Measuring longitudinal brain changes in humans and small animal models

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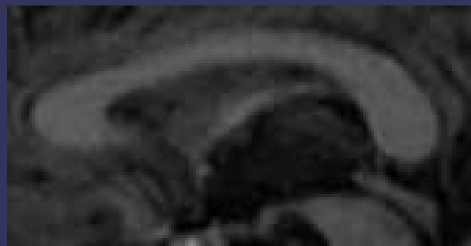
Computational Anatomy: Measuring Anatomical Structure

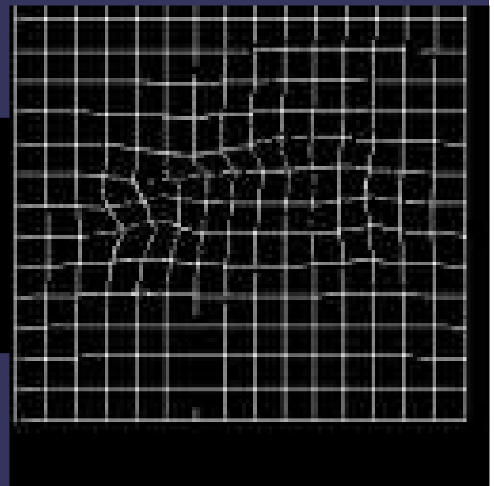
1) A reference template (e.g. an atlas or an average shape) is the unit
2) A shape transformation quantifies the shape characteristics of and individual brain with respect to the template

Template



Subject

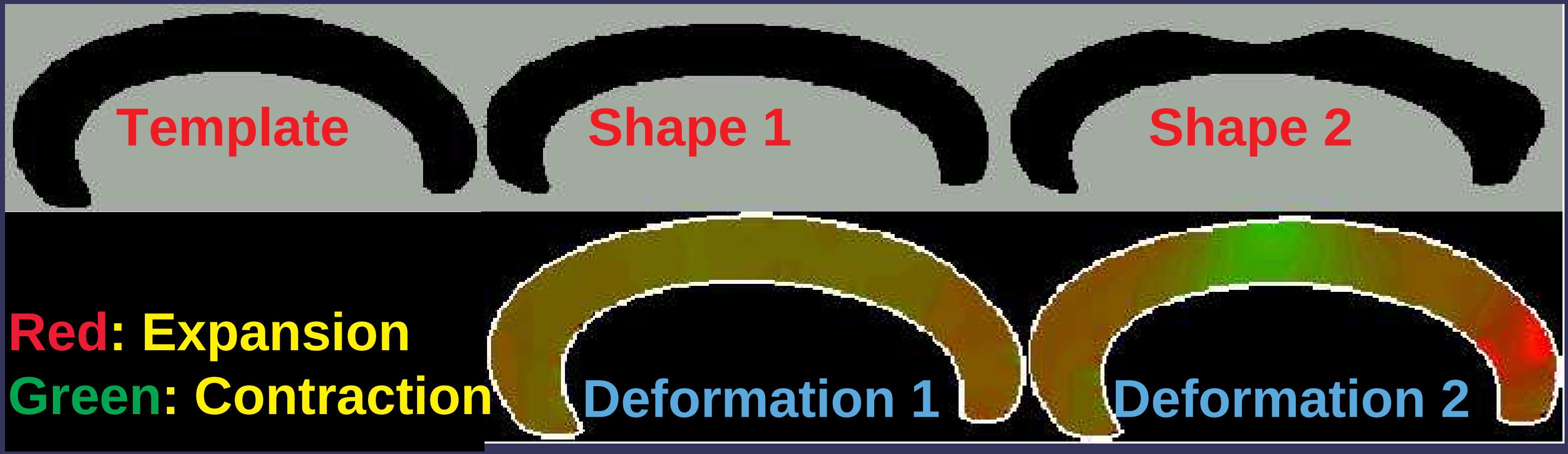
Warped template



warping of a grid

3) Two shapes are compared by comparing the corresponding transformations

• The deformation function measures the local deformation of the template:



• Deformation function measured after adaptation of the template to each shape

Local measurements of shape characteristics can be therefore measured by analyzing the deformation functions with standard statistical methodologies

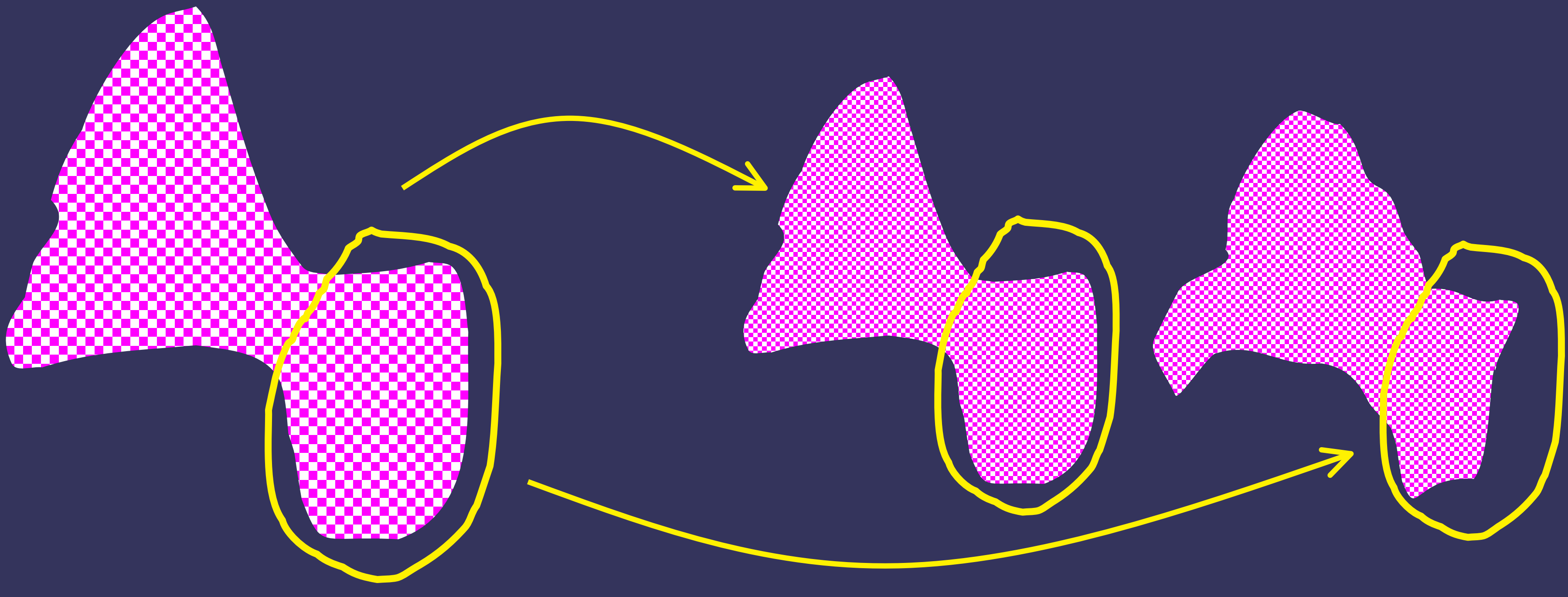
Davatzikos et.al., J. Comp. Assist. Tomogr., 1996

