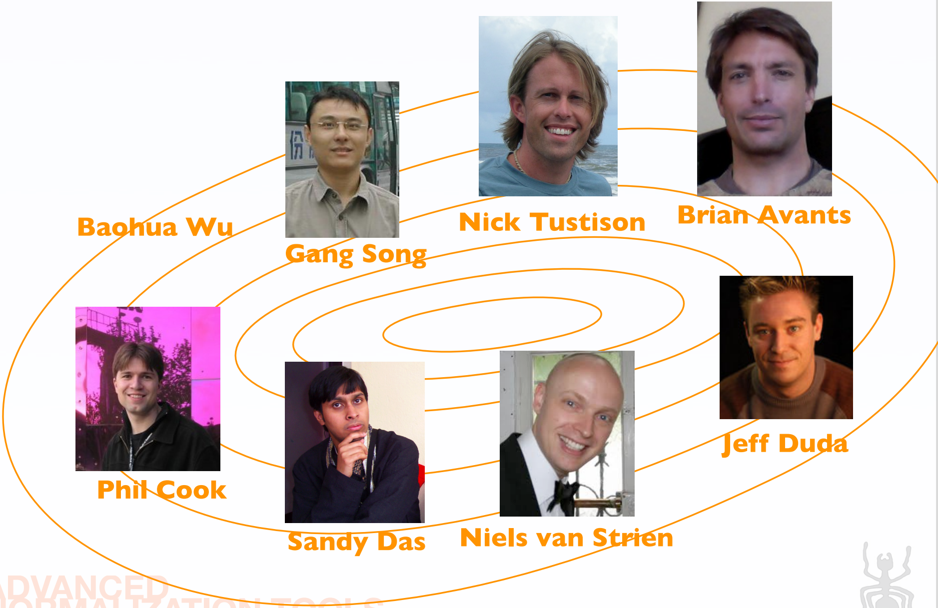
Multi-modality processing with Advanced Normalization Tools (ANTs)

Modern data fusion strategies

Brian Avants, PICSL and the ANTs Development Team

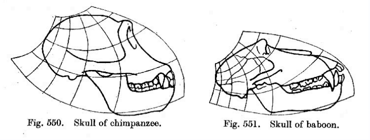
Simple hints for ...

People

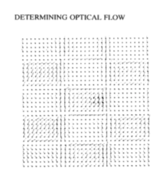

Baohua Wu
Gang Song
Nick Tustison
Brian Avants
Phil Cook
Sandy Das
Niels van Strien
Jeff Duda

History: Theory

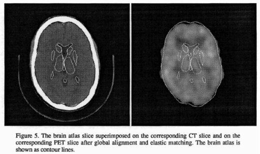
History: Implementation



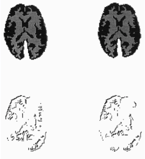
Thompson 1917



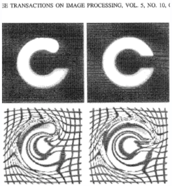
Horn 1980



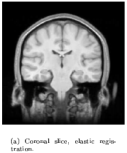
Bajcsy 1988



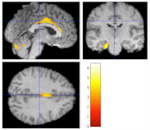
Gee 1994



Miller 1996



Guimond 1999



Ashburner 2000

Download ANTs binaries.

Go to:

link: ANTS release files

You will see folders for documentation, code, binaries.

From the folder ANTS, select a specific release, e.g.:

link: 1_9_x binaries

Install ANTs from source: Requires git/svn cmake, C++

open a terminal window and make a new directory. call it ANTs.
> mkdir ANTs
> cd ANTs
then type
> svn checkout https://advants.svn.sourceforge.net/svnroot/advants ANTS
> mkdir bin
> cd bin/
> ccmake ../ANTS/trunk/

Install ANTs from source: Requires git/svn, cmake, C++

then, in cmake, type c and then g then exit back to the terminal. then:
> make -j 4
and wait a while.
If there is an error like "cannot find 'some ITK file' " then try this:

from the bin directory, cd into ITKv4 , then type:
> git pull origin master
that will update ITK.
you can then try 'make -j 4' again.

Overview: Program + brief description 1

Tool Name	Description	Highlights	Primary Reference
ANTS	Interface to a variety of registration algorithms	Best performing normalization algorithm in multiple different studies.	A reproducible evaluation of ANTs similarity metric performance in brain image registration
antsRegistration	ITKv4 update to ANTS.	Takes full advantage of multi-core processing.	A unified registration framework for ITK, WBIR 2012.
Atropos	Multivariate probabilitic EM segmentation	Can integrate information from multiple modalities and has a DTI-specific likelihood.	An open source multivariate framework for n-tissue segmentation with evaluation on public data.
N4BiasFieldCorr...	Novel inhomogeneity field correction method	Considered new standard in bias correction by much of the medical imaging community.	N4ITK: improved N3 bias correction.
ImageMath	Basic operations on images.	Works on 2D, 3D, 4D images.	—
buildtemplateparallel	Optimal template construction in the diffeomorphic space.	Used as a standard evaluation target for new template construction methodology. New multimodality implementation.	The optimal template effect in hippocampus studies of diseased populations

