ANTs: A retrospective

Brian (Penn) and Nick (UVa)

This talk is online at `http://stnava.github.io/ANTs2015/` with colored links meant to be clicked for more information.

Retrospective

ANTs evolution

FreeSurfer, Bruce Fischl

NeuroImaging research as literature

"Contingency. AFNI is one result of unexpected events. I met a woman and fell in love."

ANTs–*begotten in SyN*

Founding developers

Brian and Edie

Nick and Bruce

Brian and Nick

ANTs Long term collaborators

+ neurodebian, slicer, brainsfit, nipype, itk and more ...

ANTs lineage

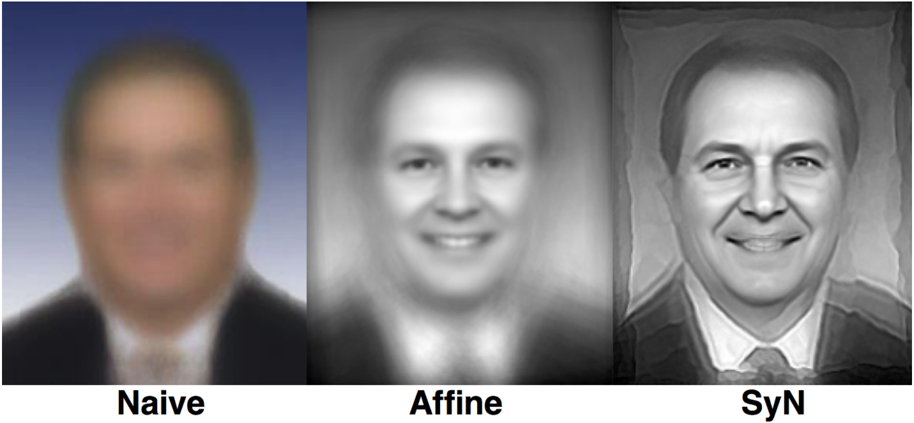
Image mapping and perception: 1877

Francis Galton: *Can we see criminality in the face?*

What about syphilis, mental illness?

Speaking of criminality. . .

Can we say anything about the U.S. Congress?



Maybe he should have used ANTs?

Image mapping & biology: 1917

D'Arcy Thompson: *Comparison of related forms*

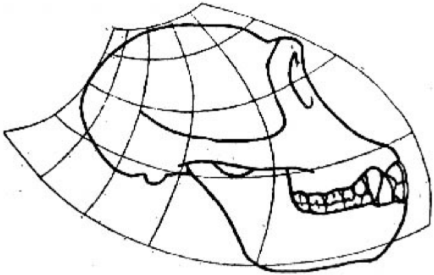


Fig. 550. Skull of chimpanzee.

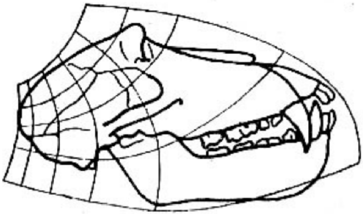
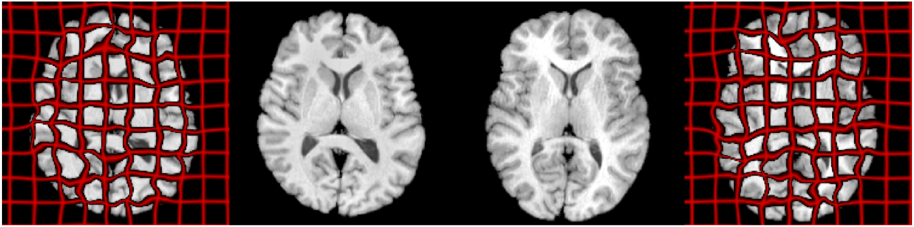


Fig. 551. Skull of baboon.

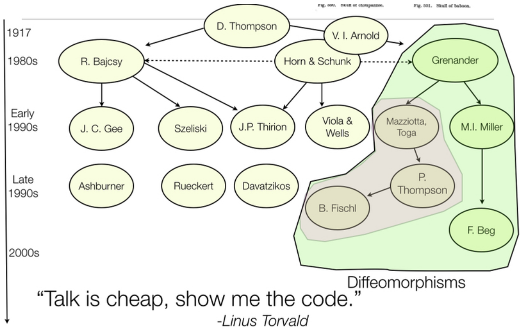
Image mapping & biology: Current

Look where we are now!