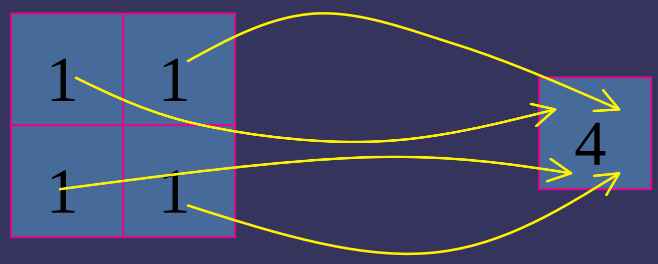
Problems when using the warping transformation:

- The target anatomy is assumed to be a diffeomorphism of the template
- Residual information is discarded
- A very accurate warping requires time and computational resources

Use the pair (Transformation, Residual) to measure shape

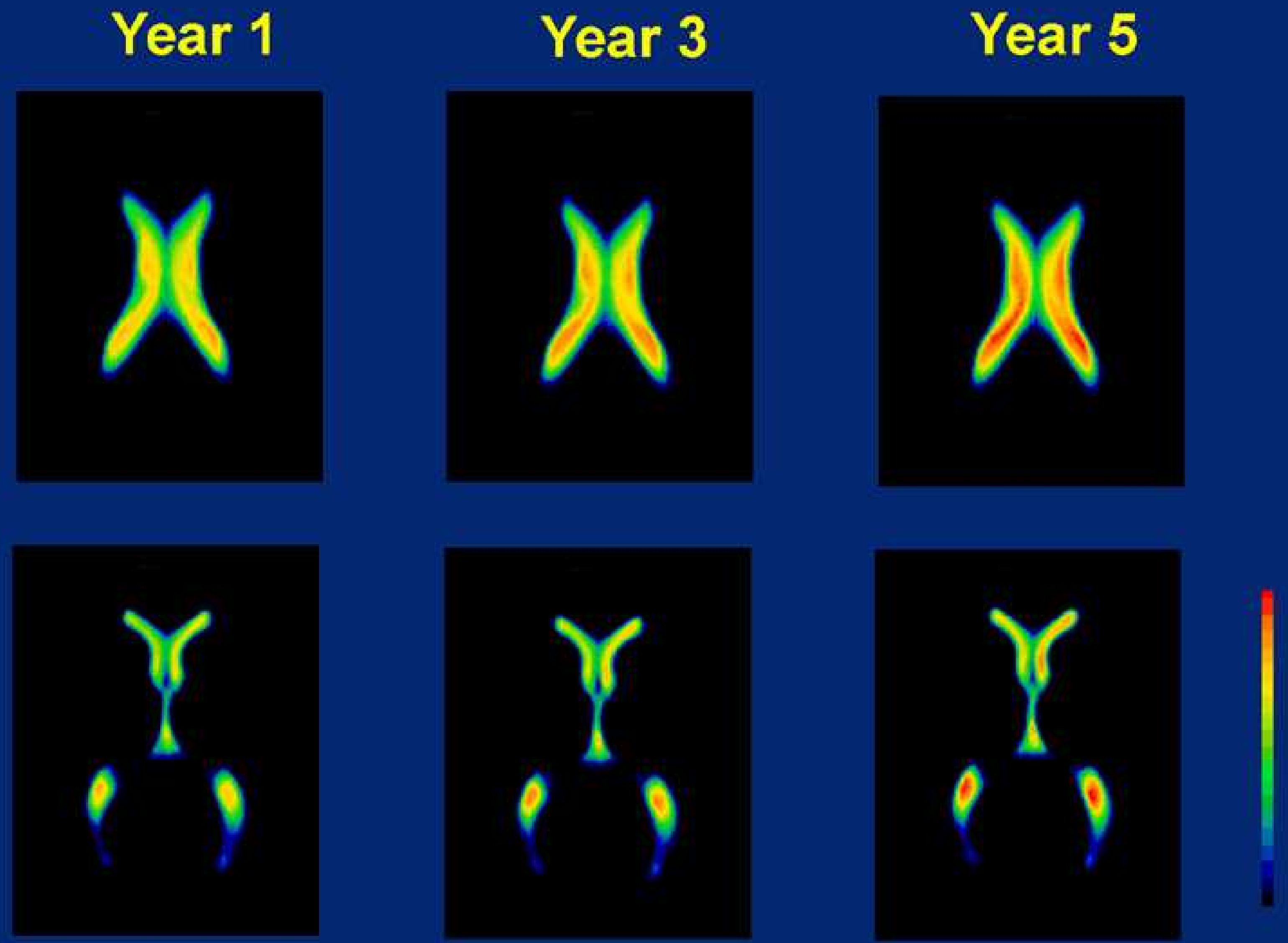
RAVENS: Mass-preserving shape transformations for morphological analysis



