-dimensional) arrays
- we can **slice** data in different ways, e.g.

```
>> data(:,:,12,1)
   % get image at z=12 at t=1
```

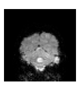
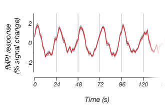


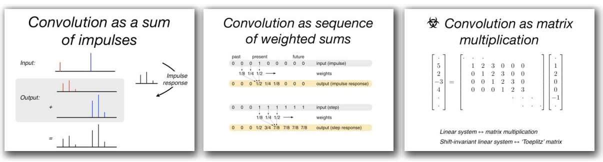
image processing, spatial filtering, ...

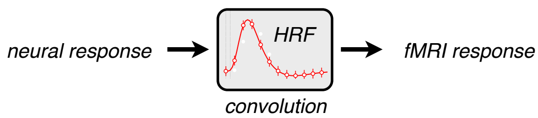
```
>> data(1,1,12,:)
   % get timeseries at [1,1,12]
```



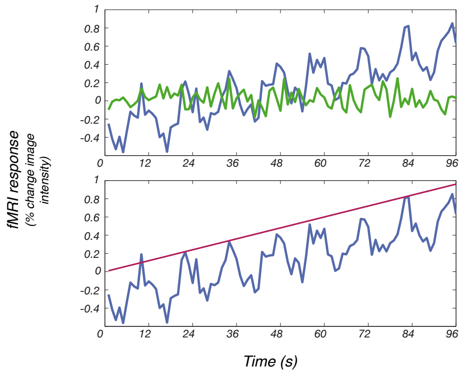
"voxel-wise" statistics, temporal filtering, ...

Convolution, 3 Ways





Noise + Drift



high-frequency noise

drift

Sources of Noise

1. **Intrinisic/thermal noise:** in subject + hardware
2. **System noise:** imaging hardware; e.g. scanner drift, small changes in B_0 over time, ...
3. **Subject motion & physiological noise:** swallowing, respiration, heartbeat, ...
4. **Non-task related neural variability:** e.g. attentional state of subject, coffee?, ...
5. **... if averaging across subjects:** differences in HRF can introduce *intersubject* variability

intra (1–4)

inter (5)

Differences in HRF across subjects

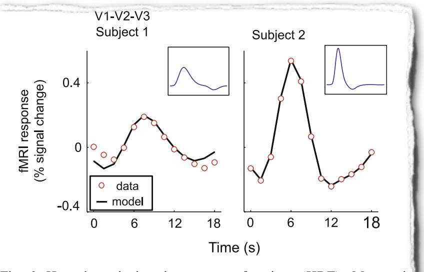


Fig. 3. Hemodynamic impulse response functions (HRF). Measured HRFs (red circles) and model fits (black curves) for early visual cortex (V1–V3) in two example subjects (Subjects 1 and 2). Data were modeled by a difference of two gamma functions. The model fits (black curves) reflect not only the best-fit HRF parameters (shown in inset) but also the specific sequence of experimental trials. Note the very different shape of the HRFs for the two subjects.

in early visual cortex

cf. time to peak

Offen et al (2008) Vis Res

Bird's eye view:
What are we trying to achieve?

... it depends!

Many cognitive studies: ***where are the areas more active in Condition A than Condition B***

"Areas involved in discriminating two vibrotactile stimuli applied to index finger [versus stimuli only]"

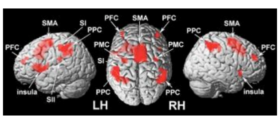


Figure 2. Cortical regions involved in frequency discrimination (contrast: discrimination trials > "null trials"). Significant signal changes were found in the SI and SII contralateral to the stimulated index finger. In addition, we found activation in the supplementary motor cortex (SMA), the premotor cortex (PMC), the posterior parietal cortex (PPC), the anterior insula, and the prefrontal cortex (PFC) of both hemispheres (MNI coordinates and *t* scores are listed in supplemental Table 1, available at www.jneurosci.org as supplemental material). LH, Left hemisphere; RH, right hemisphere.

10 subjects

Pleger et al (2006) J Neurosci

Many software packages...

AFNI *

SPM *

FSL *

FreeSurfer

caret5

SurfRelax

BrainVoyager

R

Octave

SciPy.org

Python

Matlab

C/C++
GNU Scientific Library

mrTools
Stanford / NYU tools

Steps in Analysis

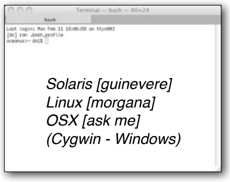
1. **Get data off scanner** & into right file format
   `PAR/REC, Nifti, Analyze, DICOM, MINC`
2. **Preprocess** (motion-correction, slice-time correction, filtering, ...)
3. Do some statistics to get a **statistical map**
4. **? Register / combine data** across subjects
5. **Render maps** in different formats
   (on high-resolution anatomy, flat maps, ...)
6. **? Plot curves**, compare data + fits, look at data in many different ways, ...