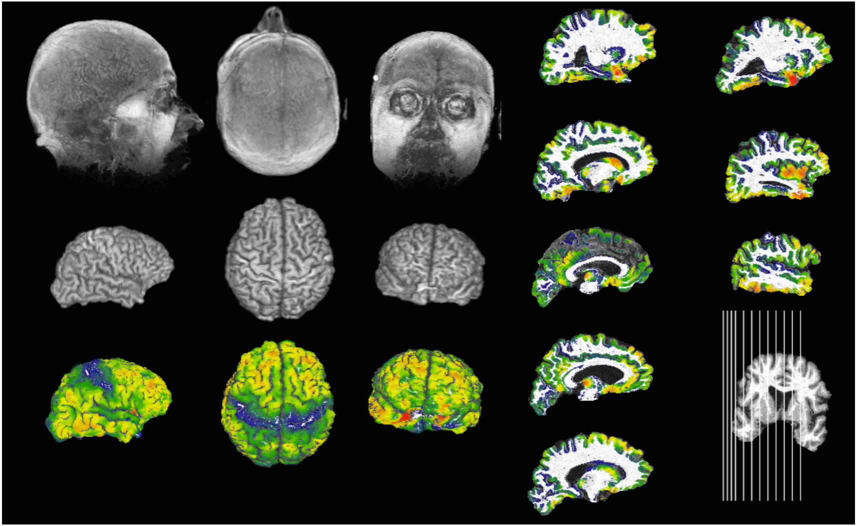


Fixed   Moving

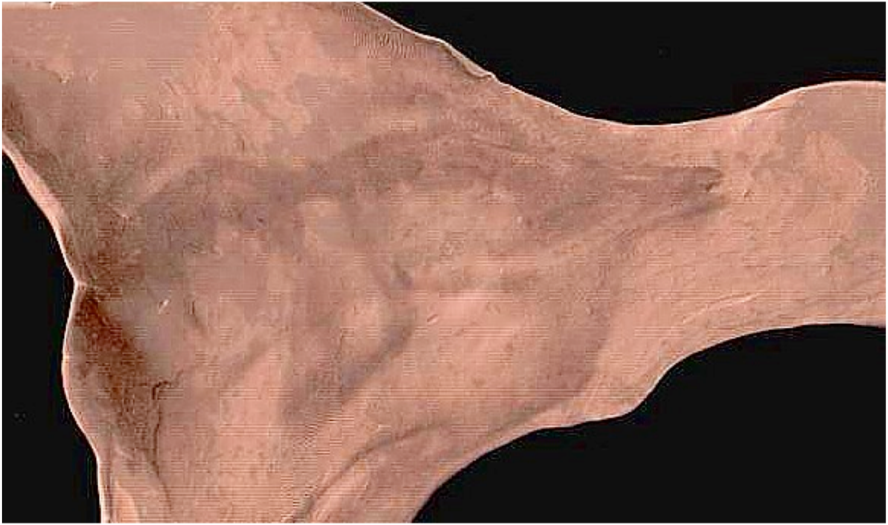
ANTs family tree



Initial scope

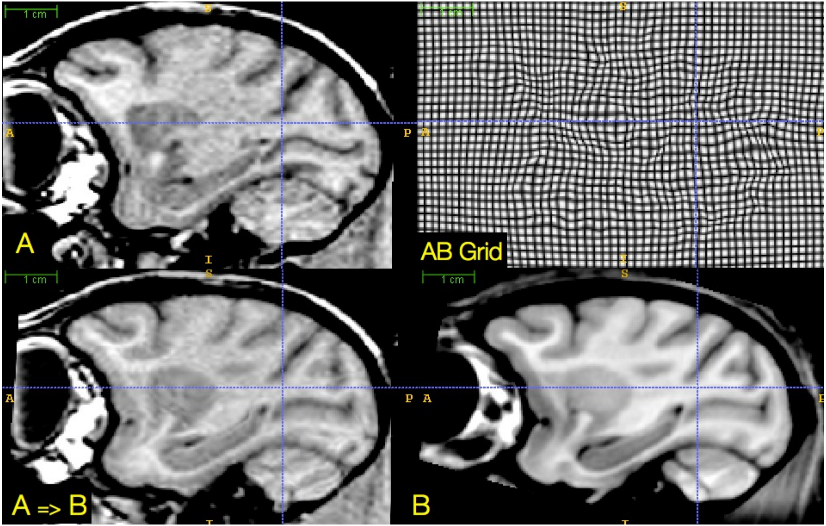


Diffeomorphisms: Occam's razor modeling



differentiable map with differentiable inverse

Diffeomoprhisms: fine-grained and flexible maps



Diffeomorphisms: image parameterization in a metric space

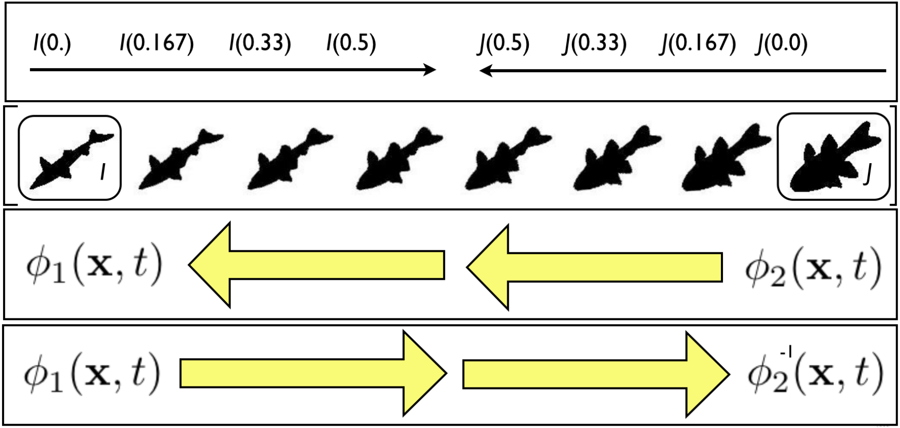
Major papers

Donoho?

"Papers are just advertisements for the science."

Symmetric Normalization (SyN)

$$\int_{t=0}^{0.5} \left(\|\mathbf{v}_1(x,t)\|_L^2 + \|\mathbf{v}_2(x,t)\|_L^2\right) dt + \|I\left(\phi_1(x,0.5)\right) - J_i\left(\phi_2(x,0.5)\right)\|^2$$



Beyond original SyN

frontiers in NEUROINFORMATICS

ORIGINAL RESEARCH ARTICLE
published: 28 April 2014
doi: 10.3389/fninf.2014.00044

The Insight ToolKit image registration framework

Brian B. Avants[1]*, Nicholas J. Tustison[2], Michael Stauffer[1], Gang Song[1], Baohua Wu[1] and James C. Gee[1]

[1] *Penn Image Computing and Science Laboratory, Department of Radiology, University of Pennsylvania, Philadelphia, PA, USA*
[2] *Department of Radiology and Medical Imaging, University of Virginia, Charlottesville, VA, USA*

frontiers in NEUROINFORMATICS

METHODS ARTICLE
published: 23 December 2013
doi: 10.3389/fninf.2013.00039

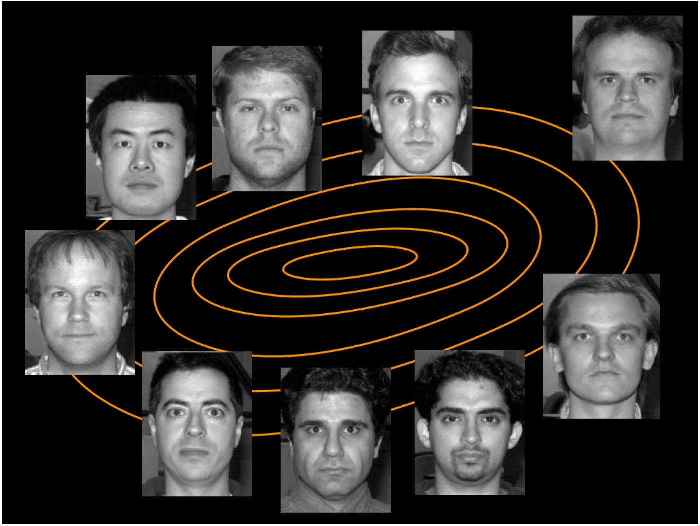
Explicit B-spline regularization in diffeomorphic image registration

Nicholas J. Tustison[1]* and Brian B. Avants[2]

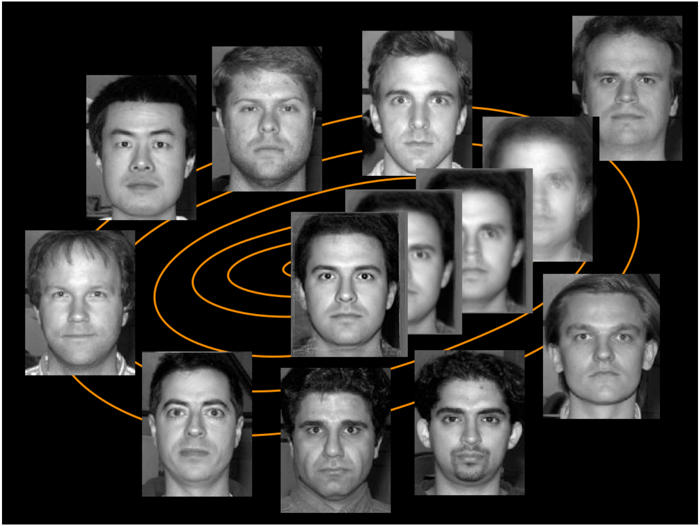
antsRegistration

```
$ antsRegistration --help

COMMAND:
     antsRegistration
          This program is a user-level registration applicatio
          ITKv4-only classes. The user can specify any number 
          consists of a transform; an image metric; and iterat
          smoothing sigmas for each level.Note that dimensiona
          output, convergence, shrink-factors and smoothing-si
          mandatory.

OPTIONS:
     --version
          Get Version Information.

     -d, --dimensionality 2/3
```

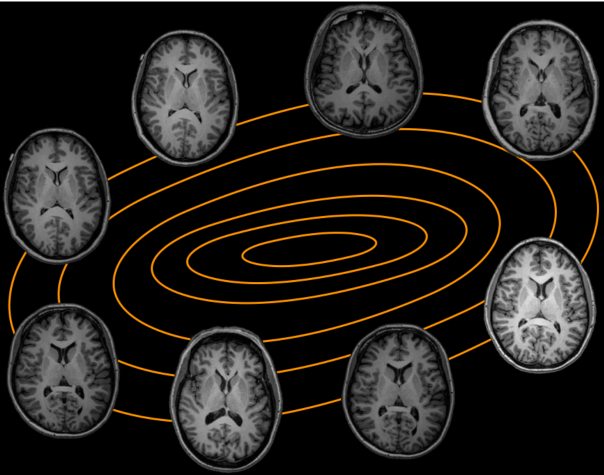
Template building: creating the average Joe



"Attractiveness" $\rightarrow$ mental processing?



What about brains?



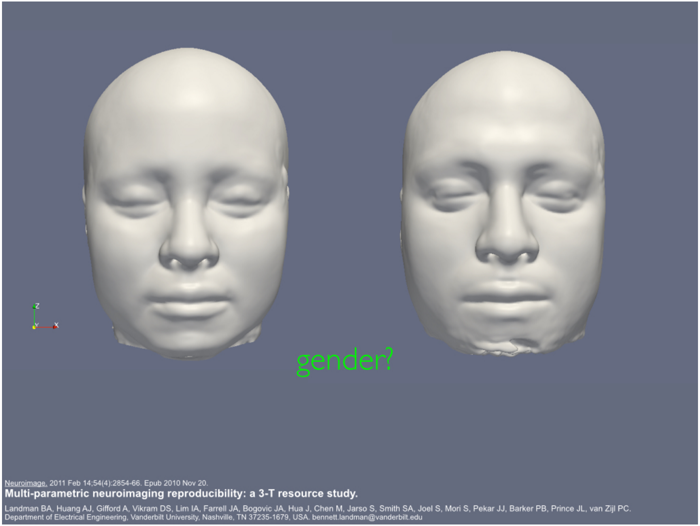
Neuroimage. 2010 Feb 1;49(3):2457-66. Epub 2009 Oct 8.