Overview: Program + brief description 2

Tool Name	Description	Highlights	Primary Reference
WarpImageMultiTrans...	Concatenates ANTS/ITK transforms	Can string together a series of N transforms to minimize interpolation error and resample.	—
antsApplyTransforms	Concatenates ANTS/ITK transforms	Can string together a series of N transforms to minimize interpolation error and resample.	—
KellyKapowski	Cortical thickness estimation based on volumetric imagery + probabilistic segmentation	The only multi-platform volumetric alternative to Freesurfer	Registration based cortical thickness measurement.
sccan	Multivariate dimensionality reduction	New tools with lots of potential for improving detection power in medical imaging.	Dementia induces correlated reductions in white matter integrity and cortical thickness: a multivariate neuroimaging study with sparse canonical correlation analysis.
antsMotionCorr	Motion correction + template construction methods for 4D images	Simple flexible rigid, affine, deformable motion correction for (mostly) functional data.	Estimation of perfusion and arterial transit time in myocardium using free-breathing myocardial arterial spin labeling with navigator-echo (not ideal but the only relevant one currently existing)

Scripting for large-scale studies

ANTs is for scripting!

```
#! /usr/bin/bash
echo ANTs likes short bash scripts

#! /usr/bin/perl
print "Longer scripts should use perl";

#! /usr/bin/Rscript
print( paste( "but ANTs prefers'',''R'' ) )
```

The Basic Toolset

Registration: Data is in Examples/Data

```
ANTS 2 -m CC[r16slice.nii.gz,r64slice.nii.gz,1,4]
-t SyN[0.25] -r Gauss[3,0] -o TEST -i 50x40x30
```

Segmentation

```
Atropos -d 2 -a r16slice.nii.gz -x r16mask.nii.gz
-m [0.1,1x1] -c [10,0] -i kmeans[3]
-o [Output.nii.gz,Output_prob_%02d.nii.gz]
```

Template building

```
bash buildtemplateparallel.sh -d 3 -m 30x50x20
-t GR -s CC -c 1 -o OutPrefix *ImageName*T1x.nii.gz
```

Basic applications

- Quantify changes in cortical thickness in an individual.

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- Asymmetry study of neuroanatomy.

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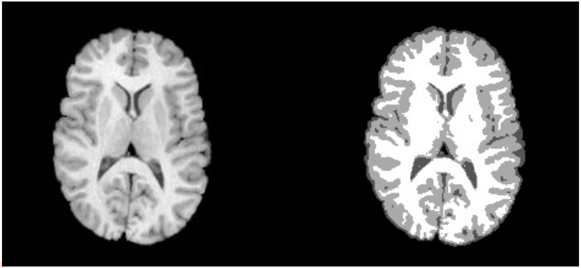
- Identify multivariate relationships between modalities and predictors.
- Single-subject BOLD fmri study of resting state connectivity.
- Asymmetry study of neuroanatomy.
- In general, optimal dimensionality reduction to increase detection power.

Segmenting anatomy from an image

See examples/segmentation_example.sh

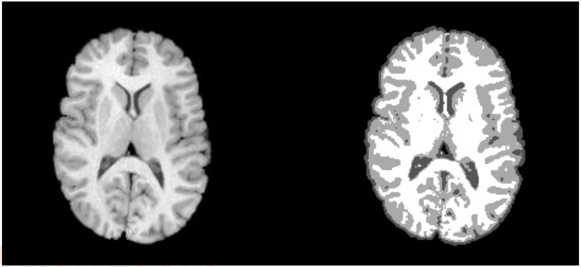
```
ThresholdImage $dim $img ${out}mk.nii.gz 0.2 1.e9
ImageMath $dim ${out}mk.nii.gz ME ${out}mk.nii.gz 2
ImageMath $dim ${out}mk.nii.gz MD ${out}mk.nii.gz 2
Atropos -d $dim -a $img -x ${out}mk.nii.gz -m [0.05,1x1] -c [10,0] -i kmeans[3] -o [${out}.nii.gz,${out}prob%02d.nii.gz]
```



Multivariate anatomical segmentation

See examples/segmentation2_example.sh

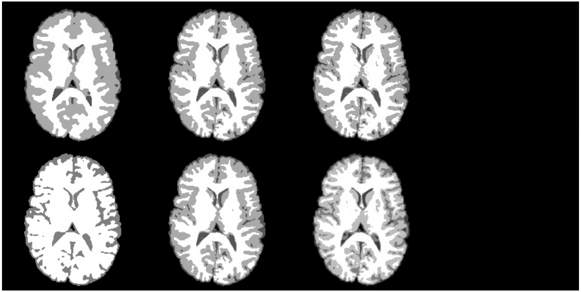
```
ImageMath $dim temp.nii.gz GO $img 2
ImageMath $dim temp1.nii.gz Laplacian $img 1
ImageMath $dim temp2.nii.gz Grad $img 1 1
Atropos -d $dim -a $img -a temp.nii.gz  -a temp1.nii.gz  -a temp2.nii.gz -x ${out}mk.nii.gz -m [0.05,1x1]   -c [10,0]  -i kmeans[3] -o [${out}.nii.gz,${out}prob%02d.nii.gz]
```