Get data off scanner

1. ... not always as trivial as you might think
2. **PAR/REC** is a Philips data format that can handle complicated data (>1 stacks, echos, mag + ph, ...)
3. many fMRI analysis tools expect **NIFTI** format

```
ds1$ ptoa
```

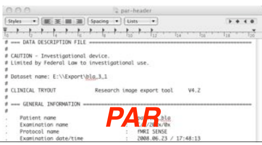
conversion tool written by
Dr Paul Morgan
(UoN, Academic Radiology; now MUSC, South Carolina)



PAR/REC

- data comes in **pairs** of files: `fname.PAR, fname.REC`
- the **PAR** part is a text file that contains information about the session, how slices were prescribes, TE, flip angles, reconstruction sizes,...
- the **REC** part is a binary file that contains the data

Text editor



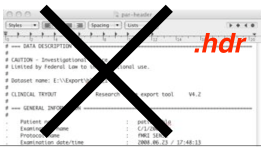
UNIX Terminal

```
ds1$ more fname.PAR
```

NIFTI/Analyze

- data comes in **pairs** of files: `fname.hdr, fname.img`
- or as a single file (header is inside file): `fname.nii`
- or even compressed: `fname.nii.gz`
- less information than in PAR/REC files, **but** more programs use it

Text editor



UNIX Terminal

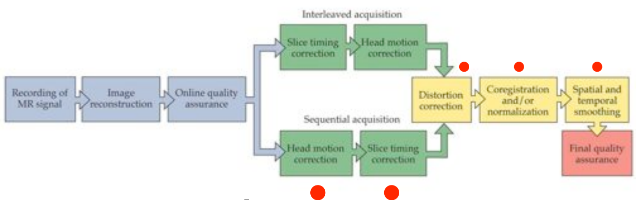
```
ds1$   fslinfo fname.img
ds1$   fslhd fname.img
```

Terminal

```
ds1$ <some unix command>
ds1$    <file that contains a bunch of unix commands>
```

- many analysis tools: can type a command in a shell/terminal, rather than clicking buttons.
- for large datasets or repetitive tasks, it is often faster to write a **script** than to click the mouse 10^6
- e.g. all commands for FSL tools can be accessed that way

Data Preprocessing



hopefully done at MR centre

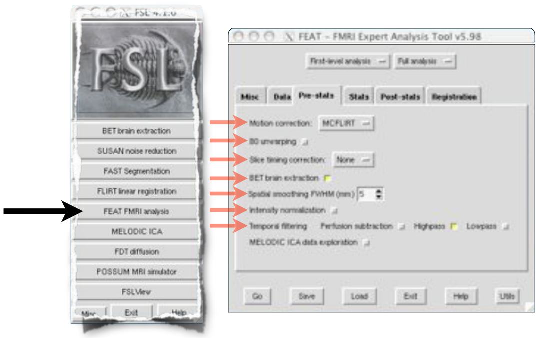
...over here, data are your responsibility!
(Also understanding what happens in analysis)

case study
FMRIB Software library (FSL)

Data Preprocessing

- most software packages implement a very similar set of preprocessing steps (because they make sense)
- ... may be called different things (specific jargon)
- check SPM, BrainVoyager, AFNI documentation for details:
  - links on my webpage *http://tinyurl.com/5kcvqv*
  - Google: *SPM, BrainVoyager, AFNI*

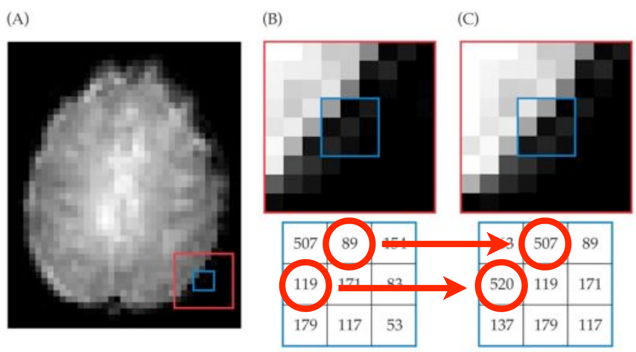
Data Preprocessing



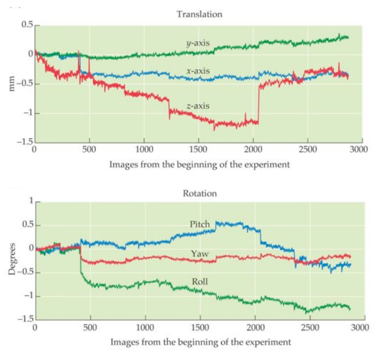
Data Preprocessing

- **Aim 1:** reduce unwanted variability in the data (this increases functional SNR)
- **Aim 2:** prepare data for statistical analysis (e.g. spatial smoothing can reduce the effective number of statistical tests).
- **Additional aim:** get data ready for display / averaging across subjects