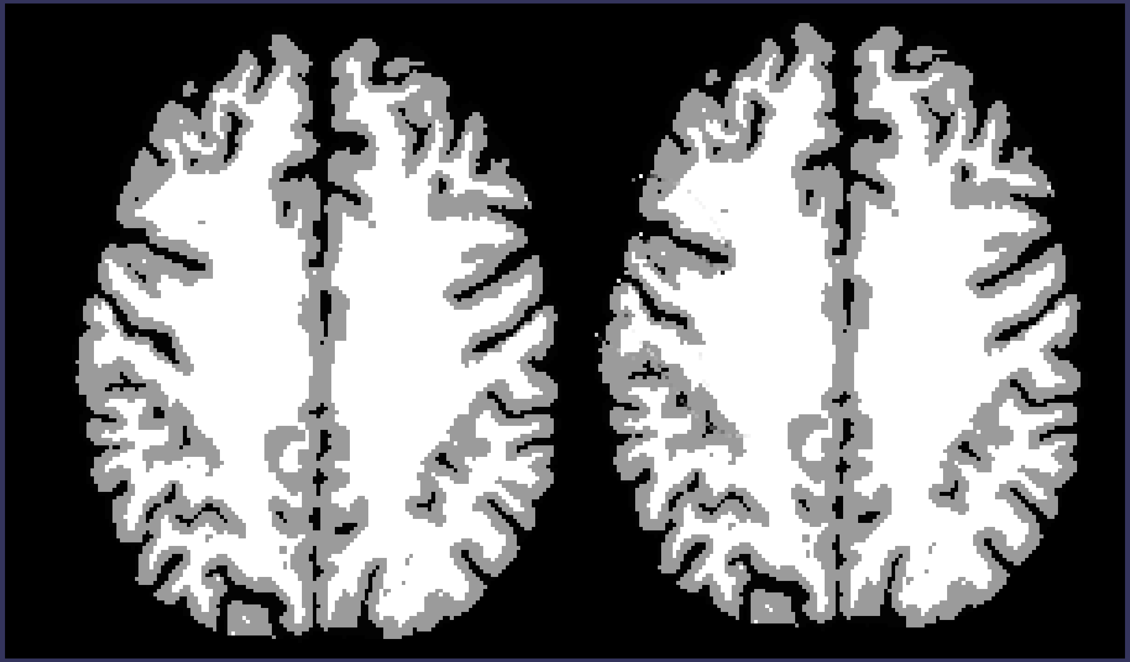


RAVENS = Regional Analysis of Volumes Examined in Normalized Space

Longitudinal Change in Ventricular Volume



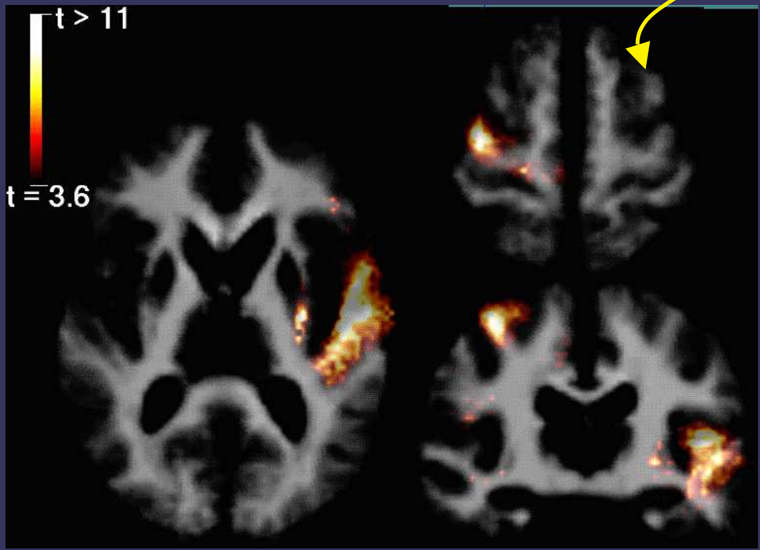
Example of Detection of Subtle Change:

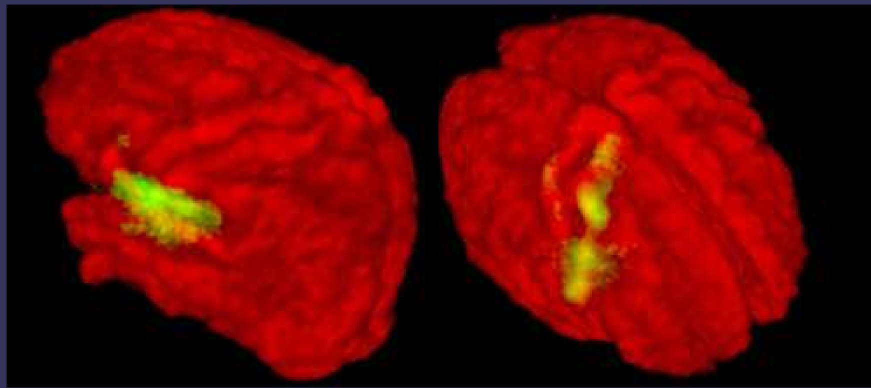


Example of Detection of Subtle Change:

Validation Experiments:

- Localized atrophy identified via t-maps of the RAVENS images
- Atrophy detected in the two gyri: PCG and STG
- T-maps are overlaid on the average WM RAVENS map of 24 subjects