Meaning of segmentation parameters

What happens when i vary each parameter?

```
-m [0.1,1x1] -m [0.2,1x1] -m [0.5,1x1]
vs.
-i kmeans[ k ] k = 2 , 3 , 4
```

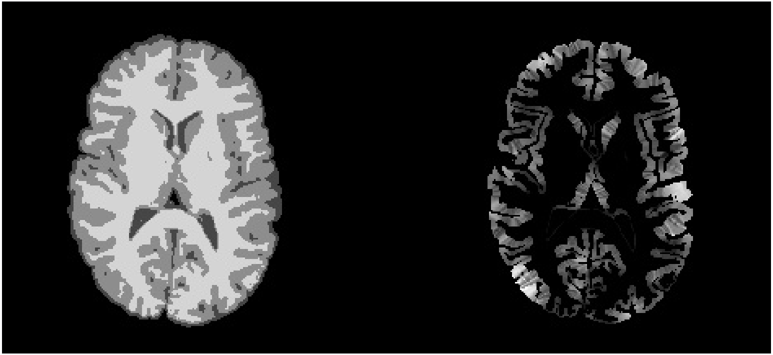


Vary MRF param and K in k-means.

Cortical thickness from imaging data

See examples/thickness_example.sh

```
KellyKapowski -d $dim -s ${out}.nii.gz -g ${out}
    prob02.nii.gz  -w ${out}prob03.nii.gz -o ${out}
    thickness.nii.gz -c [30,0] -r 0.5 -m 1.0
```



Can vary smoothness, priors on thickness, etc. See help.

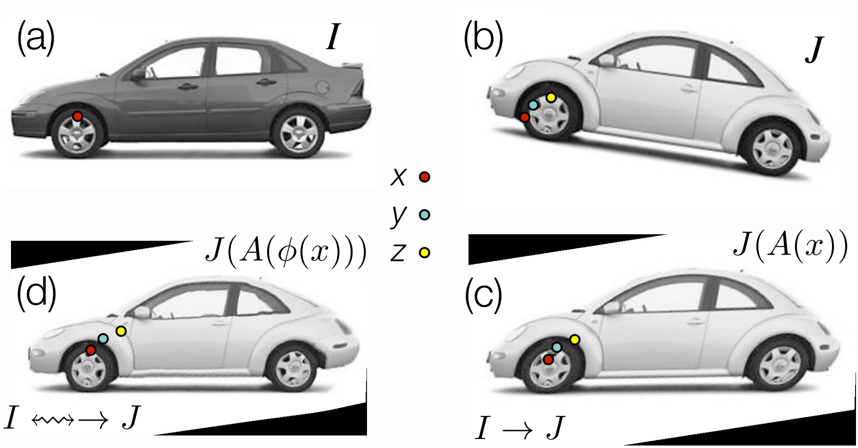
But isn't ANTs all about normalization?

But isn't ANTs all about registration?

But isn't ANTs all about mapping?

But isn't ANTs all about transformations and templates?

Template-based transformations



How did we compute that transformation?

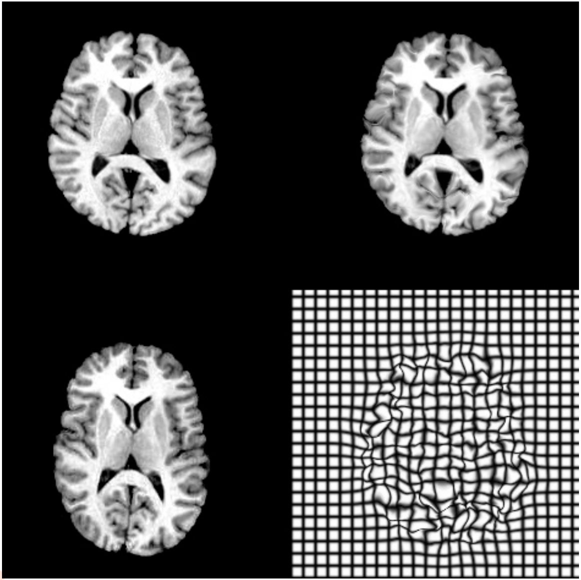
```
dim=2
m=beetle.jpg ;  f=ford.jpg
its=1500x1500x1500x300x100x0
its2=200x200x200x200x150x50
smth=5x4x3x2x1x0
down=7x6x5x4x2x1
antsRegistration -d $dim \
                        -m Mattes[  $f, $m , 1,  20,
                           Random, 0.1 ] \
                         -t affine[ 2.0 ]  \
                         -i $its  \
                        -s $smth  \
                        -f $down \
                       -u 1 \
                       -o [cars_,cars_aff.nii.gz]
antsRegistration -d $dim -r [cars_0Affine.mat] \
                        -m Mattes[ $f,$m, 1, 32 ] \
                        -t syn[ 0.25 , 3.0, 1 ] \
                        -i $its2  \
                        -s $smth  \
```