The optimal template effect in hippocampus studies of diseased populations.

Avants BB, Yushkevich P, Pluta J, Minkoff D, Korczykowski M, Detre J, Gee JC.
Department of Radiology, University of Pennsylvania, Philadelphia, PA 19104, USA. avants@grasp.cis.upenn.edu

Templates facilitate computation

Gender discernibility?



antsMultivariateTemplateConstruction2.sh

```
$ antsMultivariateTemplateConstruction2.sh

Usage:

antsMultivariateTemplateConstruction2.sh -d ImageDimension -o

Compulsory arguments (minimal command line requires SGE/PBS cl
  -j options):

     -d:  ImageDimension: 2 or 3 (for 2 or 3 dimensional regis
   ImageDimension: 4 (for template generation of time-series d

     -o:  OutputPrefix; A prefix that is prepended to all outp

<images>  List of images in the current directory, eg *_t1.nii
          of the command.  Optionally, one can specify a .csv
```

Nonparametric nonuniform intensity normalization (N3)

- Developed at the Montreal Neurological Institute (John Sled, 1998)

Nonparametric nonuniform intensity normalization (N3)

- Developed at the Montreal Neurological Institute (John Sled, 1998)
- Part of the standard preprocessing protocol in large scale projects such as ADNI

Nonparametric nonuniform intensity normalization (N3)

- Developed at the Montreal Neurological Institute (John Sled, 1998)
- Part of the standard preprocessing protocol in large scale projects such as ADNI
- The traditional de facto standard in MRI bias correction

Nonparametric nonuniform intensity normalization (N3)

- Developed at the Montreal Neurological Institute (John Sled, 1998)
- Part of the standard preprocessing protocol in large scale projects such as ADNI
- The traditional de facto standard in MRI bias correction
  - good performance

Nonparametric nonuniform intensity normalization (N3)

- Developed at the Montreal Neurological Institute (John Sled, 1998)
- Part of the standard preprocessing protocol in large scale projects such as ADNI
- The traditional de facto standard in MRI bias correction
  - good performance
  - *public availability*

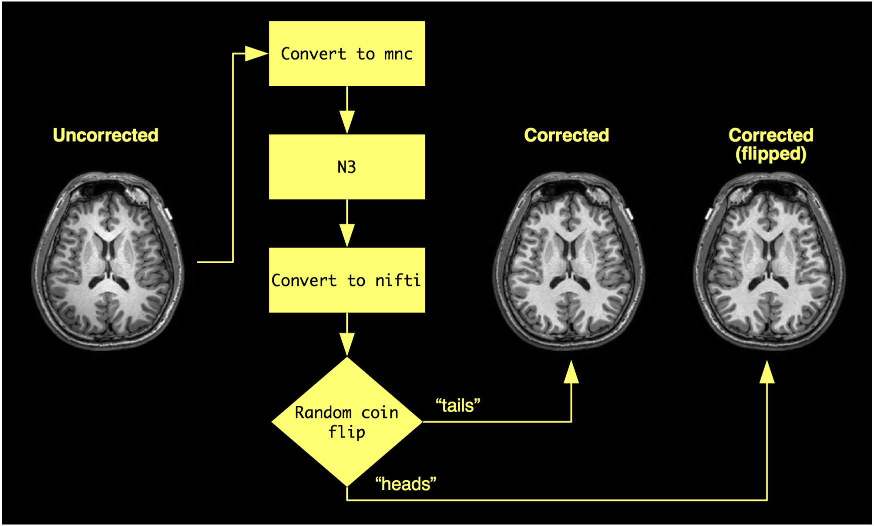
Nonparametric nonuniform intensity normalization (N3)

- Developed at the Montreal Neurological Institute (John Sled, 1998)
- Part of the standard preprocessing protocol in large scale projects such as ADNI
- The traditional de facto standard in MRI bias correction
  - good performance
  - *public availability*
- Public availability — set of perl scripts coordinating various C++ programs

Nonparametric nonuniform intensity normalization (N3)

- Developed at the Montreal Neurological Institute (John Sled, 1998)
- Part of the standard preprocessing protocol in large scale projects such as ADNI
- The traditional de facto standard in MRI bias correction
  - good performance
  - *public availability*
- Public availability — set of perl scripts coordinating various C++ programs
- "*Let's incorporate N3 into ANTs!*"

N3 adoption issues



N4

- comparative evaluation

N4

- comparative evaluation
- small spline distances (useful for higher magnet strengths)

N4

- comparative evaluation
- small spline distances (useful for higher magnet strengths)
- multiresolution

N4

- comparative evaluation
- small spline distances (useful for higher magnet strengths)
- multiresolution
- weighted regional mask (used in `antsAtroposN4.sh`)

N4

- comparative evaluation
- small spline distances (useful for higher magnet strengths)
- multiresolution
- weighted regional mask (used in `antsAtroposN4.sh`)
- fast execution times

N4

- comparative evaluation
- small spline distances (useful for higher magnet strengths)
- multiresolution
- weighted regional mask (used in `antsAtroposN4.sh`)
- fast execution times
- *publicly available*

N4

- comparative evaluation
- small spline distances (useful for higher magnet strengths)
- multiresolution
- weighted regional mask (used in `antsAtroposN4.sh`)
- fast execution times
- *publicly available*
- tested nightly within the ITK dashboard system

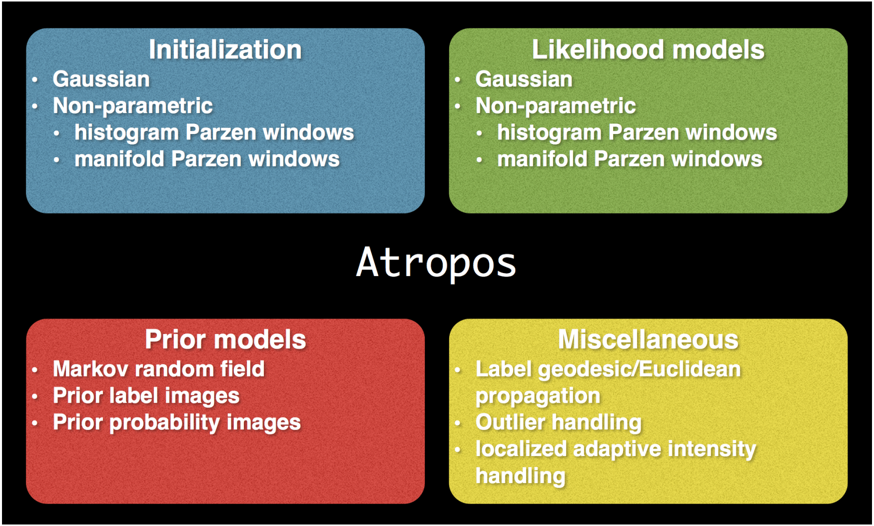
N4BiasFieldCorrection

```
$ N4BiasFieldCorrection --help

COMMAND:
     N4BiasFieldCorrection
          N4 is a variant of the popular N3 (nonparameteric no
          retrospective bias correction algorithm. Based on th
          corruption of the low frequency bias field can be mo
          the intensity histogram by a Gaussian, the basic alg
          iterate between deconvolving the intensity histogram
          the intensities, and then spatially smoothing this r
          of the bias field itself. The modifications from and
          the original N3 algorithm are described in the follo
          al., N4ITK: Improved N3 Bias Correction, IEEE Transa
          29(6):1310-1320, June 2010.

OPTIONS:
```

Atropos – cutting the threads of fate

"20+ years of development. *Show me the code!*"