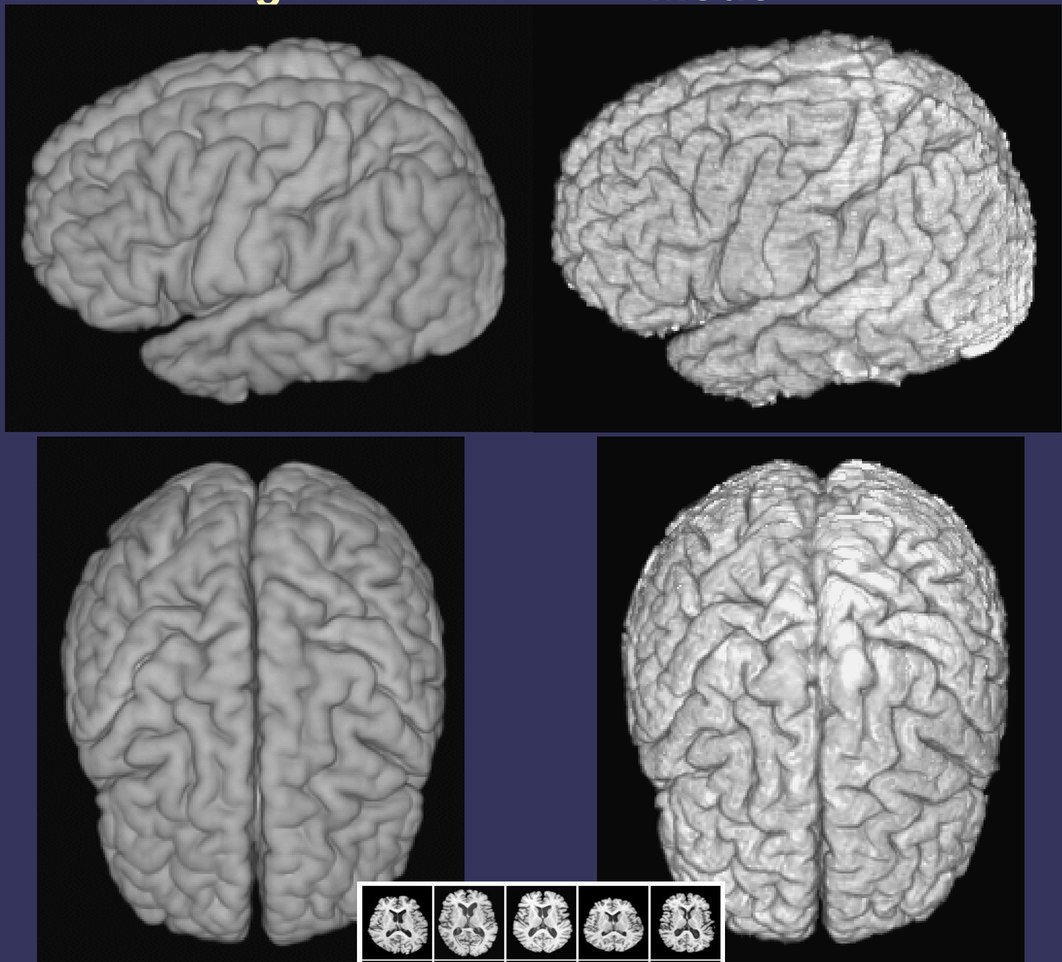




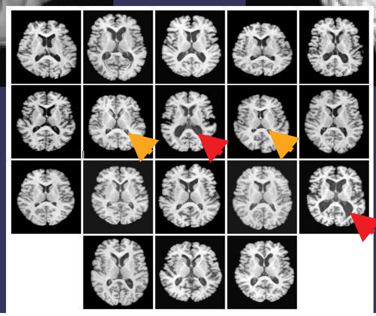
Davatzikos et.al., NeuroImage, 2001

Average brain from 158 subjects in BLSA project

Average　　　　Model

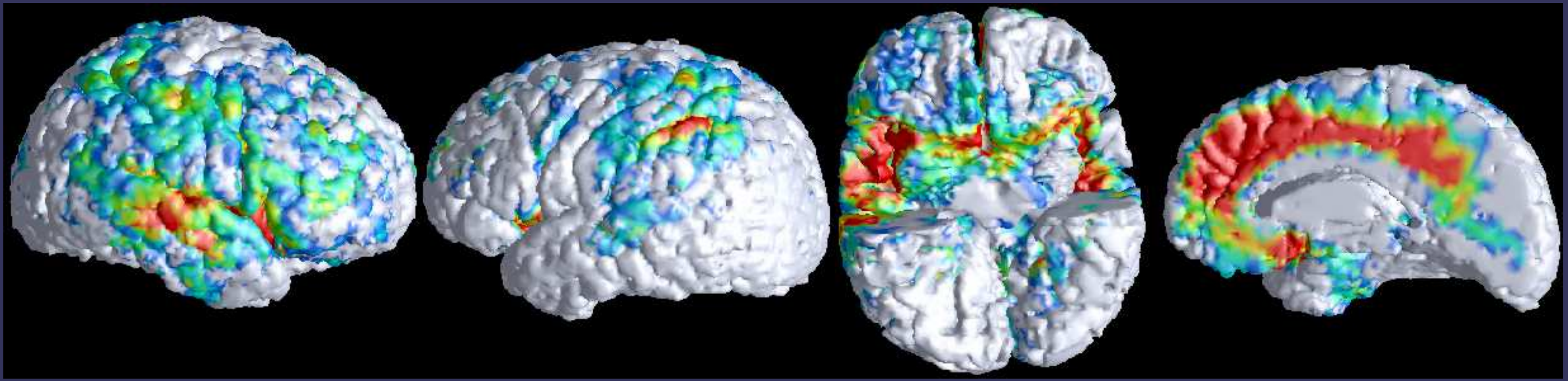


Average　　　　Template



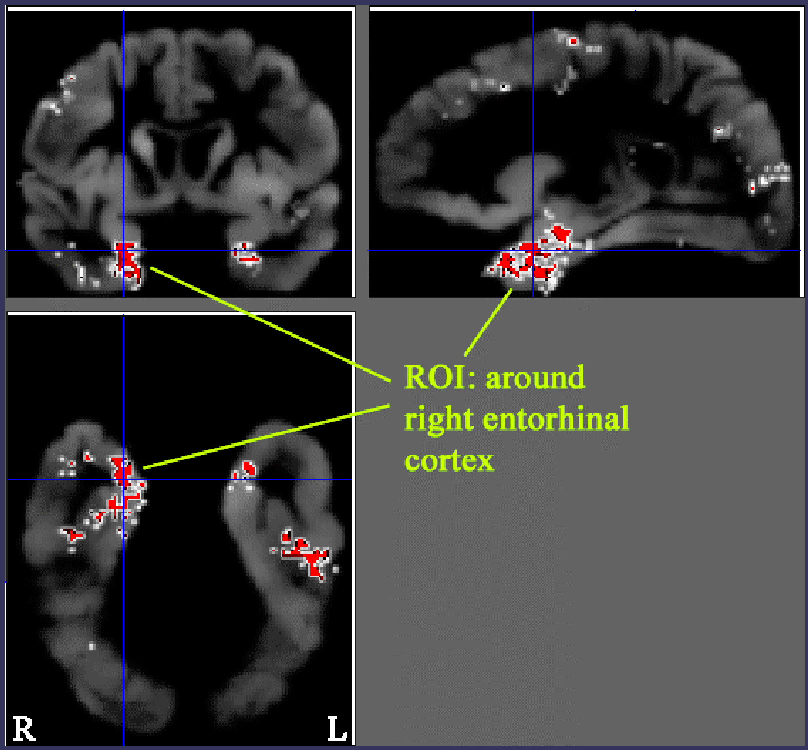
"HAMMER" image warping, by Dinggang Shen (IEEE-TMI, 2001)