Mapping two images

See examples/registration_example.sh

```
ANTS $dim -m  CC[$img1,$img2,1,4]  -t SyN[0.25]  -r Gauss[3,0] -o $out -i 50x40x30 --number-of-affine-iterations 1000x1000x500
WarpImageMultiTransform $dim $img2  ${out}.nii.gz  ${out}Warp.nii.gz ${out}Affine.txt -R $img1
CreateWarpedGridImage $dim  ${out}Warp.nii.gz ${out}grid.nii.gz 1x1 10x10 10x10
```

Mapping two images



Can vary smoothness, metrics, etc. See help.

Segmenting anatomy from an image *Now With Priors!*

See examples/segmentation3_example.sh

```
antsApplyTransforms -d 2 -i ${out}mk.nii.gz -o ${out}mk.nii.gz -t [${out}Affine.txt,1] -t ${out}InverseWarp.nii.gz -n NearestNeighbor -r $img2
  antsApplyTransforms -d 2 -i ${out}prob0${x}.nii.gz -o ${out}prob0${x}.nii.gz -t [${out}Affine.txt,1] -t ${out}InverseWarp.nii.gz -n Linear  -r $img2
for x in 1 2 3 4  ; do
  N4BiasFieldCorrection -d $dim -i $img2 -o ${out}.nii.gz -x ${out}mk.nii.gz -s 1 -b [200] -c [20x20x20,0] -w ${out}prob03.nii.gz
  Atropos -d $dim -a ${out}.nii.gz -x ${out}mk.nii.gz -m [ 0.05,1x1]   -c [10,0]   -i priorprobabilityimages[3,${out}prob%02d.nii.gz,0.25] -o [${out}.nii.gz,${out}prob%02d.nii.gz]
done
```

What is the effect of N4? Should one loop over N4 and Atropos?

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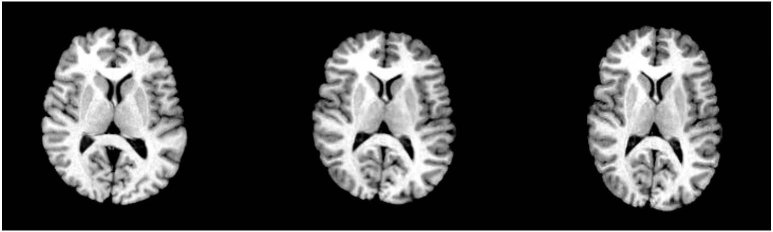
- Details matter: pre-processing, feature extraction, etc.
- Successful affine step is essential!!
- Step-size increases stability but slows convergence (SyN[0.1] more stable than SyN[0.25]).

Check the affine mapping between two images

See examples/registration_affine_example.sh

```
ANTS $dim -m  CC[$img1,$img2,1,4]  -t SyN[0.25]  -r Gauss[3,0] -o $out -i 0 --number-of-affine-iterations 1000x1000x500
WarpImageMultiTransform $dim $img2  ${out}.nii.gz  ${out}Affine.txt -R $img1
```



fixed versus affinely registered image versus original moving

Coordinates of computation time

- 2D 256^2 pixels intensity difference (MSQ) registration $\approx$ 30 seconds

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- 3D 256^3 voxels correlation-8 (CC[. , . , 1, 8]) could take 3 days if you use full-resolution and the images are very different.

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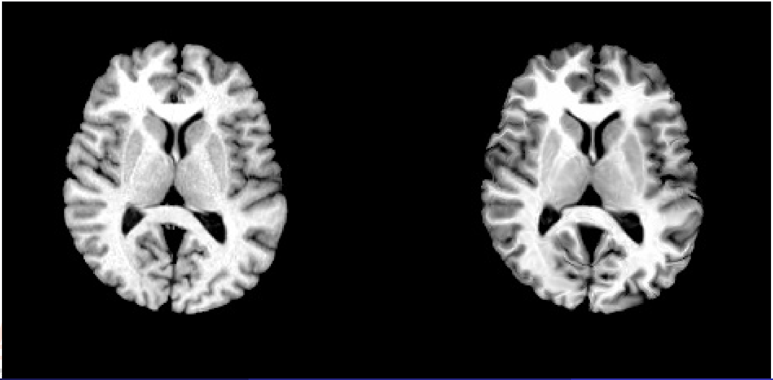
- 2D 256^2 pixels intensity difference (MSQ) registration $\approx$ 30 seconds
- 3D 256^3 voxels correlation-8 (CC[. , . , 1, 8]) could take 3 days if you use full-resolution and the images are very different.
- or it could take 15 minutes if you use low-resolution and the images are very similar.