Motion correction



Motion correction



movement for solid bodies

3 parameters for translation

3 parameters for rotation

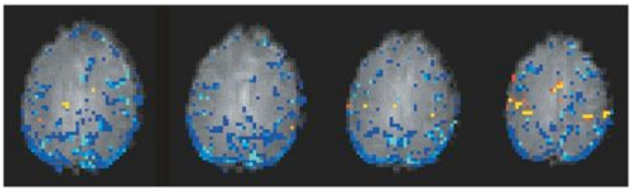
6 parameters = 6 DOF
"degrees of freedom"

Motion Correction

- **AIR** automated image registration (Woods)
- **SPM** (Ashburner)
- **FLIRT / FSL** (Jenkinson)
- **Robust alignment** (Nestares & Heeger)
- ... *...all try to minimize some **error term between a reference image** (say, the first image acquired) and **the image at each other time point.***

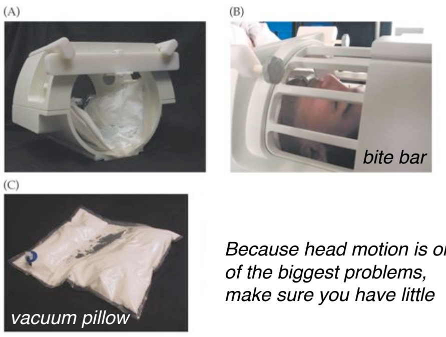
  ! By definition the algorithm finds a minimum – make sure the algorithm's solution is reasonable.

Motion Correction



Typical edge artefact in statistical images, due to (residual) motion...

Avoid Motion!



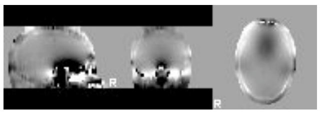
Because head motion is one of the biggest problems, make sure you have little

B_0 unwarping

- correct geometric *distortions* in EPI data (caused by inhomogeneities in local magnetic field) `fugue`
- data for this (phase images) often show wrapping, i.e. jumps from 2π back to 0 (need to correct for those jumps first...) `prelude`

your Physics colleagues have figured out a faster way:

Olivier Mougin, Sam Wharton

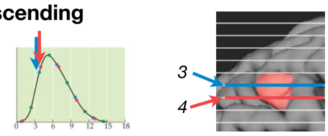


fieldmap (image intensity ∝ local field)
units: [Hz], [rad/s], [T]

http://www.fmrib.ox.ac.uk/fsl/fugue/

Slice (acquisition) time correction

- example: repetition time (TR) 2s, 10 slices
- slice order **a- / de-scending**

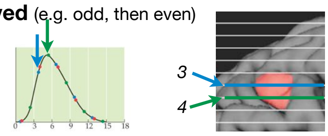


Time (s)	0.2	0.4	0.6	0.8	1.0	1.2	1.4	1.6	1.8	2.0
ascending	1	2	**3**	**4**	5	6	7	8	9	10

0.2s

Slice (acquisition) time correction

- example: repetition time (TR) 2s, 10 slices
- slice order **interleaved** (e.g. odd, then even)



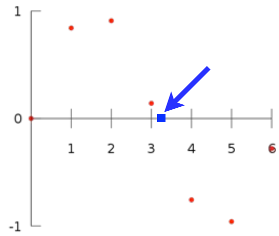
Time (s)	0.2	0.4	0.6	0.8	1.0	1.2	1.4	1.6	1.8	2.0
interleaved	1	**3**	5	7	9	2	**4**	6	8	10

1.0s

Slice (acquisition) time correction

1. Do nothing!
2. Deal with difference in timing at the time of statistical analysis (bookkeeping nightmare?)
3. Resample / interpolate data to “realign” data in time. Then proceed as before, ... (but this step might **blur** your data)

Interpolation

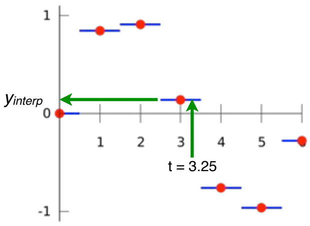


Imagine some data sampled at (time) points t = [1, 2, 3, ..., 6]

*... but you want to know what the value was at t = **3.25***

http://en.wikipedia.org/wiki/Interpolation
also Numerical Recipes in C (Press et al.)