Significant 4-year GM changes in 107 older adults

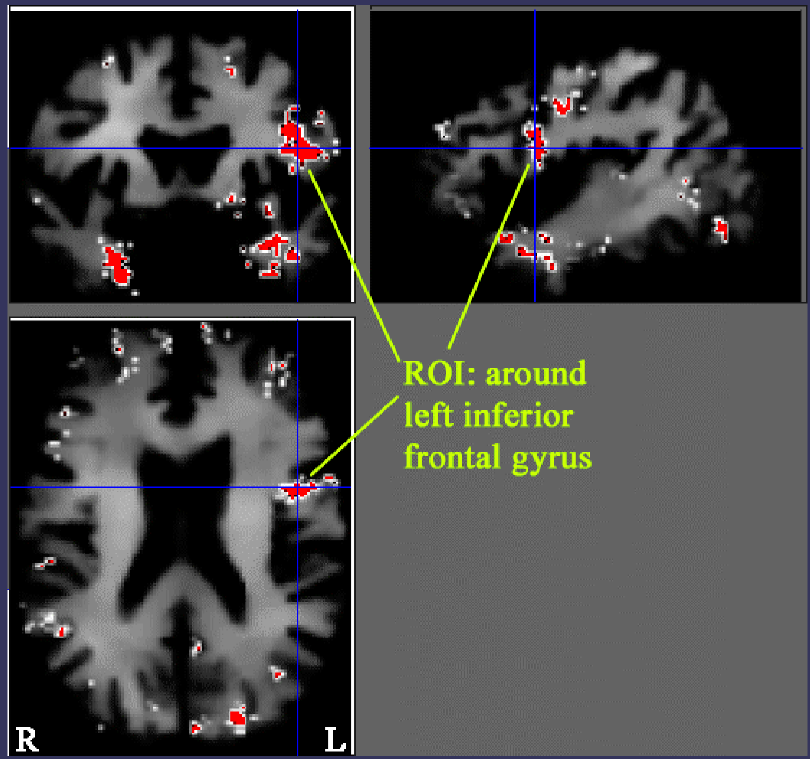


Resnick et.al., 2001, Cerebral Cortex

Finding associations between local atrophy and MCI



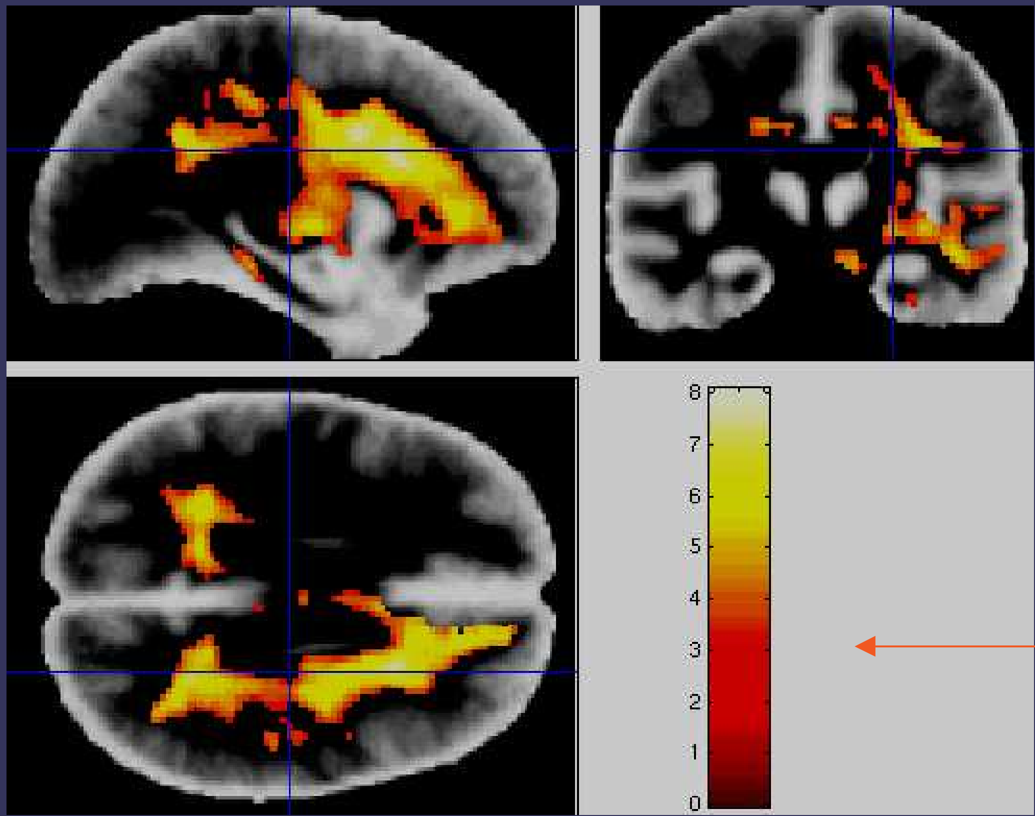
Gray matter



White matter

Longitudinal changes in WM/GM MR signal contrast

Demyelination or other degenerative processes



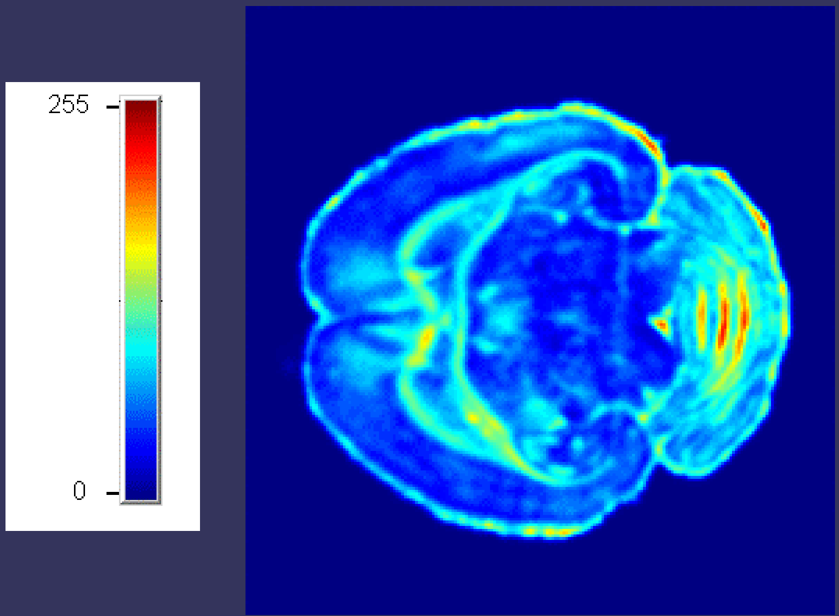
Scale of t-statistic of longitudinal changes

