

Multi-modality processing with Advanced Normalization Tools (ANTs)

Modern data fusion strategies

Brian Avants, PICSL and the ANTs Development Team

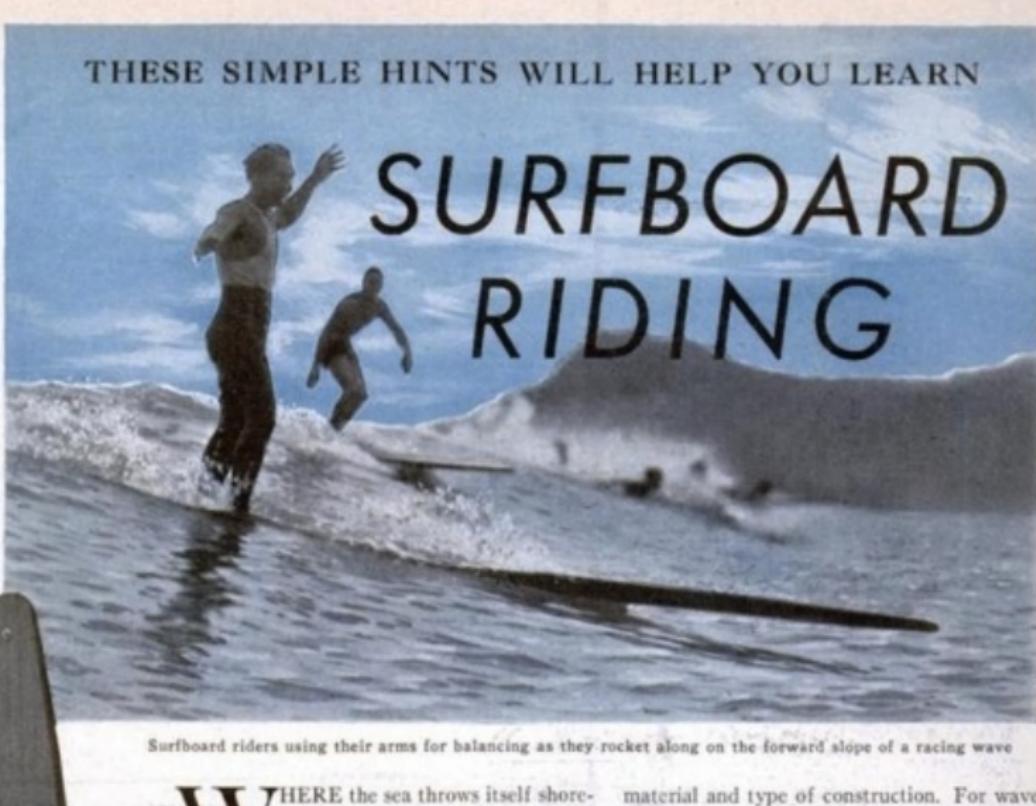
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Simple hints for ...

THESE SIMPLE HINTS WILL HELP YOU LEARN

SURFBOARD RIDING



Surfboard riders using their arms for balancing as they rocket along on the forward slope of a racing wave

WHERE the sea throws itself shore- material and type of construction. For wave

People



History: Theory



History: Implementation

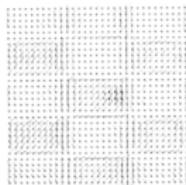


Fig. 550. Skull of chimpanzee.



Fig. 551. Skull of baboon.

DETERMINING OPTICAL FLOW

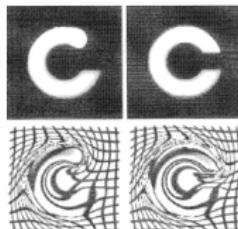


Thompson 1917

IEEE TRANSACTIONS ON IMAGE PROCESSING, VOL. 5, NO. 10, I

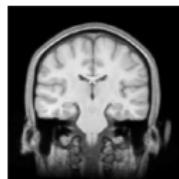


Gee 1994



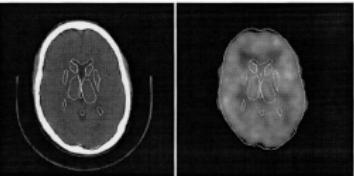
Miller 1996

Horn 1980

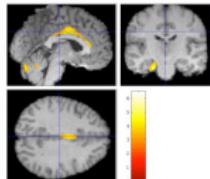


(a) Coronal slice, elastic registration.

Guimond 1999



Bajcsy 1988



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 probabilistic 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
WarlImageMultiTrans...	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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- Perform a template-based study of thickness, gray matter probability, FA, rs connectivity ...



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- Single-subject BOLD fmri study of resting state connectivity.



Basic applications

- Quantify changes in cortical thickness in an individual.
- Perform a template-based study of thickness, gray matter probability, FA, rs connectivity ...
- Identify multivariate relationships between modalities and predictors.
- Single-subject BOLD fmri study of resting state connectivity.
- Asymmetry study of neuroanatomy.



Basic applications

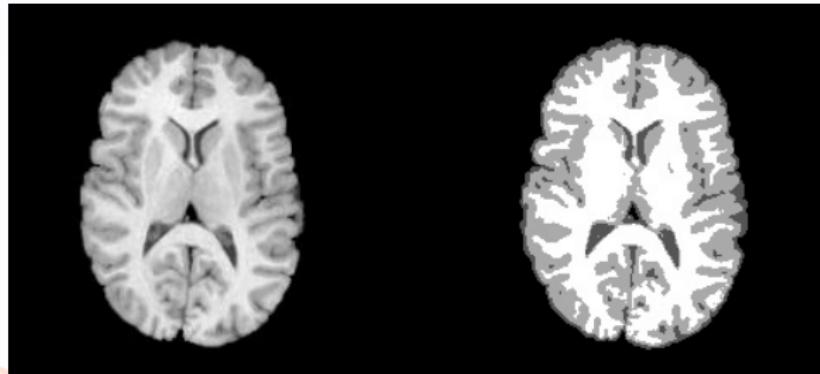
- Quantify changes in cortical thickness in an individual.
- Perform a template-based study of thickness, gray matter probability, FA, rs connectivity ...
- Identify multivariate relationships between modalities and predictors.
- Single-subject BOLD fmri study of resting state connectivity.
- Asymmetry study of neuroanatomy.
- In general, optimal dimensionality reduction to increase detection power.