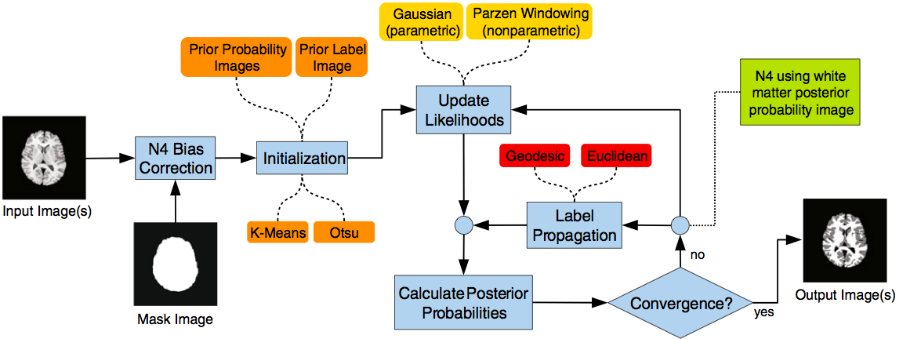
Atropos: flexible code base



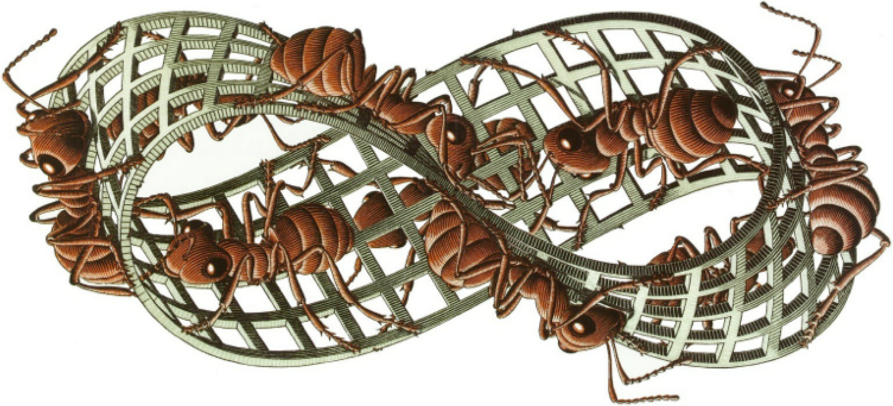
Atropos

```
$ Atropos --help

COMMAND:
     Atropos
          A finite mixture modeling (FMM) segmentation approac
          specifying prior constraints. These prior constraint
          of a prior label image, prior probability images (or
          MRF prior to enforce spatial smoothing of the labels
          FAST and SPM. Reference: Avants BB, Tustison NJ, Wu
          source multivariate framework for n-tissue segmentat
          public data. Neuroinformatics. 2011 Dec;9(4):381-400

OPTIONS:
     -d, --image-dimensionality 2/3/4
          This option forces the image to be treated as a spec
          not specified, Atropos tries to infer the dimensiona
```

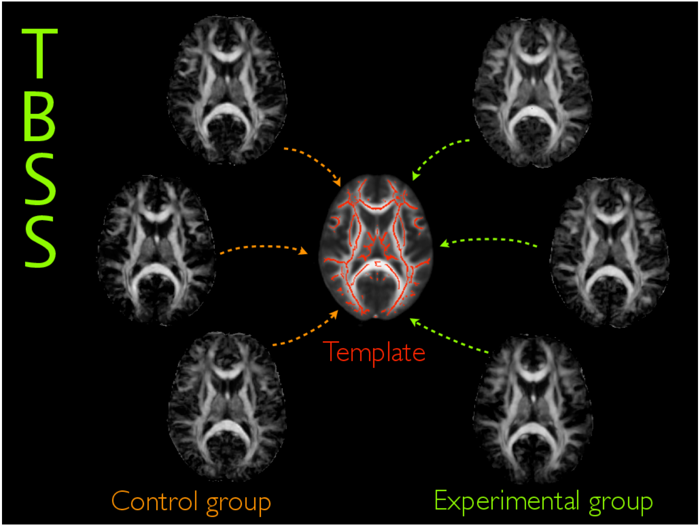
Atropos + N4 → `antsAtroposN4.sh`



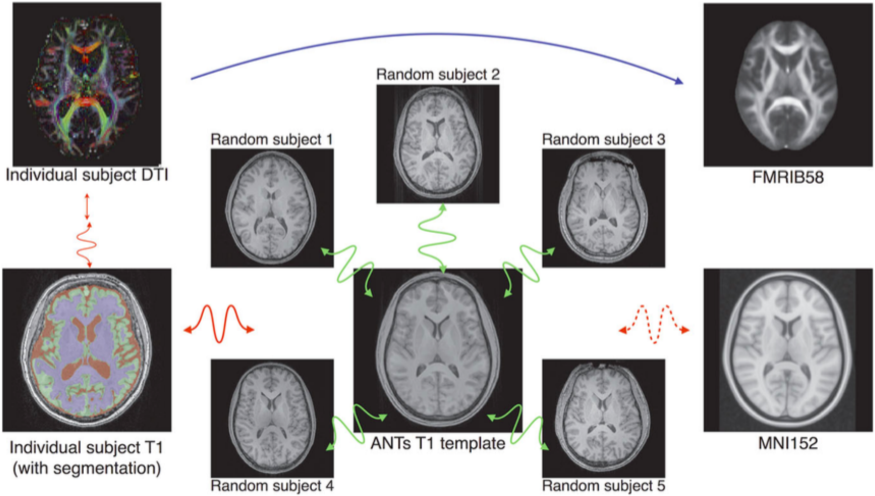
ANTs and the perils of circularity



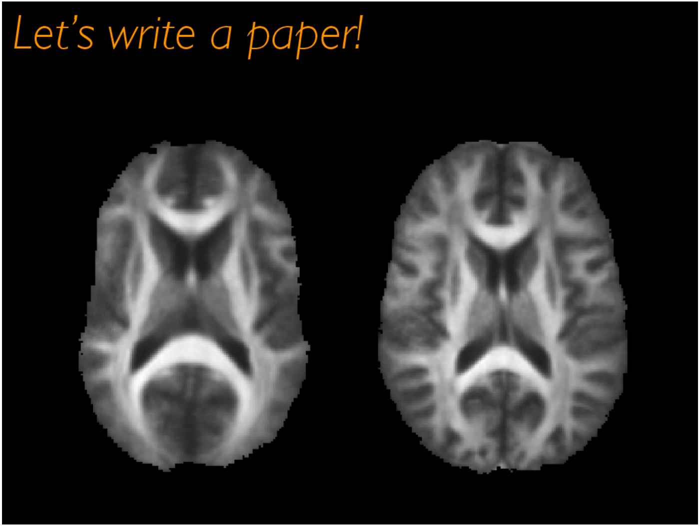
"Hey Brian, have you ever used TBSS?"