☆ Shape and signal changes with aging were uncorrelated

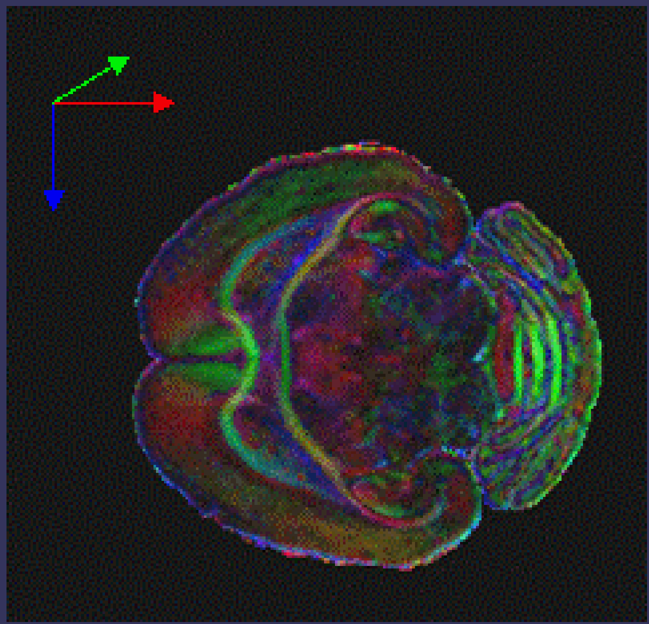
Davatzikos and Resnick, 2000

Measuring longitudinal change in early postnatal development of the mouse brain

• Standard T1, T2 imaging is inadequate → Diffusion tensor imaging

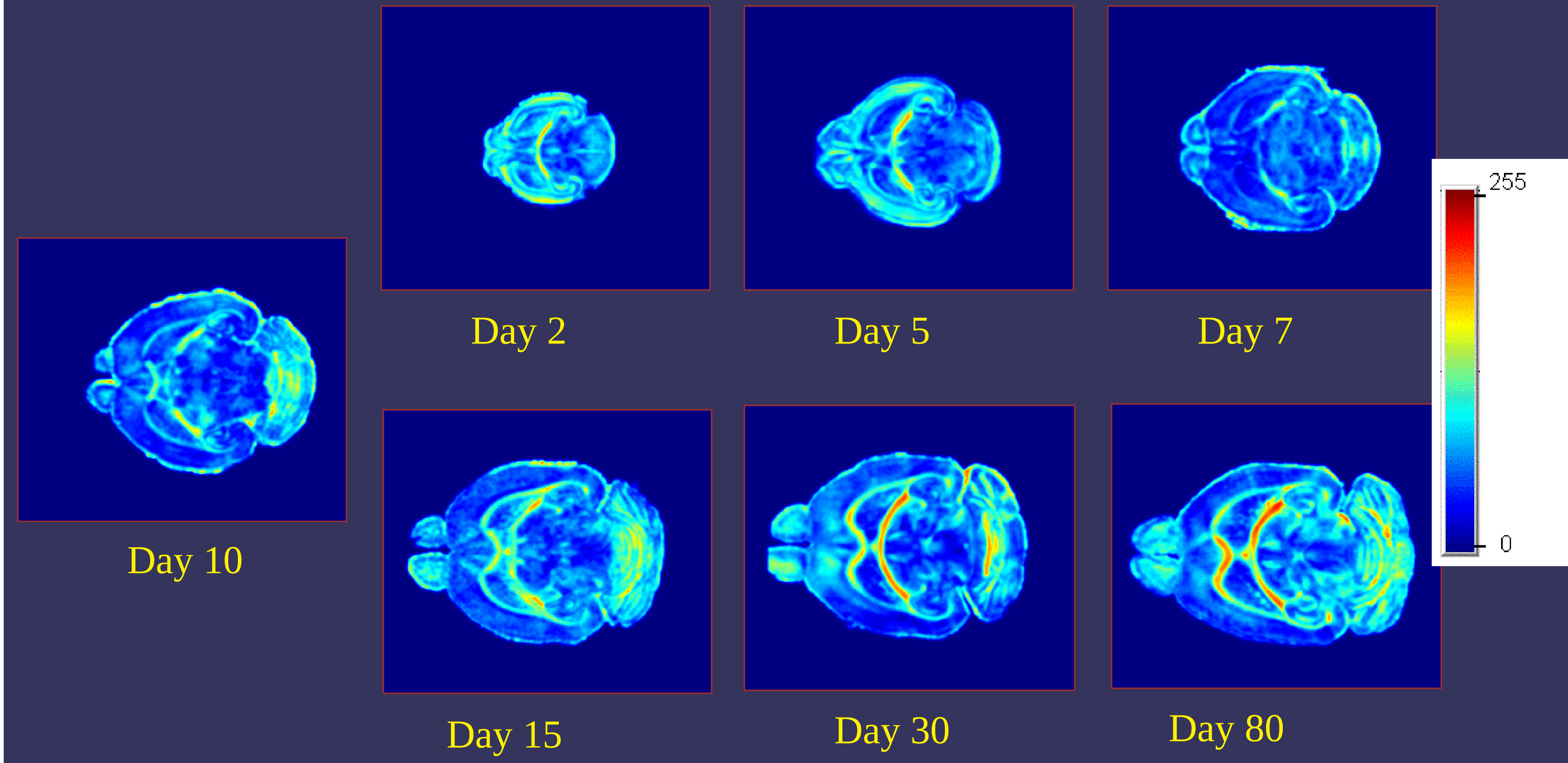


color coded FA map

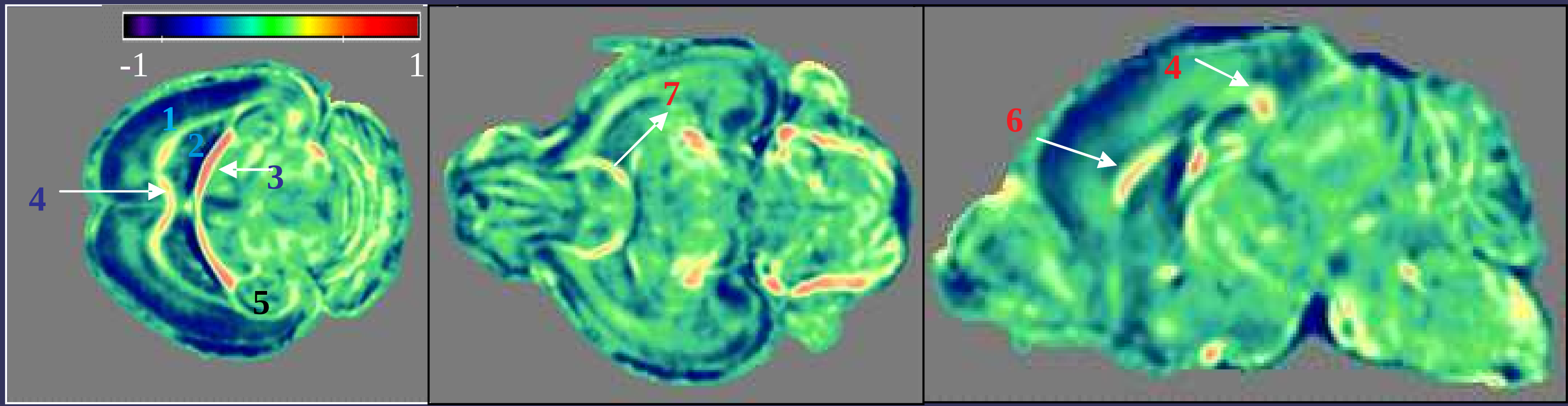


orientation map