Segmenting anatomy from an image

See examples/segmentation_example.sh

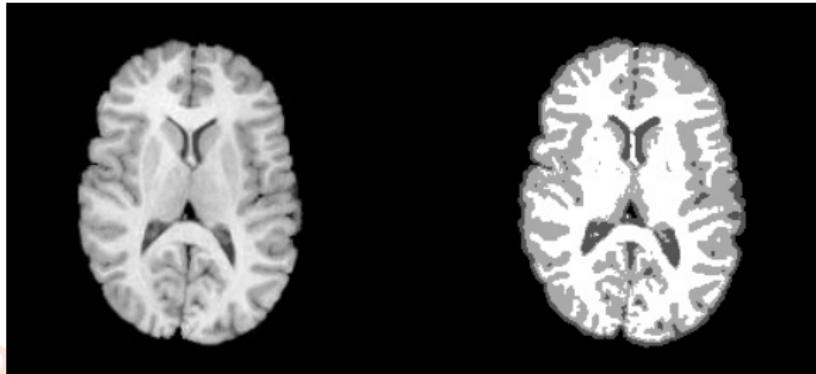
```
1 ThresholdImage $dim $img ${out}mk.nii.gz 0.2 1.e9
2 ImageMath $dim ${out}mk.nii.gz ME ${out}mk.nii.gz 2
3 ImageMath $dim ${out}mk.nii.gz MD ${out}mk.nii.gz 2
4 Atropos -d $dim -a $img -x ${out}mk.nii.gz -m [0.05,1
    x1] -c [10,0] -i kmeans[3] -o [${out}.nii.gz,${out}prob%02d.nii.gz]
```



Multivariate anatomical segmentation

See examples/segmentation2_example.sh

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



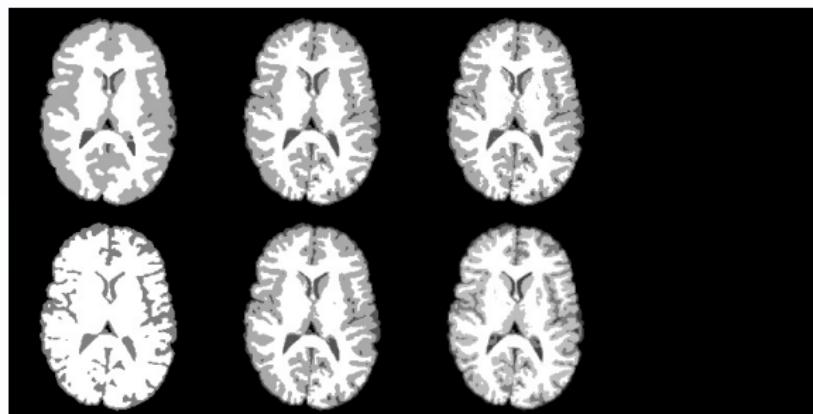
Meaning of segmentation parameters

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



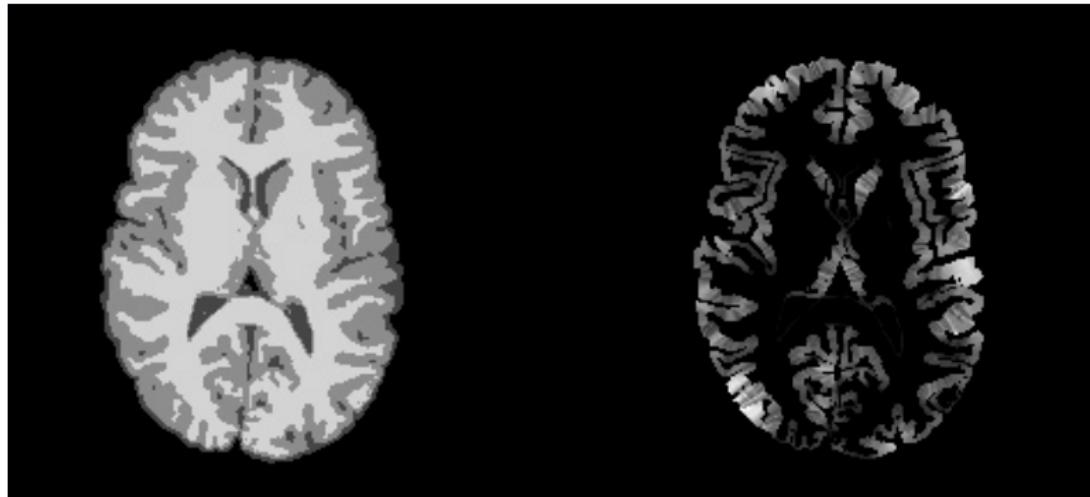
Vary MRF param and K in k-means.



Cortical thickness from imaging data

See examples/thickness_example.sh

```
1 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
```



ADVANCED
PICS

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



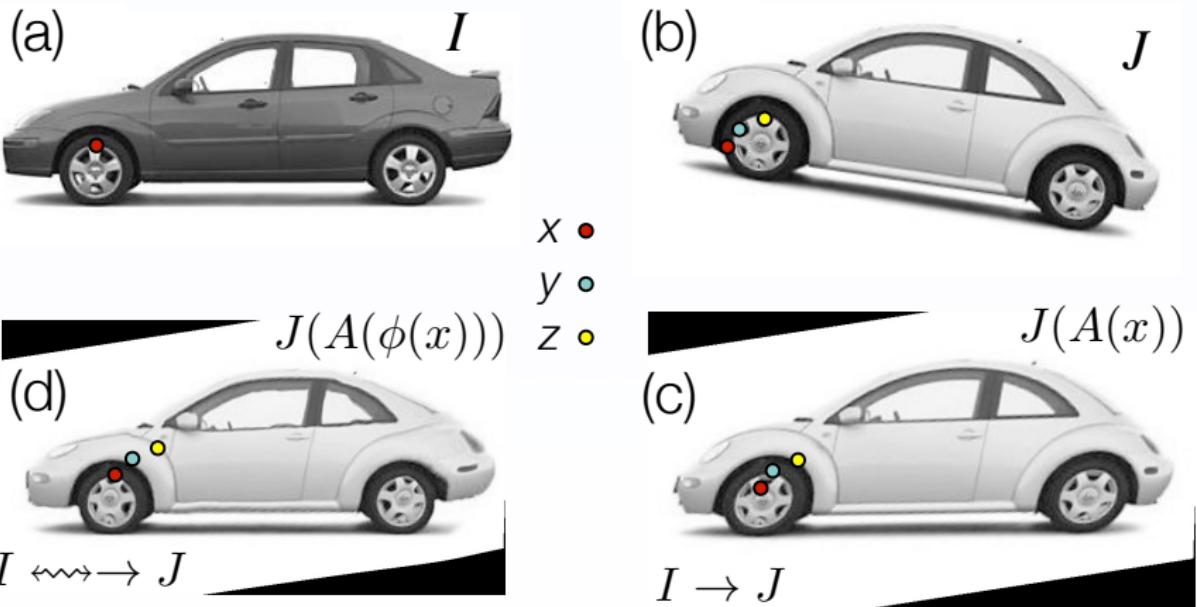
But isn't ANTs all
about normalization?