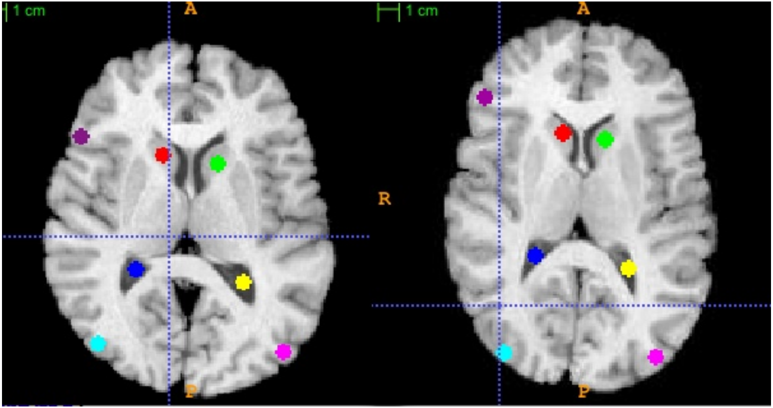
Multiple metrics driving registration

See examples/registration_mm_example.sh

```
ANTS $dim -m MSQ[$lm1,$lm2,0.5,0] -m MSQ[$lm1b,$lm2b,0.5,0] -m CC[$img1,$img2,1,4] -t SyN[0.25] -r Gauss[3,0] -o $out -i 50x50x20 --number-of-affine-iterations 1000x1000x500 --use-all-metrics-for-convergence 1
```



Landmark-based registration 1



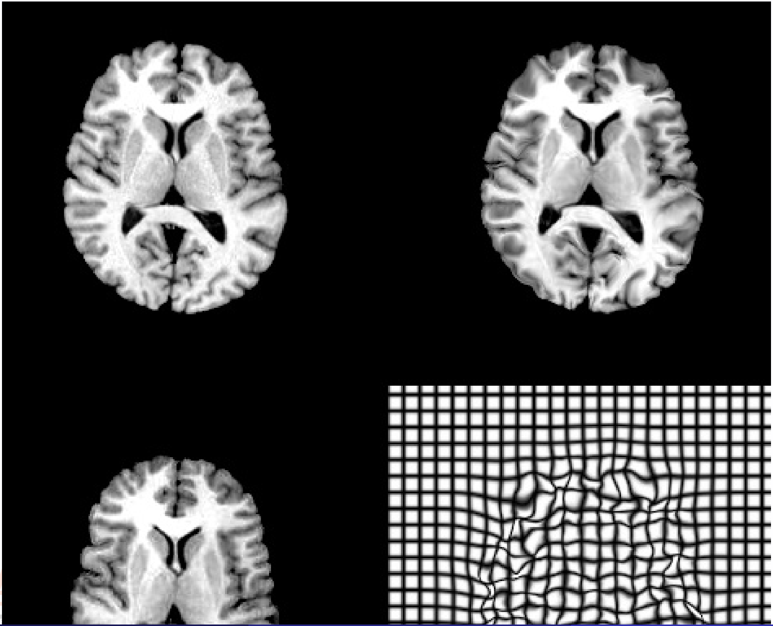
.

Landmark-based registration 2

See examples/registration_lm_example.sh

```
WarpImageMultiTransform $dim $lm2  ${out}lm.nii.gz  ${out}preAffine.txt -R $img1 --use-NN
WarpImageMultiTransform $dim $img2 ${out}img.nii.gz ${out}preAffine.txt -R $img1
wt=1 ; pct=0.5 ; sig=50
 ANTS $dim  -i 55x40x30  -r Gauss[8,0] -t SyN[ 0.25 ]
 -m PSE[ $lm1 ,  ${out}lm.nii.gz  , $lm1 ,  ${out}lm.nii.gz  ,$wt,$pct,$sig,0,10,10000 ]
  -m  CC[$img1,${out}img.nii.gz,1,4] -o $out -i 50x50x50 --number-of-affine-iterations 0
 --use-all-metrics-for-convergence 1 --continue-affine 0
```

Landmark-based registration 3



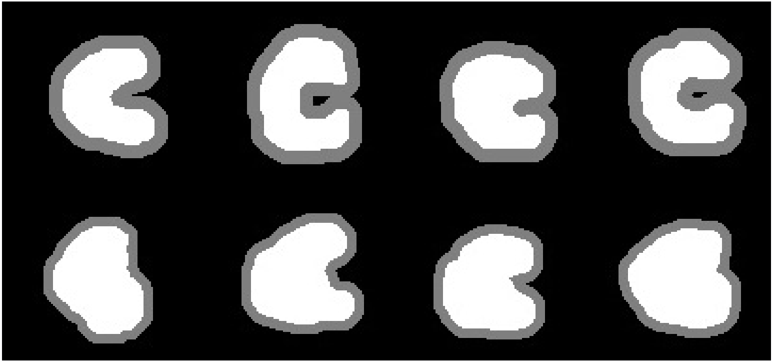
Other Landmark-based registration tools

- for 3D
- ANTSUseLandmarkImagesToGetAffineTransform Im1.nii.gz Im2.nii.gz affine outaffine.txt
- ANTSUseLandmarkImagesToBSplineDisplacementField Im1.nii.gz Im2.nii.gz outLMWarp.nii.gz 10x10x10 6 3 0
- Then use WarpImageMultiTransform / antsApplyTransform to apply the warp to the relevant image.