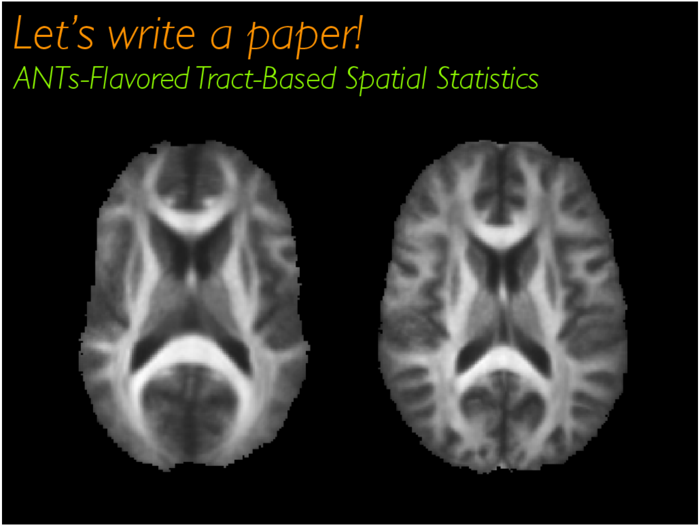
Use ANTs template building



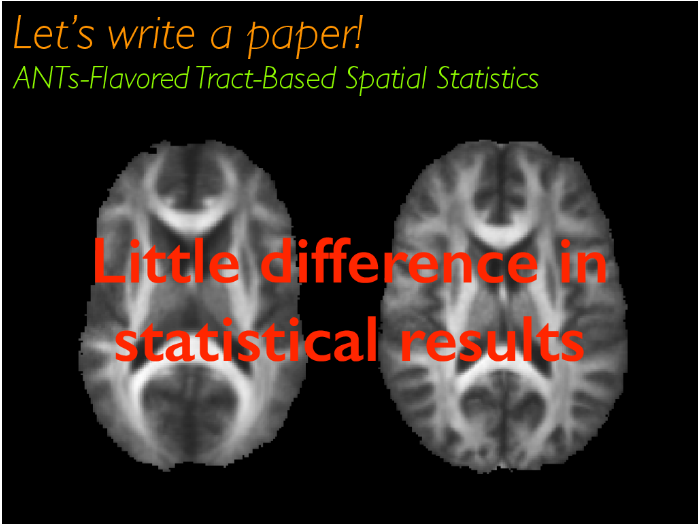
Evaluation



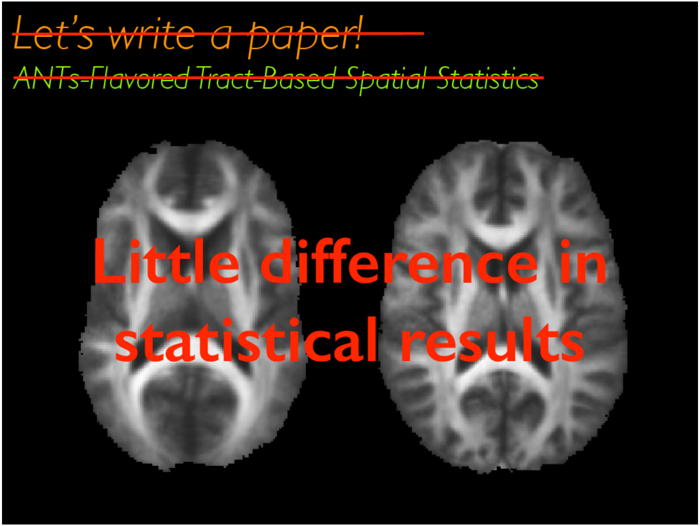
We'll call the approach. . .



Quantitative results



So much for that idea. :(

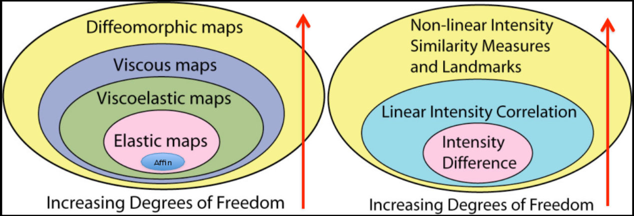


What happened?

Possible causes

Transformation model

Appearance model



Other possible causes

- smoothing
- statistical testing (parametric vs. non-parametric)
- skeletal projections (TBSS)

Insight to the major stumbling block

brian avants
to Nick

May 8

nick

the only point i understand clearly is that the ssd metric + smoothing and standard fsl + smoothing have similar detection power and both are dissimilar to the other metrics (and t1 based mapping) .

regarding this question

> So, Brian, is all this smoothing simply spreading out the FA differences
> between groups which is why the statistical power is higher?

i still dont know.   a t-test is

(mean_1 - mean_2) / variance

so either the difference in means (on the skeleton) is increased by the ssd+smoothing approaches or the variance is decreased. my guess is that it's the latter.

perhaps it's worth looking explicitly at each of these three values.

...

Academically “counting sheep”

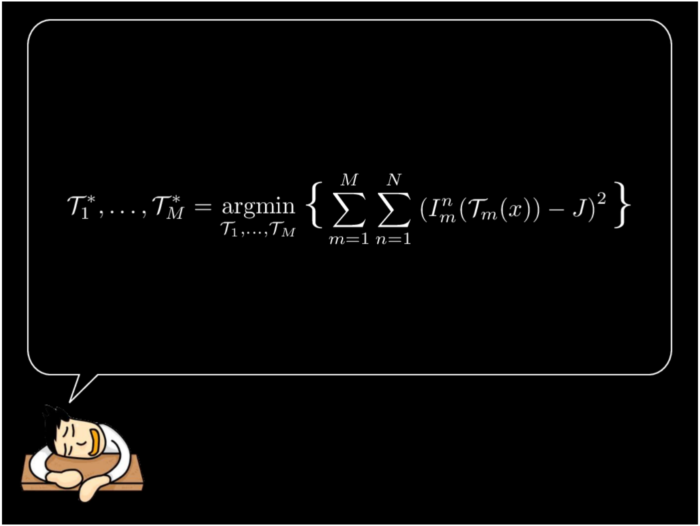
$$\mathcal{T}^* = \underset{\mathcal{T}}{\operatorname{argmin}} \left\{ SSD(I, J, \mathcal{T}) = \frac{1}{N} \sum_{n=1}^{N} \left(I^n(\mathcal{T}(\mathbf{x})) - J \right)^2 \right\}$$

It sort of looks like the variance but the N

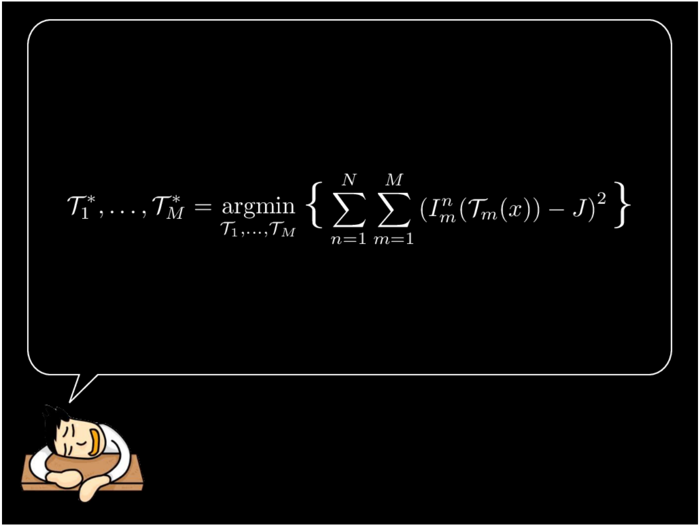
$$\mathcal{T}^* = \underset{\mathcal{T}}{\operatorname{argmin}} \left\{ SSD(I, J, \mathcal{T}) = \frac{1}{N} \sum_{n=1}^{N} \left(I^n(\mathcal{T}(\mathbf{x})) - J \right)^2 \right\}$$

Wait, that's not right.

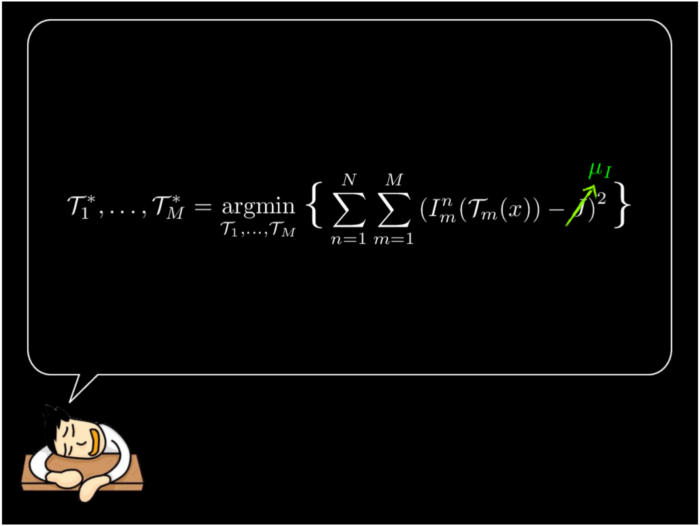
There's a missing summation!