Interpolation

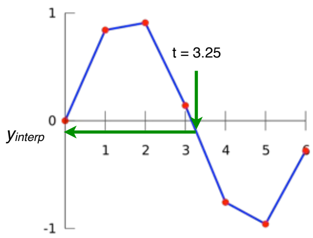


Nearest neighbour

pick the (y) value of the closest sampled point on t

http://en.wikipedia.org/wiki/Interpolation
also Numerical Recipes in C (Press et al.)

Interpolation



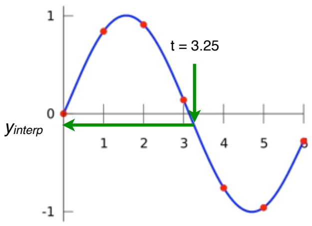
Linear interpolation

pick the (y) value on a line segment that joins adjacent sampled points on t

linear

http://en.wikipedia.org/wiki/Interpolation
also Numerical Recipes in C (Press et al.)

Interpolation



Polynomial interpolation

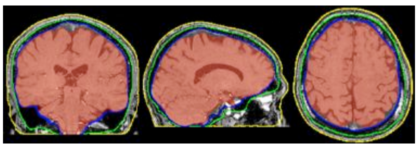
pick the (y) value on a polynomial that goes through sampled points on t

... you may also see
Spline interpolation
Sinc interpolation
(highest quality, but slow)

http://en.wikipedia.org/wiki/Interpolation
also Numerical Recipes in C (Press et al.)

Brain extraction

- remove skull / skin / fat before further processing (which are *a priori* not interesting for most fMRI)
- may improve alignment across subjects (but ! within suject alignment... there is information in the skull!)

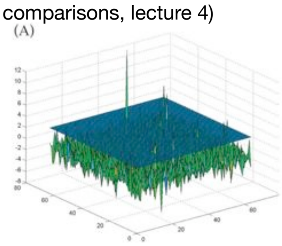


S.M. Smith. (2002) Fast robust automated brain extraction. HBM, 17(3):143-155

http://www.fmrib.ox.ac.uk/fsl/bet2/

Spatial smoothing

1. reduce noise in images
2. introduce **known** spatial correlations, e.g. with gaussian blurring (gaussian random fields, lecture 4)
3. ...reduce number of 'independent' samples in image (multiple comparisons, lecture 4)



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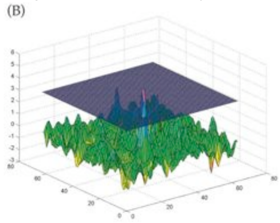
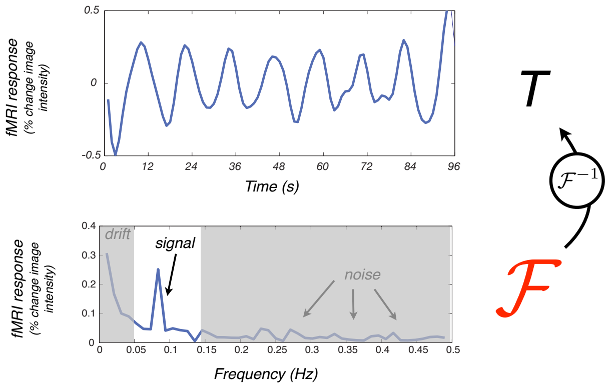


☣ *Terminal*

```
ds1$ fslmaths
ds1$ fslstats
ds1$ fslsplit
ds1$ fslmerge
ds1$ fsl<bla>
```

Temporal filtering

1. If we know the characteristics of **unwanted variability** (noise), then we can try to filter it out.
2. trend-removal, high-pass filtering (to get rid of drift)
3. smoothing, low-pass filtering (to get rid of high-frequency ripples)



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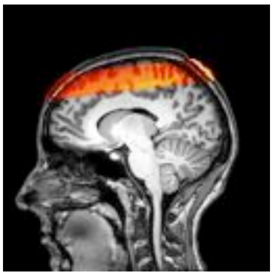
Make sure not to remove signal...

Check that filtering doesn't introduce statistical dependencies that might hurt you later...