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?

```
1 dim=2
2 m=beetle.jpg ; f=ford.jpg
3 its=1500x1500x1500x300x100x0
4 its2=200x200x200x200x150x50
5 smth=5x4x3x2x1x0
6 down=7x6x5x4x2x1
7 antsRegistration -d $dim \
8                         -m Mattes[ $f, $m , 1, 20,
9                               Random, 0.1 ] \
10                          -t affine[ 2.0 ] \
11                          -i $its \
12                          -s $smth \
13                          -f $down \
14                          -u 1 \
15                          -o [cars_,cars_aff.nii.gz]
16 antsRegistration -d $dim -r [cars_OAffine.mat] \
17                         -m Mattes[ $f,$m, 1, 32 ] \
18                         -t syn[ 0.25 , 3.0, 1 ] \
19                         -i $its2 \
20                         -s $smth
```

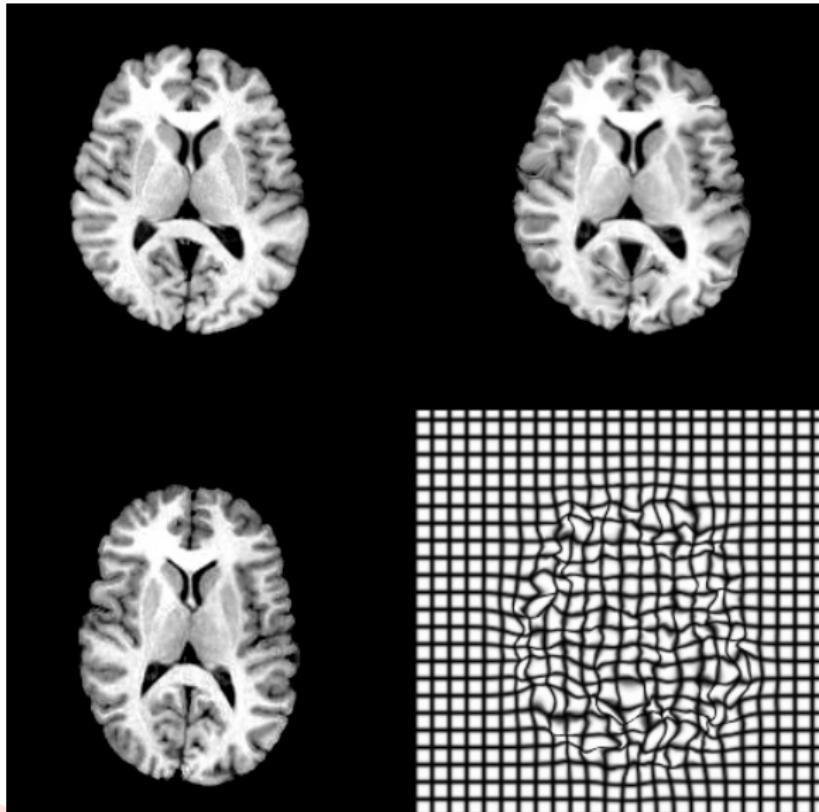
Mapping two images

See examples/registration_example.sh

```
1 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
2 WarpImageMultiTransform $dim $img2 ${out}.nii.gz ${
   out}Warp.nii.gz ${out}Affine.txt -R $img1
3 CreateWarpedGridImage $dim ${out}Warp.nii.gz ${out}
   grid.nii.gz 1x1 10x10 10x10
```



Mapping two images



ADVANCED
NORMALIZATION TOOLS

Can vary smoothness metrics etc. See help

(PICS)

ANTsMM



Segmenting anatomy from an image *Now With Priors!*

See examples/segmentation3_example.sh

```
1 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
2 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
3 for x in 1 2 3 4 ; do
4     N4BiasFieldCorrection -d $dim -i $img2 -o ${out}.
        nii.gz -x ${out}mk.nii.gz -s 1 -b [200] -c [20
        x20x20,0] -w ${out}prob03.nii.gz
5     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]
6 done
```

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

Meaning of ANTs registration parameters

What happens when i vary each parameter?

- Robustness increases with regularization (-r Gauss[6,3] > -r Gauss[3,0])



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What happens when i vary each parameter?

- Robustness increases with regularization ($-r$ Gauss[6,3] > $-r$ Gauss[3,0])
- Flexibility decreases with regularization ($-r$ Gauss[6,3] < $-r$ Gauss[3,0])



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What happens when i vary each parameter?

- Robustness increases with regularization ($-r$ $\text{Gauss}[6,3] > -r \text{Gauss}[3,0]$)
- Flexibility decreases with regularization ($-r \text{Gauss}[6,3] < -r \text{Gauss}[3,0]$)
- Robustness increases with correlation window ($-m$ $\text{CC}[\dots, 1, 4] < -m \text{CC}[\dots, 1, 6]$) but computation time also increases



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- Successful affine step is essential!!