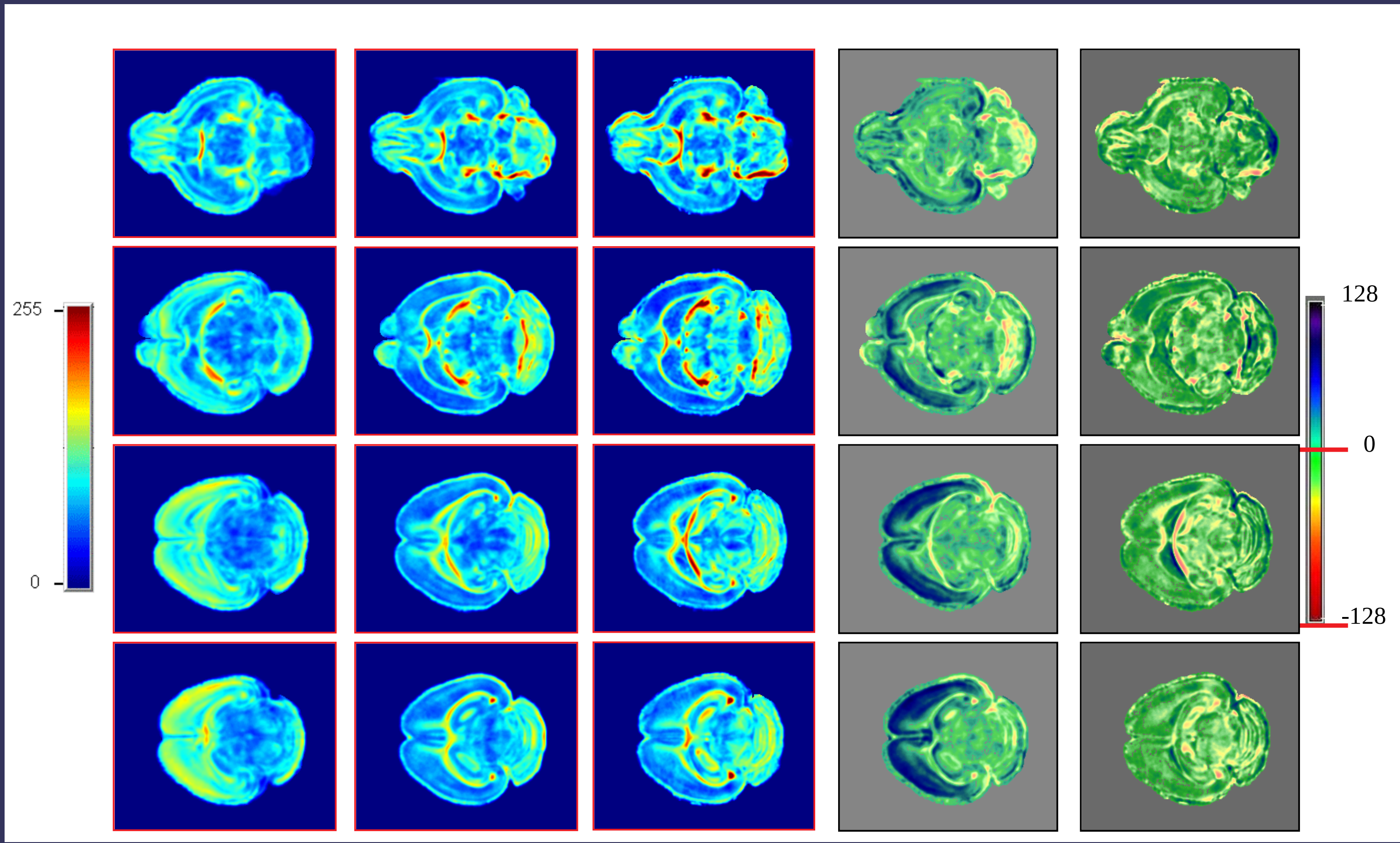
Longitudinal change of fractional anisotropy



Correlation of FA and age



- Cortex
- Caudate-putamen
- Internal capsule and ventr/hippo. commisure
- Corpus callosum
- Hippocampus
- Splenium of the corpus callosum
- Anterior commisure



Young mice (days 2 – 7)

Adolescent mice (days 10 – 30)

Old mice (days 45 – 80)

Difference between young and adolescent mice