Registration / Flat maps

Aligning across sessions (same subject)

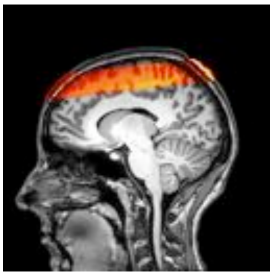


EPI data is blurry

image contrast different: anatomy and functional data

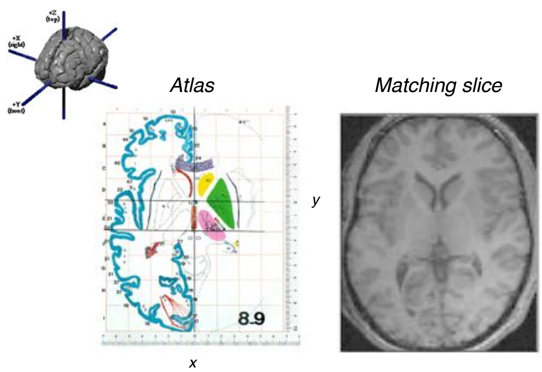
consider collecting anatomy data with the same slice prescription

Aligning across sessions (different subject)



?

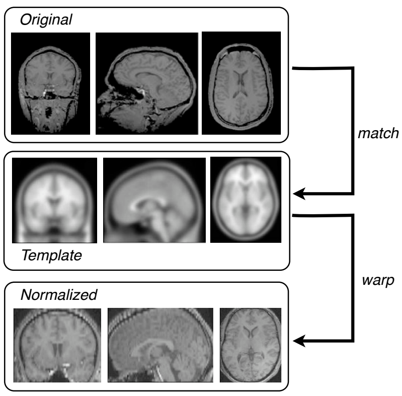
Talairach coordinates



+x (right), +y (front), +z (top)

Talairach & Tournoux (1988)

Transforming to Talairach coordinates



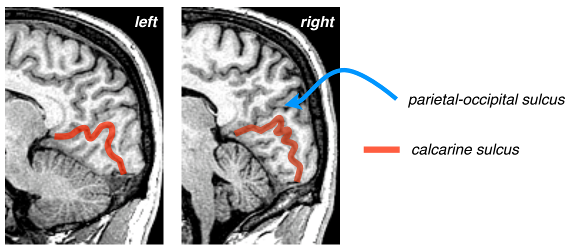
Find landmarks
anterior/posterior commisure
AP, LR, inf-sup borders

Talairach template
MNI templates
Montreal Neurological Institute

Find landmarks
anterior/posterior commisure
AP, LR, inf-sup borders

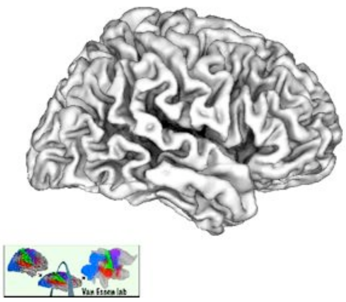
A word of caution:
Problem with Talairach coordinates

Individual differences & asymmetries:



Sagittal slices of the two hemispheres in one subject.

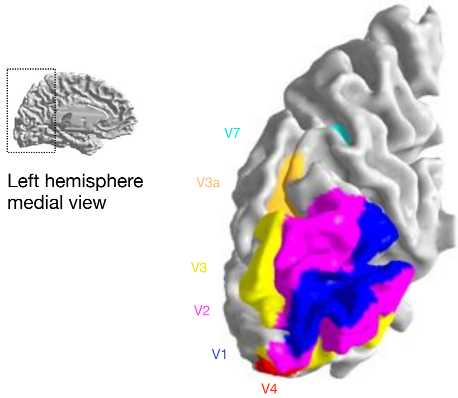
Flat maps of cortical surface



caret software

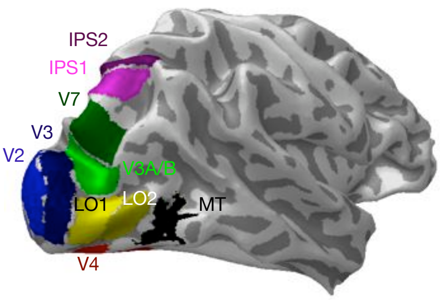
Google: *Van Essen lab*

Human visual areas

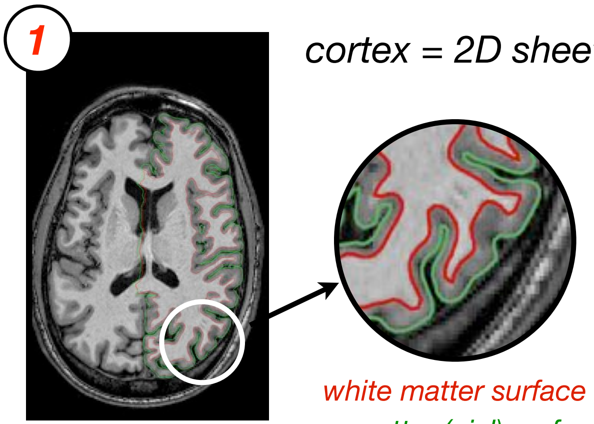


Human visual areas

Lateral view



LO1 and LO2:
Larsson & Heeger, J Neurosci (2006)
IPS1 and IPS2:
Schluppeck, Glimcher, & Heeger, J Neurophysiol (2005)
Silver, Ress, & Heeger, J Neurophysiol (2005)