Meaning of ANTs registration parameters

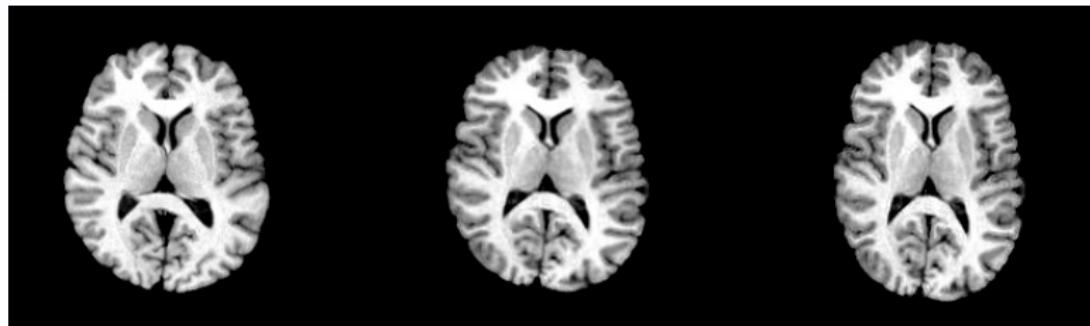
What happens when i vary each parameter?

- Robustness increases with regularization ($-r$ Gauss[6,3] > $-r$ Gauss[3,0])
- Flexibility decreases with regularization ($-r$ Gauss[6,3] < $-r$ Gauss[3,0])
- Robustness increases with correlation window ($-m$ CC[. , . , 1 , 4] < $-m$ CC[. , . , 1 , 6]) but computation time also increases
- 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

```
1 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  
2 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



Coordinates of computation time

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



Coordinates of computation time

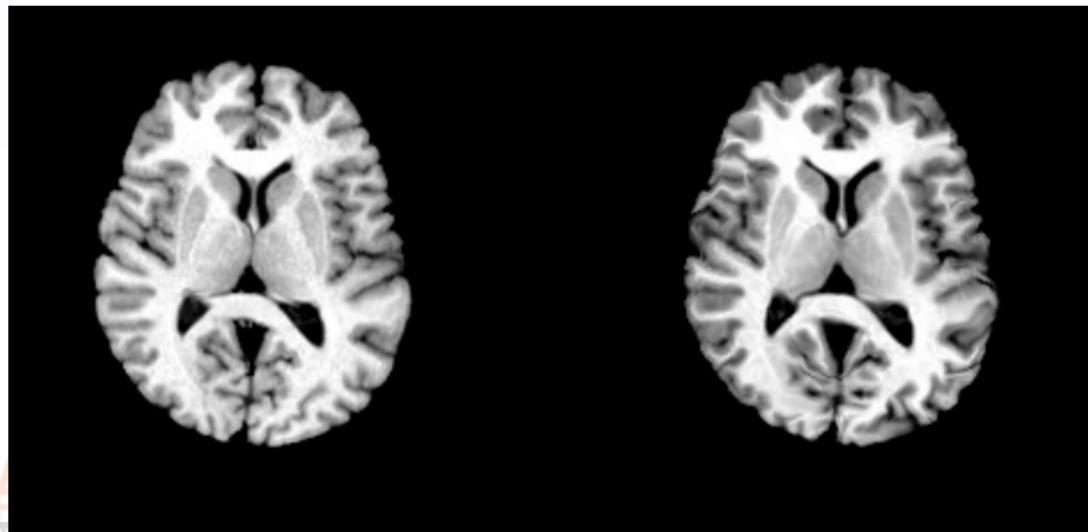
- 2D 256^2 pixels intensity difference (MSQ) registration
 \approx 30 seconds
- 3D 256^3 voxels correlation-8 ($CC[\dots, 1, 8]$) could take 3 days if you use full-resolution and the images are very different.
- or it could take 15 minutes if you use low-resolution and the images are very similar.



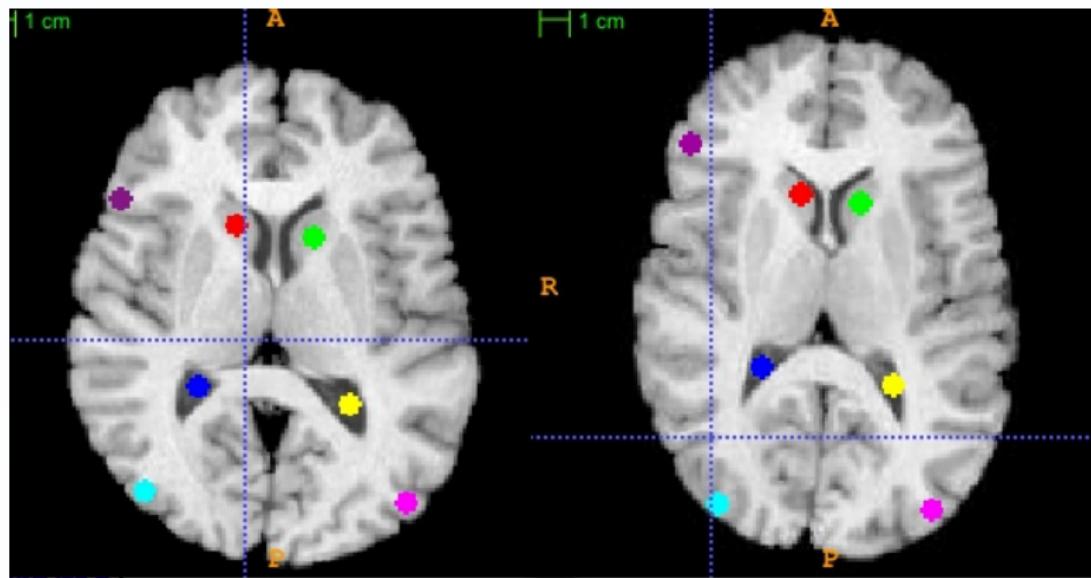
Multiple metrics driving registration

See examples/registration_mm_example.sh