We switch the summations,



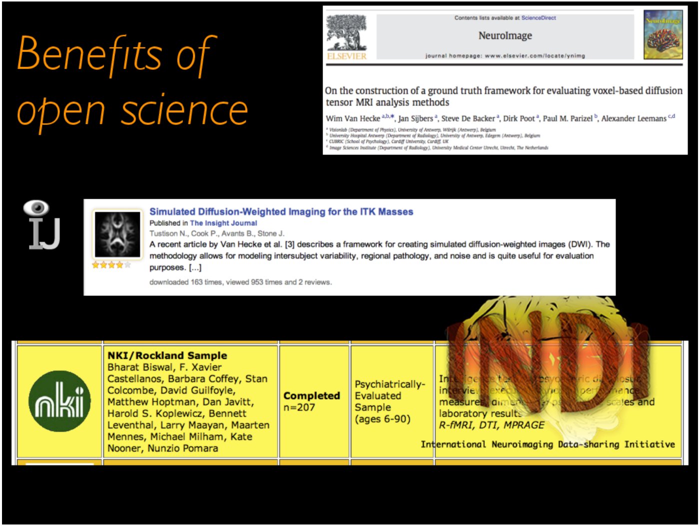
recast J as the mean image, and



there it is!

$$\mathcal{T}_1^*, \ldots, \mathcal{T}_M^* = \operatorname*{argmin}_{\mathcal{T}_1, \ldots, \mathcal{T}_M} \left\{ \sum_{n=1}^{N} \underbrace{\sum_{m=1}^{M} \left(I_m^n(\mathcal{T}_m(x)) - \cancelto{\mu_I}{J} \right)^2}_{\text{voxelwise variance}} \right\}$$

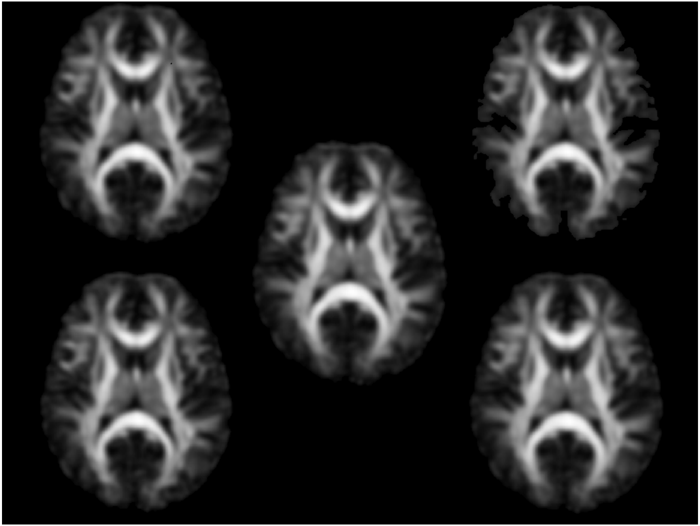
Okay, so now how do we show this?



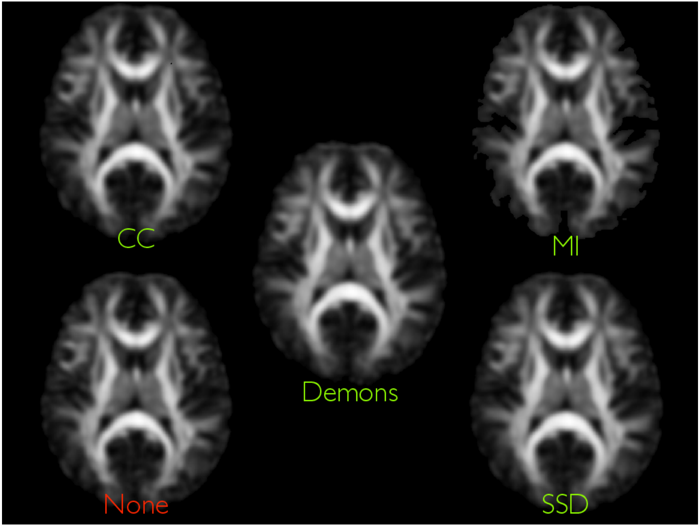
Open science evaluation

```
$ CreateDTICohort -h

COMMAND:
     CreateDTICohort

OPTIONS:
     -d, --image-dimensionality 2/3
     -a, --dti-atlas inputDTIAtlasFileName
     -x, --label-mask-image maskImageFileName
                            lowerThresholdFunction
     -n, --noise-sigma <noiseSigma=18>
     -p, --pathology label[<percentageChangeEig1=-0.05>,<perce
     -w, --dwi-parameters [B0Image,directionFile,bvalue]
                          [B0Image,schemeFile]
     -r, --registered-population textFileWithFileNames.txt
     -o, --output [outputDirectory,fileNameSeriesRootName,<num
```

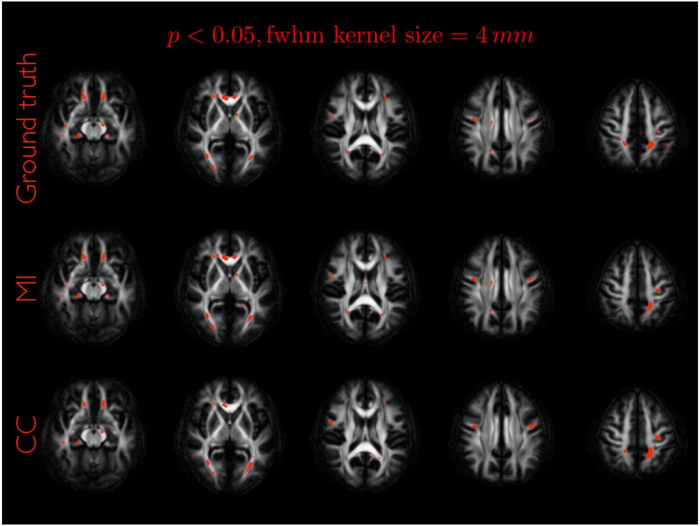
Which one is not warped?



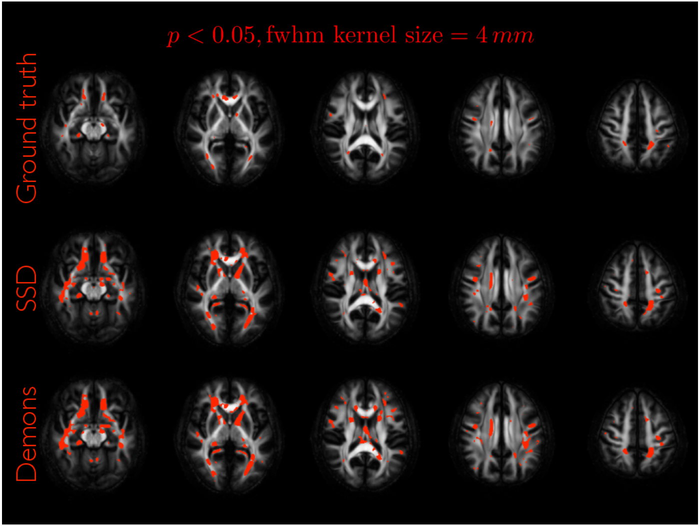
Answer



How does this vary with similarity metric?



How does this vary with similarity metric?



Bookstein review (blurb 1)

This is a signed review by Fred Bookstein.

This manuscript has an excellent point to make, and I would think so even if either (1) I did not agree with its position, or (2) my own work were not cited so gently and appropriately within it, and even though (3) the title is truly terrible, since "circularity" has two ENTIRELY different meanings, one having to do with GEOMETRIC circularity and the other with LOGICAL circularity, and the meaning the authors intended is (I trust) the second one whereas the one that instantly leaps to the mind of the typical member of the medical imaging community must necessarily be the first one, which is to say, the wrong one. The title should instead be something like

Circular reasoning about circles:
logical circularity in voxel-based analysis

or the like.

Anyway, assuming the title is repaired, it is impossible to disagree with the authors' position. My comment is only that this is old news, and that is not meant as a destructive criticism, but only as the suggestion that the literature review be made deeper and wiser than it is.

Bookstein review (blurb 2)

of any statistician's toolkit. In fact, my own articleof 2001, which is appropriately cited by these authors, makes exactly the same point: the information in the registration is confounded with the information in the registered images; you can't say you are testing just one and not the other.

Bookstein review (blurb 3)

algebraically by a variant of the Akaike formula. I happen to think I said most of this already in 2001, but that was before the widespread availability of diffusion tensor data, which looks like it is susceptible to different paradoxes instead. But they are at root the same.