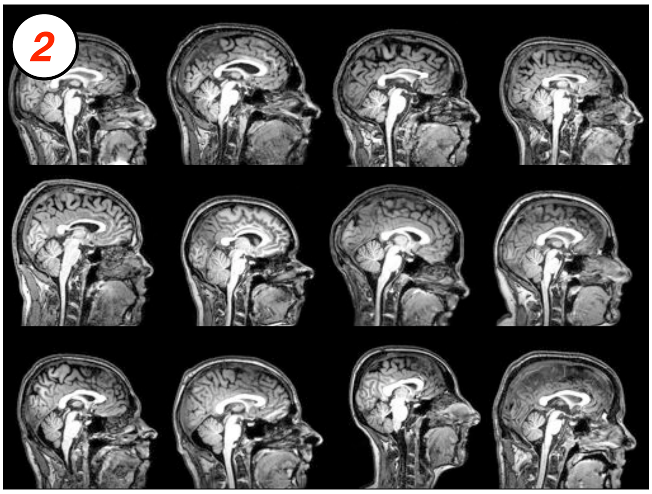


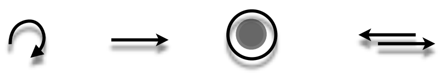
cortex = 2D sheet

horizontal slice, ds

white matter surface

gray matter (pial) surface

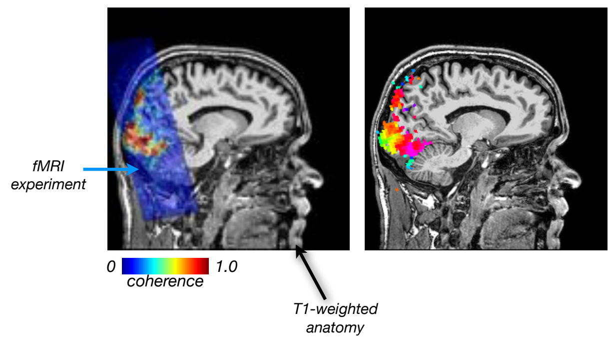


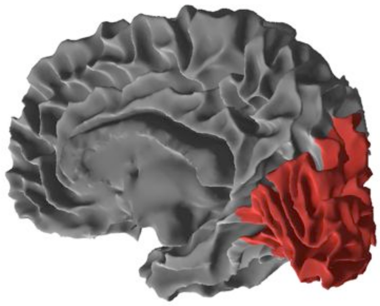


rotation, translation, dilation, and shear

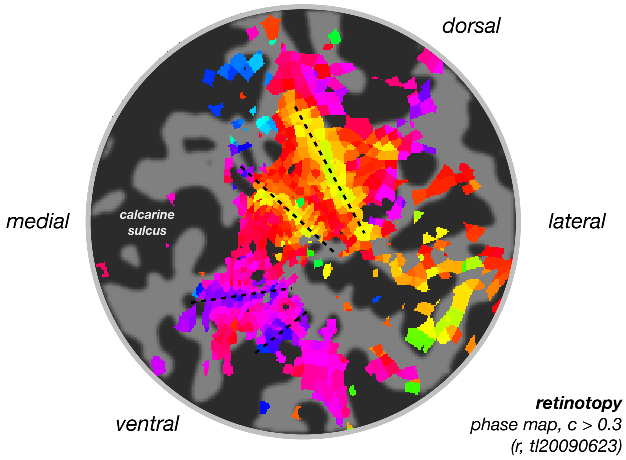
3

a statistical map *... and another*



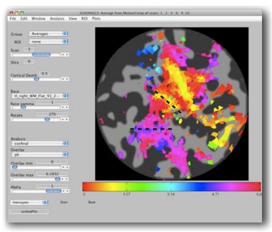


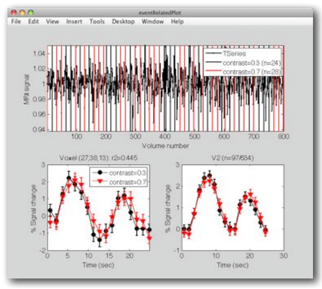
if we flatten out the cortical sheet...