```
1 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



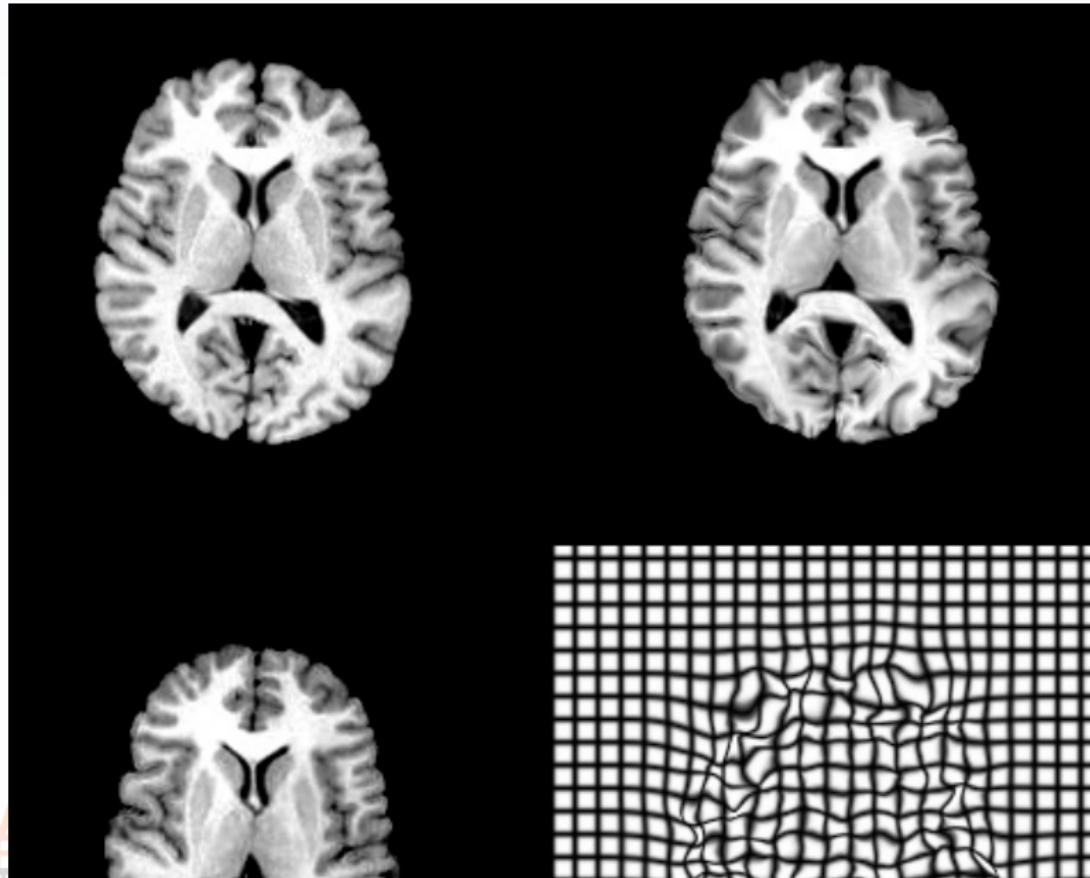
Landmark-based registration 2

See examples/registration_lm_example.sh

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



Landmark-based registration 3



(PICS-L)

ANTsMM



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 WarplImageMultiTransform / antsApplyTransform to apply the warp to the relevant image.



Template construction

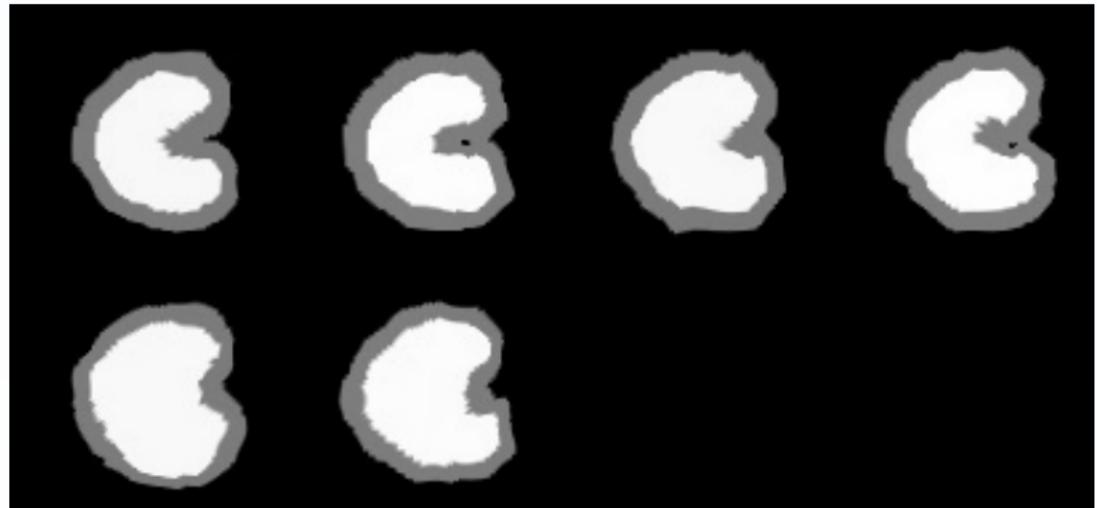
See examples/btp_example.sh

```
1 ln -s ./data/phantom* .
2 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

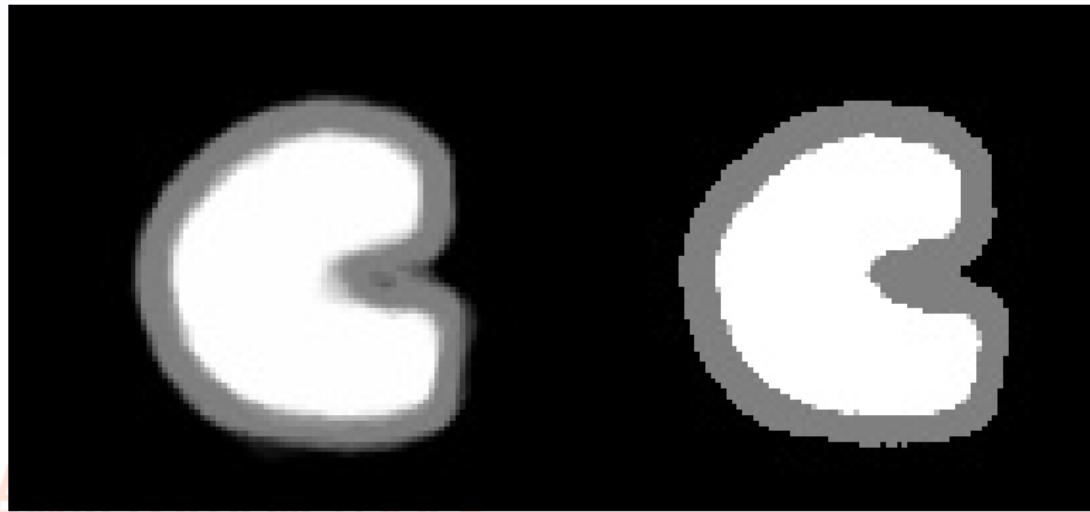


subjects after iteration 2



Multi-template labeling