Template construction

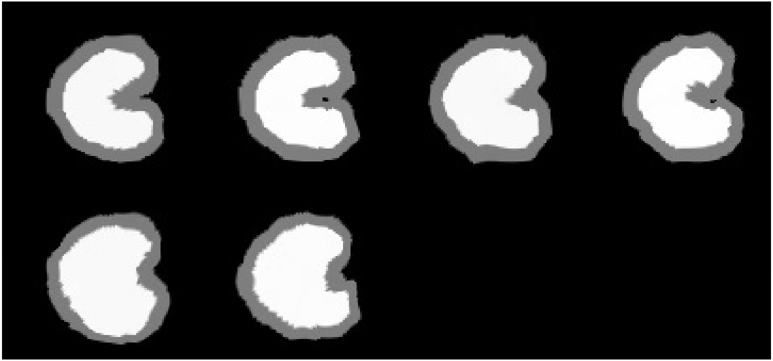
See examples/btp_example.sh

```
ln -s ../data/phantom* .
buildtemplateparallel.sh -d 2 -o PH -c 0 -s CC -i 3 -m 50x0x0 -t GR  phantom*jpg
```



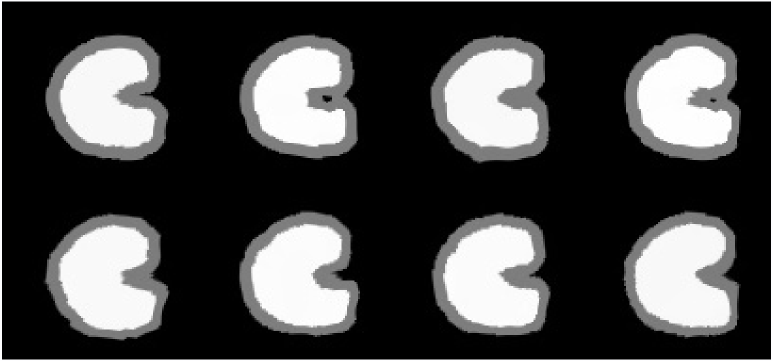
all “subjects”

Template construction output



subjects after iteration 1

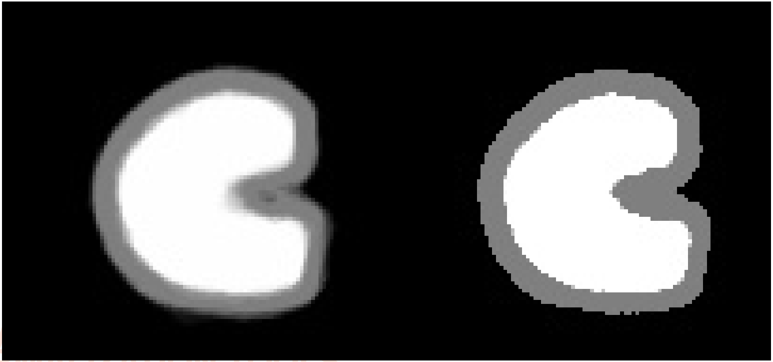
Template construction output



subjects after iteration 2

Multi-template labeling

```
for x in *deformed.nii.gz ; do
  Atropos -d 2 -a $x -m [0.1,1x1] -i kmeans[2] -x
     mask.nii.gz -o [temp${ct}seg.nii.gz] -c [3,0]
ls temp*seg.nii.gz > list.txt
ImageSetStatistics 2 list.txt PHtemplateseg.nii.gz
    0
```



Identifying local predictors of global differences

$$\text{volume}_{\text{local}} \approx 1 + \text{volume}_{\text{global}}$$

ANTs multivariate voxel-wise statistics

```
ThresholdImage 2 PHtemplateseg.nii.gz  maskg.nii.gz 127 127
for x in PHphantom*wmgmWarp.nii.gz ; do
  ANTSJacobian 2 $x phantomG${ct} 1 maskg.nii.gz 0

ls phantomG*logjacobian.nii.gz > list.txt
sccan --imageset-to-matrix [list.txt,maskg.nii.gz] -o phantomGlogjacs.csv
sccan --scca two-view[phantomGlogjacs.csv,globalvols.csv,maskg.nii.gz, NA ,-0.1,-1] -o CCA.nii.gz -n 1 -p 1000 -i 10 --PClusterThresh 100
```

The p-value is reported to the screen

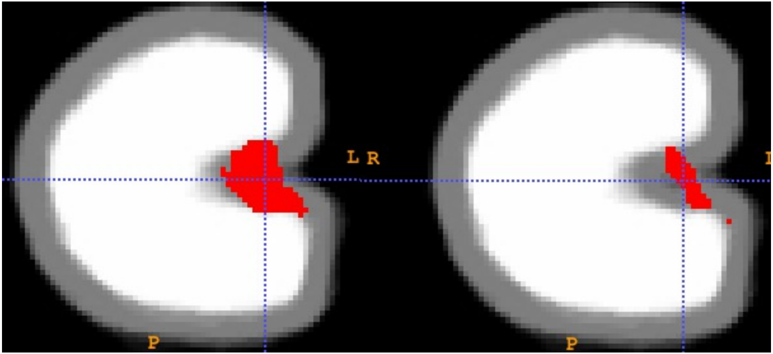
"0.363314 p-value **0.002997** ct 1000 true 0.978359 "

Now we can compare to standard voxel-wise statistics using **R** ...