retinotopy
phase map, c > 0.3
(r, tl20090623)

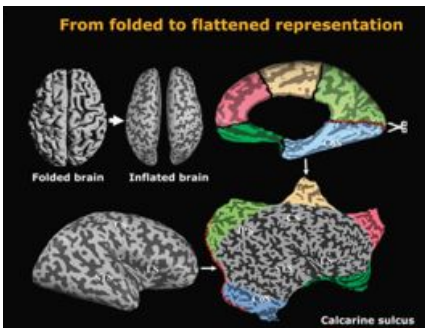
e.g. restrict analysis to different visual areas





Lily (Yue) Xing's PhD project

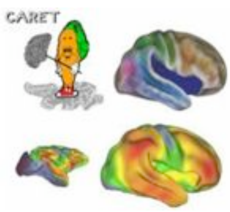
***BrainVoyager* (€ !)**

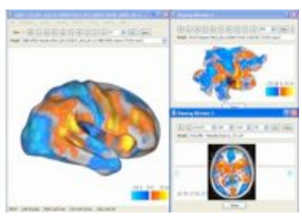


some flattened brains in different conventions

from Humphreys et al (2008) *Autism Research*

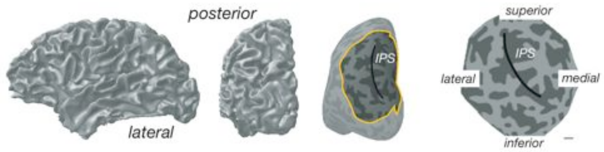
Caret





! only computes a subset of what most people need

SurfRelax

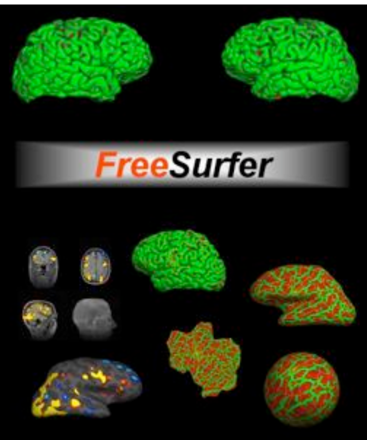


white matter surface (left hemisphere) *inflated surface* *flattened patch*

SurfRelax
Jonas Larsson's Tools
http://www.pc.rhul.ac.uk/staff/J.Larsson/software.html

64-bit Linux

FreeSurfer

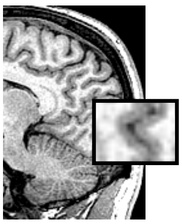


Linux
Mac OS X

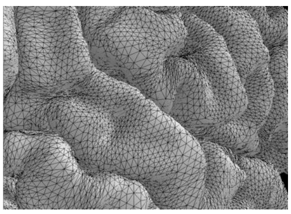
fully automated !
http://surfer.nmr.mgh.harvard.edu/

---

volume versus ***surface***



pixels / voxels in 3D 'intensity at a point' (image)

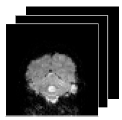


vertices in 3D, connected to form triangles / polygons (mesh)

---

volume versus surface

- for a volume we need 3 "indices" to uniquely identify a voxel (x,y,z)
- 4 for timeseries (x,y,z,t)
- multi-dimensional arrays
- we can slice these data in different ways:



```
>> data(:,:,12,1) % get slice z=12 at t=1
>> data(32,:,:,1) % ??
>> data(1,1,12,:) % get timeseries at [1,1,12]
```

---

volume versus ***surface***

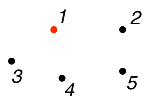
```
>> surf = loadSurfOFF('tl_left_WM.off')

surf =

    filename: 'tl_left_WM.off'
       Nvtcs: 154610
       Ntris: 309216
      Nedges: 0
        vtcs: [154610x3 double]
        tris: [309216x3 double]

>> curv = loadVFF('tl_left_Curv.vff');
```

Justin Gardner's demo *http://tinyurl.com/lenl5d*

---

mesh

x,y,z coordinates

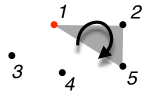


x,y,z

```
>> surf.vtcs(1,:)
ans =
   75.2111   20.4095  115.7857
```

position (mm)

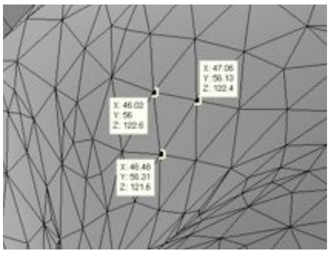
polygons / triangles




```
>> surf.tris(1,:)
ans =
     1     2     5
```

clockwise ordering (viewed from outside)