```
1 for x in *deformed.nii.gz ; do
2     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]
3     ls temp*seg.nii.gz > list.txt
4     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

```
1 ThresholdImage 2 PHtemplateseg.nii.gz maskg.nii.gz 127 127
2 for x in PHphantom*wmgmWarp.nii.gz ; do
3     ANTSJacobian 2 $x phantomG${ct} 1 maskg.nii.gz
4         0
5
6 ls phantomG*logjacobian.nii.gz > list.txt
7 sccan --imageset-to-matrix [list.txt,maskg.nii.gz]
8     ] -o phantomGlogjacs.csv
9 sccan --scca two-view[phantomGlogjacs.csv,
10   globalvols.csv,maskg.nii.gz, NA ,-0.1,-1] -o
11   CCA.nii.gz -n 1 -p 1000 -i 10 --PClusterThresh
12   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** ...

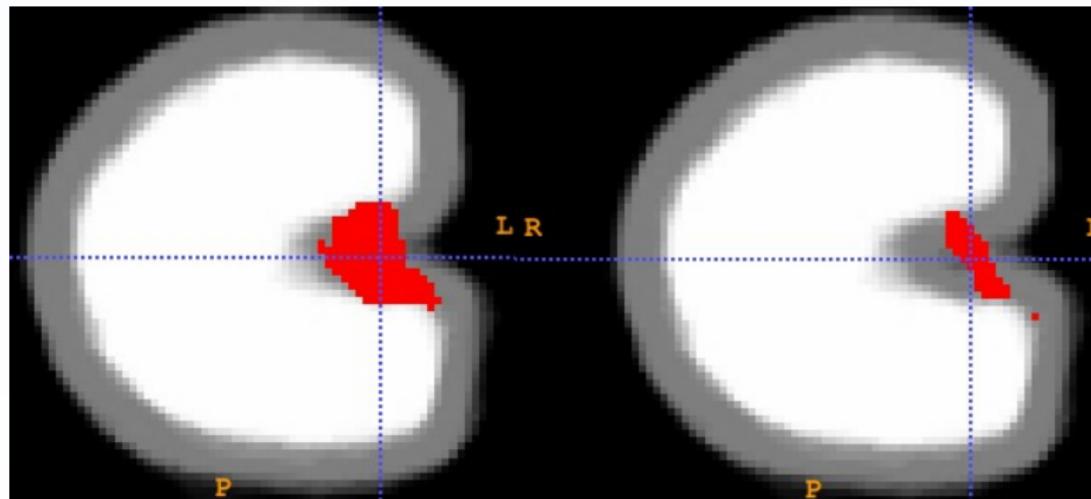


.... voxel-wise statistics in R

```
1 predictor<-read.csv("data/phantpredictors.csv")
2 predictor<-read.csv("templateex/globalvols.csv")
3 logjac<-read.csv("templateex/phantomGlogjacs.csv")
4 attach( logjac ) ; attach( predictor )
5 nvox<-ncol(logjac)
6 pvals<-rep(NA,nvox)
7 for ( x in c(1:nvox) )
8 {
9   voxels<-logjac[,x]
10  lmres<-summary(lm( voxels ~ vol ))
11  coeff<-coefficients( lmres )
12  pval<-coeff[2,4]
13  pvals[x]<-pval
14 }
15 qvals<-p.adjust(pvals)
16 print(min(qvals))
17 write.csv(1-qvals,'templateex/qvals.csv')
18 # sccan --vector-to-image [ templateex/qvals.csv ,
  templateex/maskg.nii.gz , 1] -o temp.nii.gz
```



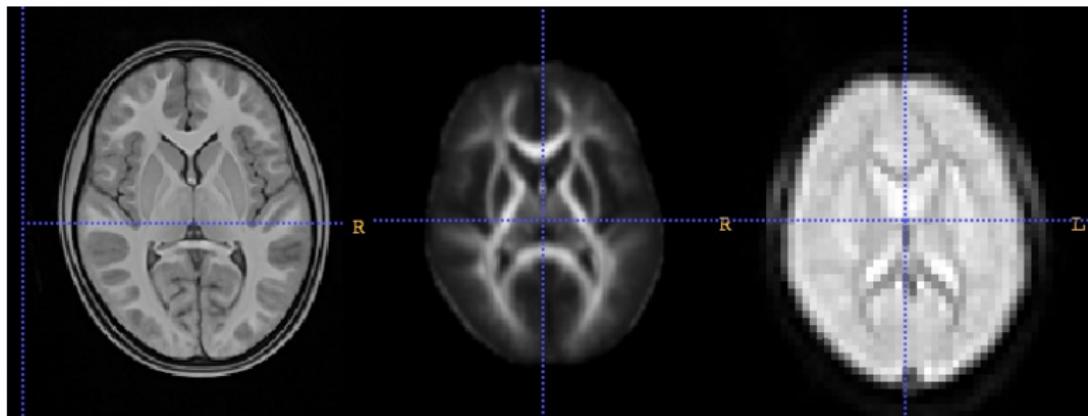
Comparison of results



**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.



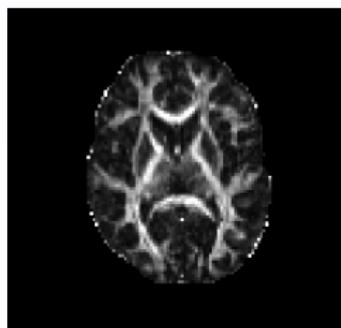
Longitudinal analysis with ANTs

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

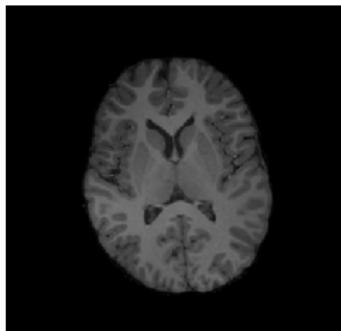


Processing of diffusion tensor data.

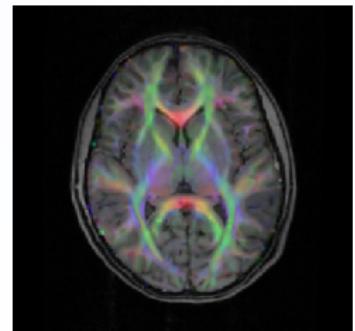
- ① Intra-subject matching (T1 → FA)
- ② Compose warps for template space warp
- ③ Warp and reorient with preservation of principal direction
- ④ Get derived images (FA, MD, RGB, etc) principal direction)



Subject FA



Subject T1



Aligned composite

Time series / rsfMRI analysis with ANTs

See examples/motioncorr_example.sh