.... voxel-wise statistics in **R**

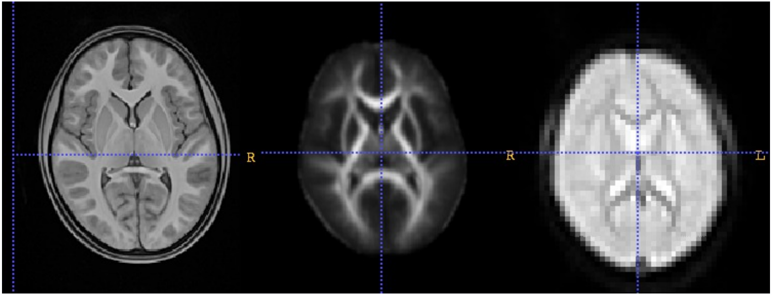
```
predictor<-read.csv("data/phantpredictors.csv")
predictor<-read.csv("templateex/globalvols.csv")
logjac<-read.csv("templateex/phantomGlogjacs.csv")
attach( logjac ) ; attach( predictor )
nvox<-ncol(logjac)
pvals<-rep(NA,nvox)
for ( x in c(1:nvox) )
{
  voxels<-logjac[,x]
  lmres<-summary(lm( voxels ~  vol ))
  coeff<-coefficients( lmres )
  pval<-coeff[2,4]
  pvals[x]<-pval
}
qvals<-p.adjust(pvals)
print(min(qvals))
write.csv(1-qvals,'templateex/qvals.csv')
# sccan --vector-to-image [ templateex/qvals.csv ,
    templateex/maskg.nii.gz , 1] -o temp.nii.gz
```

Comparison of results



SCCAN p-value ≈ 0.003 **minimum FDR-corrected p-value** ≈ 0.009 **but results are similar. FDR threshold** $= 0.05$.

Templates for all modalities



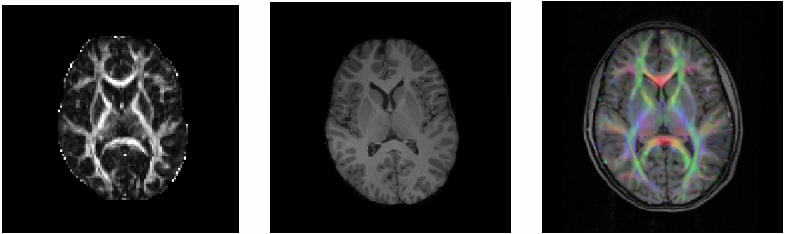
Templates for the same population T1, FA and BOLD.
We exploit population templates to extract the brain and set-up modality specific brain extraction and segmentation.

Longitudinal analysis with ANTs

Look at your data to verify the quality of the rigid mapping!

Processing of diffusion tensor data.

1. Intra-subject matching (T1 $\rightarrow$ FA)
2. Compose warps for template space warp
3. Warp and reorient with preservation of principal direction
4. Get derived images (FA, MD, RGB, etc) principal direction)



Subject FA   Subject T1   Aligned composite

Time series / rsfMRI analysis with ANTs

See examples/motioncorr_example.sh

```
antsMotionCorr  -d 3 -a $img -o ${out}avg.nii.gz
antsMotionCorr  -d 3 -o [${out},${out}.nii.gz,${out}avg.nii.gz] -m mi[ ${out}avg.nii.gz , $img , 1 , 32 , Regular, 0.01 ]  -t Rigid[ 0.05 ] -i 100 -u 1 -e 1 -s 0.0 -f 1 -n 10
```

- mi — mutual information metric

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    32 , Regular, 0.01 ]  -t Rigid[ 0.05 ] -i 100 -u 1
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- mi — mutual information metric
- Rigid — use rigid map to the average with gradient step 0.05