Fred L. Bookstein
University of Vienna,
University of Washington
March 23, 2012

Competitions

Algorithmic fight club

International competitions

- Klein 2009

International competitions

- Klein 2009
- EMPIRE 2010

International competitions

- Klein 2009
- EMPIRE 2010
- Multi-Atlas Label Challenge 2012

International competitions

- Klein 2009
- EMPIRE 2010
- Multi-Atlas Label Challenge 2012
- SATA Challenge 2013

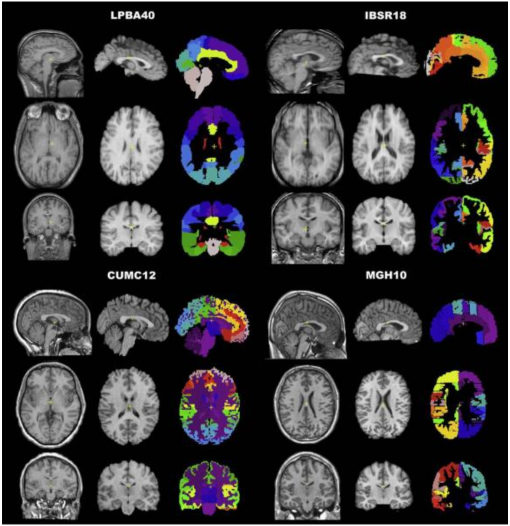
International competitions

- Klein 2009
- EMPIRE 2010
- Multi-Atlas Label Challenge 2012
- SATA Challenge 2013
- BRATS 2013

International competitions

- Klein 2009
- EMPIRE 2010
- Multi-Atlas Label Challenge 2012
- SATA Challenge 2013
- BRATS 2013
- STACOM 2014 MoCo Challenge

Klein, NeuroImage 2009



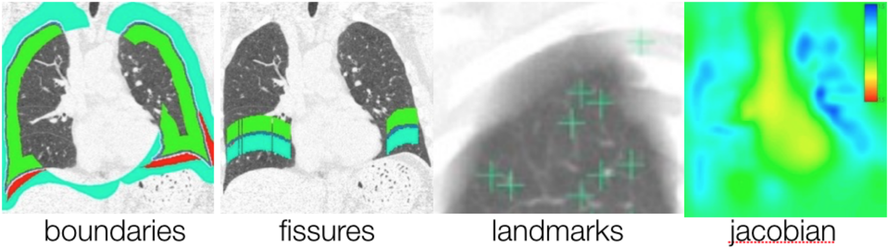
Klein results

	LPBA40	μ (SD)	IBSR18	μ (SD)	CUMC12	μ (SD)	MGH10	μ (SD)
rank 1	ART	.82 (.35)	SPM_D	.83 (.27)	SPM_D	.76 (.24)	SyN	.77 (.37)
	SyN	.60 (.38)	SyN	.72 (.51)	SyN	.74 (.51)	ART	.72 (.45)
	FNIRT	.49 (.66)	IRTK	.67 (.53)	IRTK	.74 (.50)	IRTK	.61 (.51)
	JRD-fluid	.49 (.66)	ART	.60 (.70)	ART	.60 (.70)		
2	IRTK	.43 (.63)	JRD-fluid	.30 (.82)			SPM_D	.27 (.23)
	D.Demons	.13 (.82)					D.Demons	.27 (.69)
	SPM_US	.11 (.83)					JRD-fluid	.24 (.66)
							ROMEO	.06 (.63)
3	ROMEO	.08 (.73)	FNIRT	.16 (.82)	D.Demons	.20 (.84)		
	SPM_D	.07 (.29)	D.Demons	.05 (.84)	FNIRT	.18 (.81)		
					JRD-fluid	.17 (.81)		

Take-away message

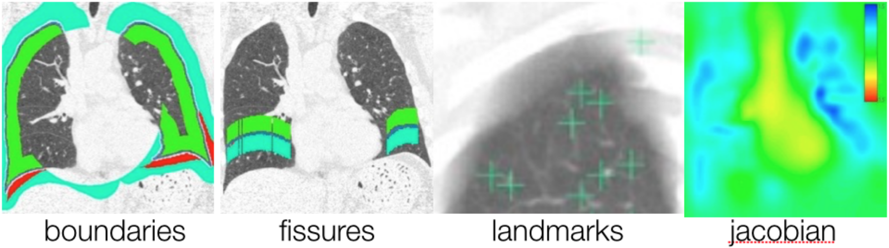
"One of the most significant findings of this study is that the relative performances of the registration methods under comparison appear to be little affected by the choice of subject population, labeling protocol, and type of overlap measure. . . . ART, SyN, IRTK, and SPM's DARTEL Toolbox gave the best results according to overlap and distance measures, with ART and SyN delivering the most consistently high accuracy across subjects and label sets."

EMPIRE 2010



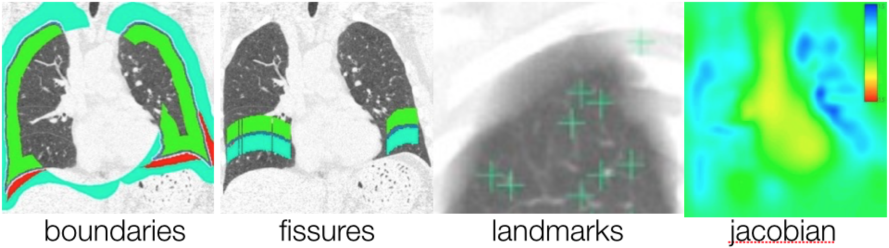
- Alignment of lung boundaries,

EMPIRE 2010



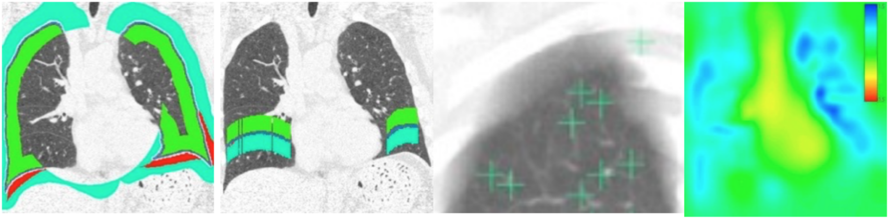
- Alignment of lung boundaries,
- major fissures,

EMPIRE 2010



- Alignment of lung boundaries,
- major fissures,
- annotated landmark pairs, and

EMPIRE 2010



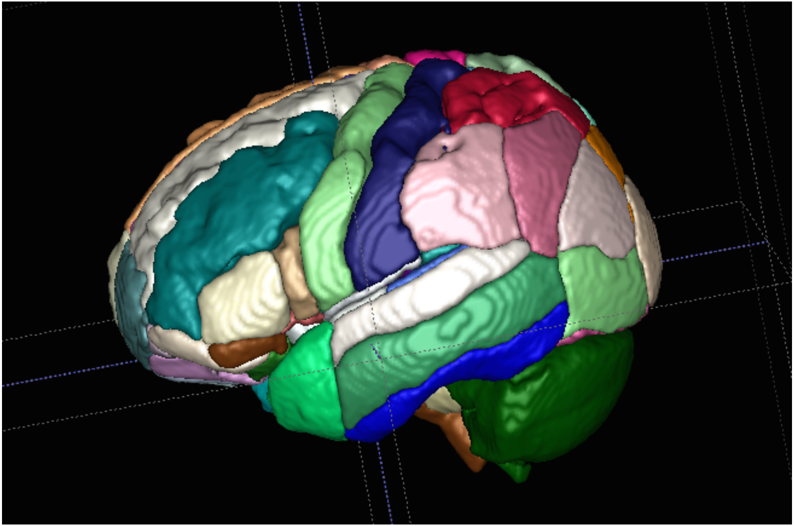
boundaries fissures landmarks jacobian

- Alignment of lung boundaries,
- major fissures,
- annotated landmark pairs, and
- topology of displacement field.