```
1 antsMotionCorr -d 3 -a $img -o ${out}avg.nii.gz
2 antsMotionCorr -d 3 -o [${out}],${out}.nii.gz,${out}
    avg.nii.gz] -m mi[ ${out}avg.nii.gz , $img , 1 ,
    32 , Regular , 0.05 ] -t Rigid[ 0.5 ] -i 25 -u 1 -
    e 1 -s 0.0 -f 1 -n 10
```

- mi — mutual information metric



Time series / rsfMRI analysis with ANTs

See examples/motioncorr_example.sh

```
1 antsMotionCorr -d 3 -a $img -o ${out}avg.nii.gz
2 antsMotionCorr -d 3 -o [${out}],${out}.nii.gz,${out}
    avg.nii.gz] -m mi[ ${out}avg.nii.gz , $img , 1 ,
    32 , Regular , 0.05 ] -t Rigid[ 0.5 ] -i 25 -u 1 -
    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



Time series / rsfMRI analysis with ANTs

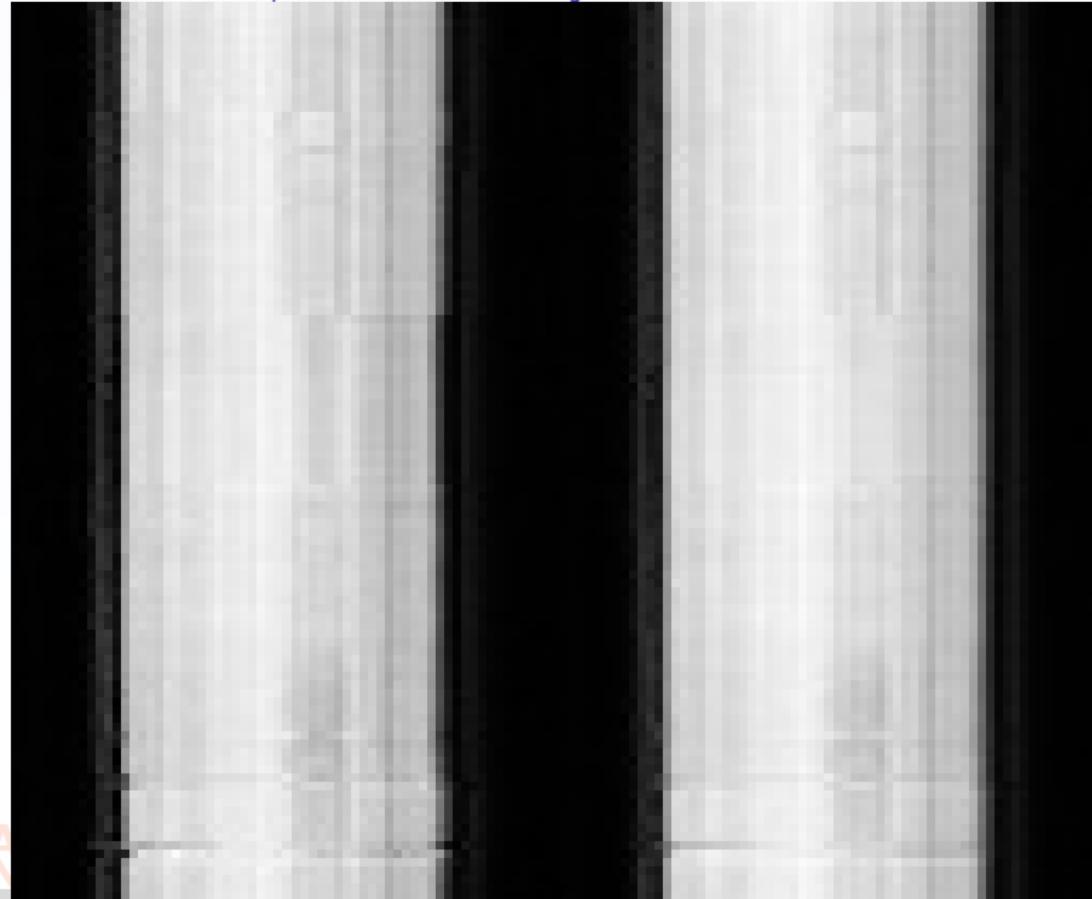
See examples/motioncorr_example.sh

```
1 antsMotionCorr -d 3 -a $img -o ${out}avg.nii.gz
2 antsMotionCorr -d 3 -o [${out}],${out}.nii.gz,${out}
    avg.nii.gz] -m mi[ ${out}avg.nii.gz , $img , 1 ,
    32 , Regular , 0.05 ] -t Rigid[ 0.5 ] -i 25 -u 1 -
    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 ...

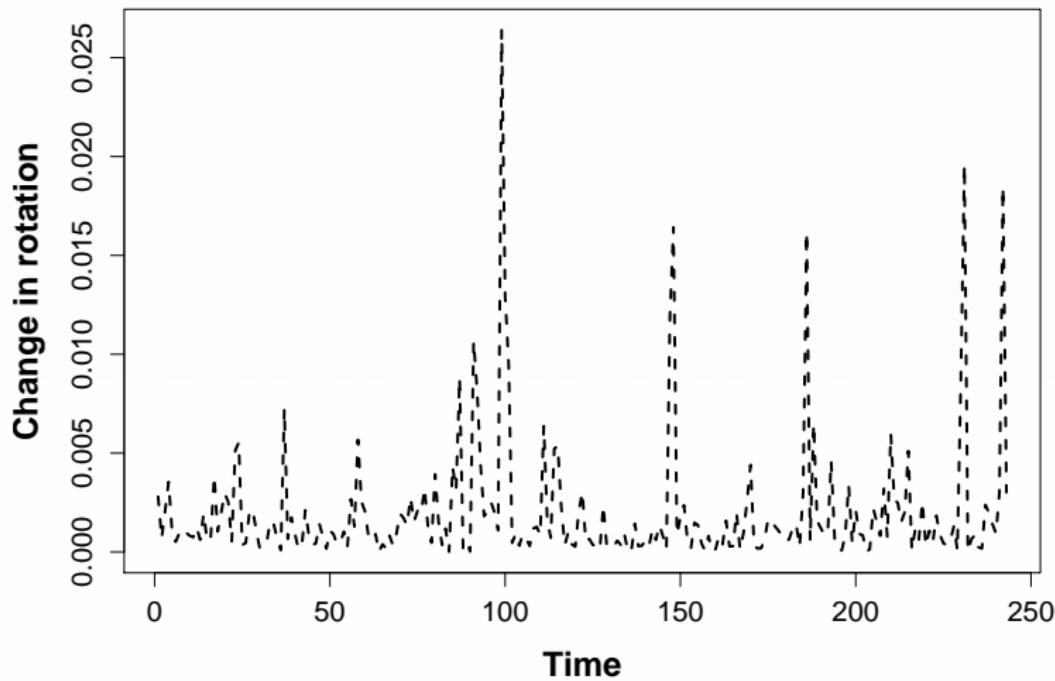


Time series / rsfMRI analysis with ANTs



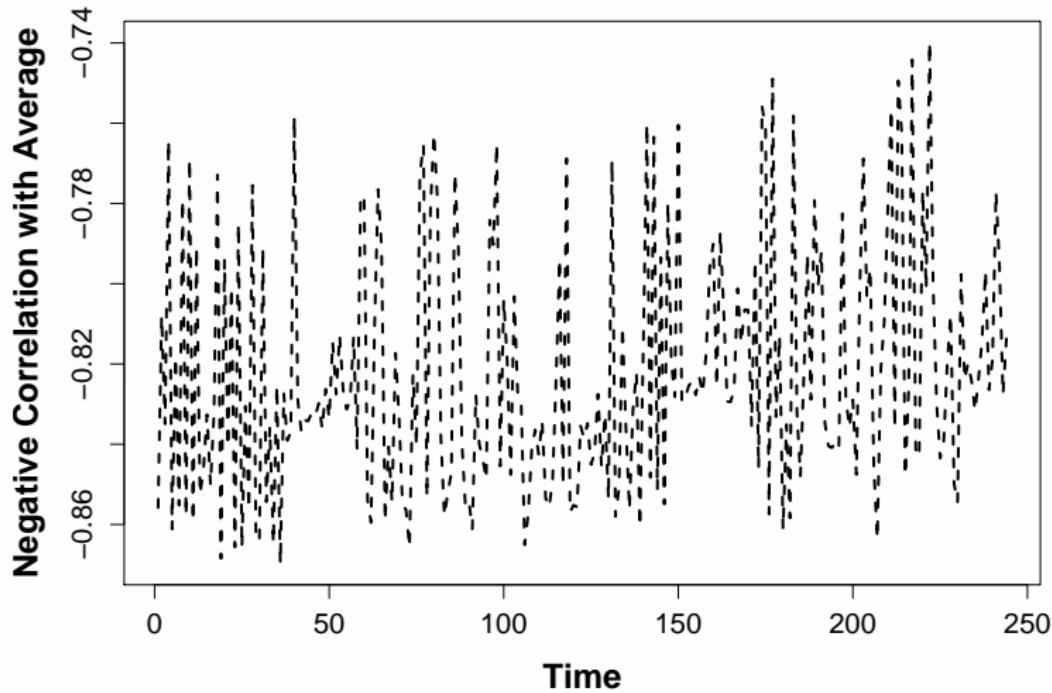
Time series / rsfMRI analysis with ANTs

Outlier Rejection



Time series / rsfMRI analysis with ANTs

Outlier Rejection



Extracting a resting state network

See examples/rsfnodes_example.sh

```