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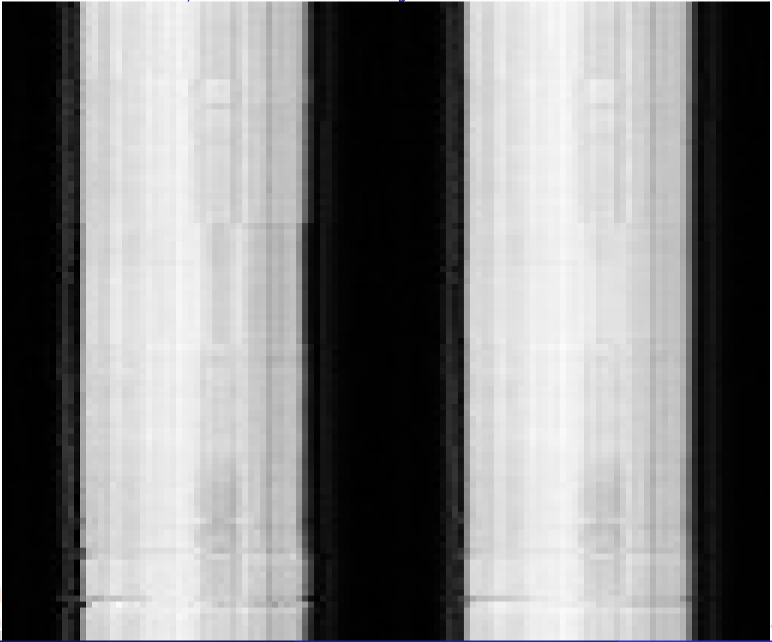
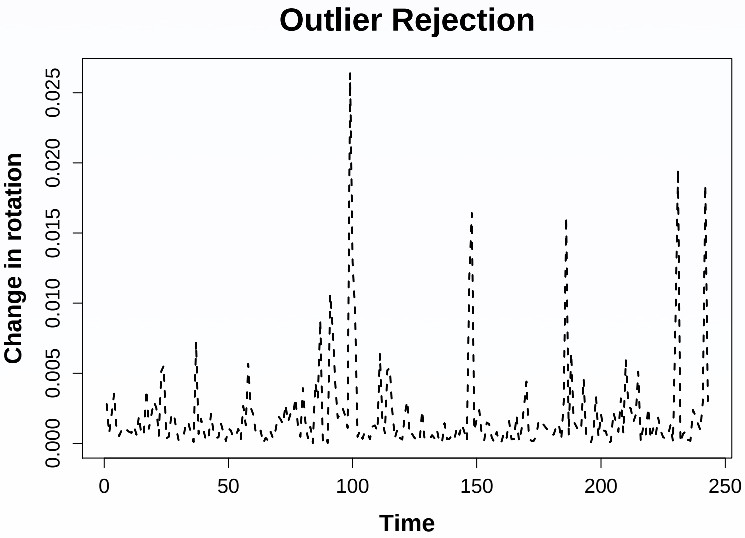
     -e 1 -s 0.0 -f 1 -n 10
```

- mi — mutual information metric
- Rigid — use rigid map to the average with gradient step 0.05
- other params — smoothing, scale estimation, iterations ...

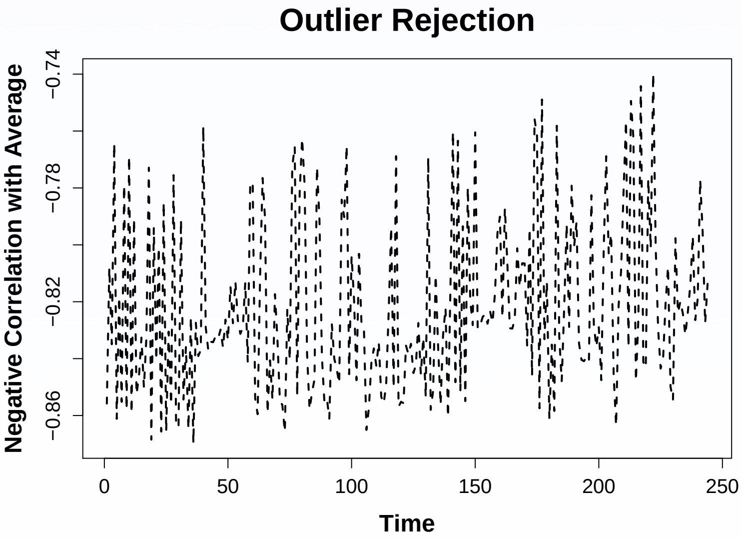
Time series / rsfMRI analysis with ANTs



Time series / rsfMRI analysis with ANTs



Time series / rsfMRI analysis with ANTs



Extracting a resting state network

See examples/rsfnodes_example.sh

```
ThresholdImage 3 ${out}avg.nii.gz  ${out}_bmask.nii.gz 300 9999
ImageMath 3 ${out}_bmask.nii.gz GetLargestComponent ${out}_bmask.nii.gz
ImageMath 4 ${out}compcorr.nii.gz CompCorrAuto ${out}.nii.gz ${out}_bmask.nii.gz 6
sccan --timeseriesimage-to-matrix [ ${out}compcorr_corrected.nii.gz , ${out}_bmask.nii.gz , 0 , 1.0 ] -o ${out}.csv
sccan --svd sparse[ ${out}.csv ,  ${out}_bmask.nii.gz , -0.05 ] -n 20 -i 10 --PClusterThresh 50 -o ${out}RSFNodes.nii.gz
```

Then build a graph (see iGraph).

How does structure and functional connectivity elaborate during development?

open data

Reproducibility

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- We aim to support user needs so if you can't find something, just ask .... Questions?

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- NIBIB for software development support under grant R01-EB006266-01.
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