EMPIRE 2010 results

	Lung Boundaries		Fissures		Landmarks		Folding		Overall			
Team Name	Avg Score	Avg Rank	Avg Score	Avg Rank	Avg Score	Avg Rank	Avg Score	Avg Rank	Avg Rank	Placed	Last Update	Method Type
picsl gsyn	0.12	8.00	0.03	9.52	0.75	3.65	0.00	13.77	8.73	1	25 Jun 2010	Fully Auto
Nifty Reggers	0.00	7.57	0.27	12.30	0.75	7.25	0.00	12.50	9.90	2	26 Jun 2010	Fully Auto
Iowa sstvd [illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	26 Jun [illegible]	Fully [illegible]

Multi-atlas 2012

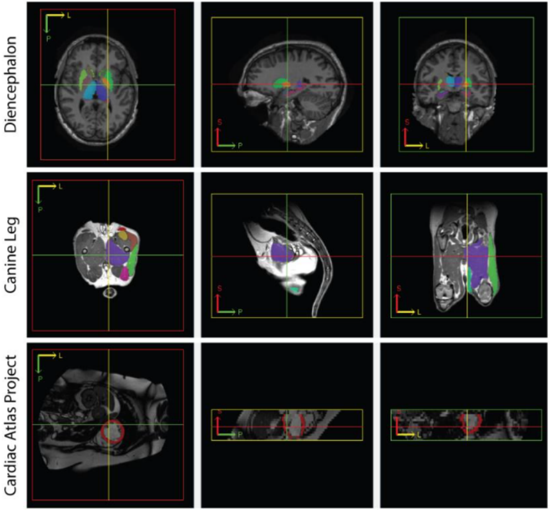


Multi-atlas 2012 results

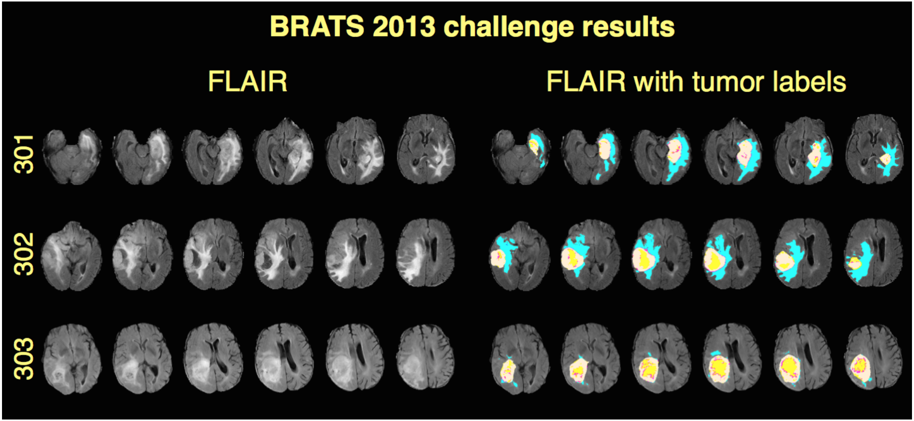
Overall Rank †	Repro. Rank‡	Team Name	Mean DSC Overall	Mean DSC Cortical	Mean DSC Non-Cortical
1	1	PICSL_BC	0.7654	0.7388	0.8377
2	2	NonLocalSTAPLE	0.7581	0.7318	0.8296
3	3	MALP_EM	0.7576	0.7328	0.8252
4	4	PICSL_Joint	0.7499	0.7216	0.8271
5	6	MAPER	0.7413	0.7144	0.8144
6	7	STEPS	0.7372	0.7107	0.8095
7	5	SpatialSTAPLE	0.7372	0.7093	0.8130
8	9	CIS_JHU	0.7357	0.7131	0.7971
9	8	CRL_Weighted_STAPLE ANTS+Baloo	0.7344	0.7122	0.7950
10	10	CRL_Weighted_STAPLE ANTS	0.7308	0.7066	0.7966

SATA 2013

Three very different problem domains



BRATS 2013


BRATS 2013 challenge results
FLAIR
FLAIR with tumor labels
301
302
303

BRATS 2013 results

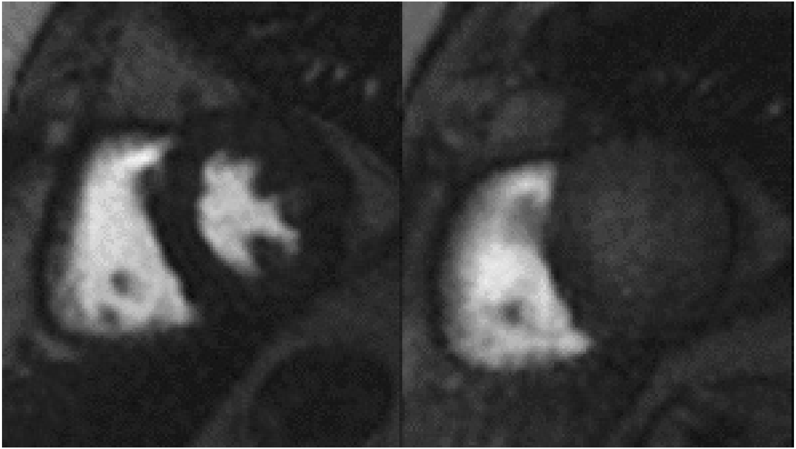
Results

Patient

Position	User	Dice			Positive Predictive Value			Sensitivity			Kappa	Complete tumor Rank	Tumor core Rank	Enhancing tumor Rank
		complete	core	enhancing	complete	core	enhancing	complete	core	enhancing				
1	Nick Tustison	0.87 (1)	0.78 (1)	0.74 (1)	0.85 (2)	0.74 (4)	0.69 (4)	0.89 (2)	0.88 (1)	0.83 (1)	0.99 (1)	1.67	2.00	1.89
2	Raphael Meier	0.82 (5)	0.73 (2)	0.69 (3)	0.76 (6)	0.78 (2)	0.71 (1)	0.92 (1)	0.72 (4)	0.73 (3)	0.99 (4)	4.00	2.67	3.00
3	Syed Reza	0.83 (4)	0.72 (3)	0.72 (2)	0.82 (3)	0.81 (1)	0.70 (3)	0.86 (5)	0.69 (6)	0.76 (2)	0.99 (3)	4.00	3.33	3.22
4	Liang Zhao	0.84 (3)	0.70 (4)	0.65 (5)	0.80 (4)	0.67 (5)	0.65 (6)	0.89 (3)	0.79 (3)	0.70 (4)	0.99 (5)	3.33	4.00	4.11
5	Nicolas Cordier	0.84 (2)	0.68 (5)	0.65 (6)	0.88 (1)	0.63 (6)	0.68 (5)	0.81 (6)	0.82 (2)	0.66 (6)	0.99 (2)	3.00	4.33	4.33
6	Joana Festa	0.72 (6)	0.66 (6)	0.67 (4)	0.77 (5)	0.77 (3)	0.70 (2)	0.72 (7)	0.60 (7)	0.70 (5)	0.98 (6)	6.00	5.33	5.00
7	Senan Doyle	0.71 (7)	0.46 (7)	0.52 (7)	0.66 (7)	0.38 (7)	0.58 (7)	0.87 (4)	0.70 (5)	0.55 (7)	0.98 (7)	6.00	6.33	6.44

Optimal symmetric multimodal templates and concatenated random forests for supervised brain tumor segmentation (simplified) with ANTsR, *Neuroinformatics*.

STACOM 2014



ANTs: in summary

Show me the code!

General purpose library for multivariate image registration, segmentation & statistical analysis tools

- 170,000+ lines of C++, 6$+$ years of work, 15+ collaborators.

Show me the code!

General purpose library for multivariate image registration, segmentation & statistical analysis tools

- 170,000+ lines of C++, $6+$ years of work, 15+ collaborators.
- Generic mathematical methods that are tunable for application specific domains.

Show me the code!

General purpose library for multivariate image registration, segmentation & statistical analysis tools

- 170,000+ lines of C++, 6+ years of work, 15+ collaborators.
- Generic mathematical methods that are tunable for application specific domains.
- no free lunch: *An algorithm must use prior knowledge about a problem to do well on that problem.*

Still quite a bit to do

On documentation

We are blind to deficiencies. Users blind to features.