1 ThresholdImage 3 ${out}avg.nii.gz ${out}_bmask.nii  
     .gz 300 9999  
2 ImageMath 3 ${out}_bmask.nii.gz GetLargestComponent  
     ${out}_bmask.nii.gz  
3 ImageMath 4 ${out}compcorr.nii.gz CompCorrAuto ${  
     out}.nii.gz ${out}_bmask.nii.gz 6  
4 sccan --timeseriesimage-to-matrix [ ${out}  
     compcorr_corrected.nii.gz , ${out}_bmask.nii.gz  
     , 0 , 1.0 ] -o ${out}.csv  
5 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

- ANTs is ideal for producing reproducible research.



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- It is multi-platform and portable.



Reproducibility

- ANTs is ideal for producing reproducible research.
- It is multi-platform and portable.
- It can easily be modified for + + + different types of studies.

Reproducibility

- ANTs allows one to access the powers of both ITK and R.



Reproducibility

- ANTs allows one to access the powers of both ITK and R.
- We aim to support user needs so if you can't find something, just ask Questions?



Acknowledgements

Need a QA slide also ...

RSF nodes — automatically label then select nodes and stuff ...

Show a menu and let people use it.



Acknowledgements

- NIBIB for software development support under grant R01-EB006266-01.
- The ITK development team.
- Dr. Murray Grossman for pushing application development.
- The NLM for providing stimulus funding in support of ITKv4.