!freesurfer: *counter-clockwise ordering*



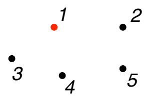
mesh

```
>> surfdata = ones(1, surf.Nvtcs);
>> patch('vertices', surf.vtcs, ...
        'faces',surf.tris,...
        'FaceVertexCData', surfdata,...
        'facecolor','flat','edgecolor','k');
>> colormap(gray)
```

Matlab

mesh + surface data

coordinates of vertex



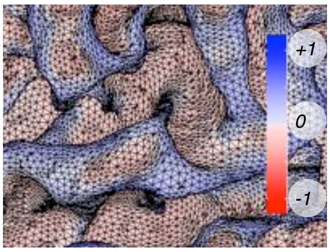
x,y,z

```
>> surf.vtcs(1:5,:)
ans =
   75.2111   20.4095  115.7857
   75.0598   20.4986  115.7333
   78.4137   20.4357  114.6386
   78.1711   20.4412  114.9014
   75.2228   20.4066  115.3947
```

value at vertex

vertex	value
1	0.21
2	0.19
3	0.31
4	0.29
.	.

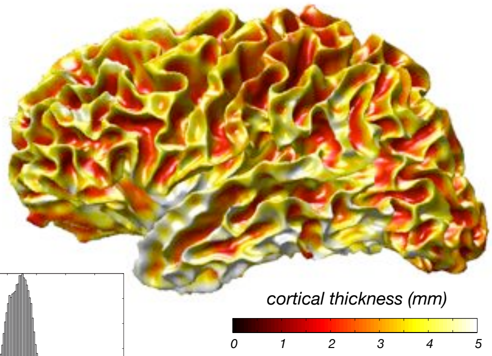
```
>> size(curv)
ans =
           1      154610
>> curv(1:5)
ans =
    0.21 0.19 0.31 0.29 0.20
```

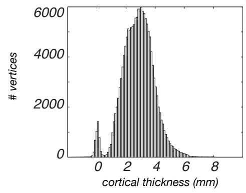


mesh + surface data
map of local curvature

```
>> surfdata = curv;
>> patch('vertices', surf.vtcs, ...
        'faces',surf.tris,...
        'FaceVertexCData', surfdata,...
        'facecolor','flat','edgecolor','k');
>> colormap(twoCondCmap)
```

Matlab






```
% surf2image -type distance -surface outer.off \
    inner.off corticalThickness.vff
```

Autorecon Processing StagesMotion Correction and Conform

1. NU (Non-Uniform intensity normalization)
2. Talairach transform computation
3. Intensity Normalization 1
4. Skull Strip
5. EM Register (linear volumetric registration)
6. CA Intensity Normalization
7. CA Non-linear Volumetric Registration
8. Remove Neck
9. LTA with Skull
10. CA Label (Volumetric Labeling) and Statistics
11. Intensity Normalization 2 (start here for control points)
12. White matter segmentation
13. Edit WM With ASeg
14. Fill (start
15. Tessella
16. Smooth
17. Inflate1
18. QSpher
19. Automa
20. Final Surfs (start here for brain edits for pial surf)
21. Smooth2
22. Inflate2
23. Cortical Ribbon Mask
24. Spherical Mapping
25. Spherical Registration
26. Spherical Registration, Contralateral hemisphere
27. Map average curvature to subject
28. Cortical Parcellation - Desikan_Killiany and Christophe (Labeling)
29. Cortical Parcellation Statistics
30. ...

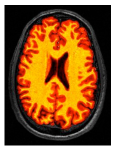
Worth the hassle?

```
% recon-all -subject ds -i ds_MPRAGE.img -all
```

source:
`http://surfer.nmr.mgh.harvard.edu/fswiki/recon-all`

What do I need?

- T1-weighted anatomy with good contrast
- a computer with Linux / Mac OSX (freesurfer runs SPMMRC incl. **morgana**)
- correctly set-up your UNIX .bashrc file
- ~12h compute time for 1mm^3 data set
- ... a bit of patience, if things break



- **demo:** Matlab, data from Justin Gardner's demo on mrTools wiki: http://tinyurl.com/lenl5d

For an overview of tools

60+ tools compatible with NIFTI-1

NITRC The Source for Neuroimaging Tools and Resources

NITRC website
`http://www.nitrc.org/`

Summary

- recap
- **Matlab (... + Unix, terminals, ...)**
- software packages
- preprocessing steps, how, why?
- registration / flat maps