Difference between old and adolescent mice

Problem with 3D warping:

-- Either independent warping between the template and the individual, for each time-point

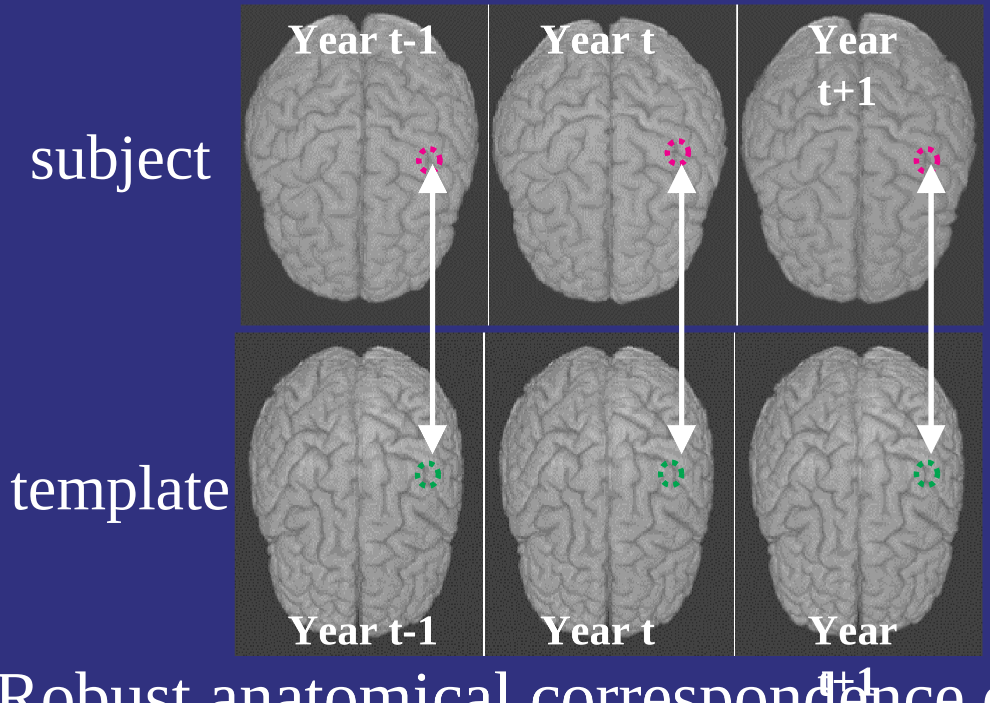
-- …or warping from time $t-1$ to time t, and from time t to time $t+1$, etc.

Sequence of independent warpings → inconsistencies

$\boxed{\text{4D Warping}}$

4D template warping

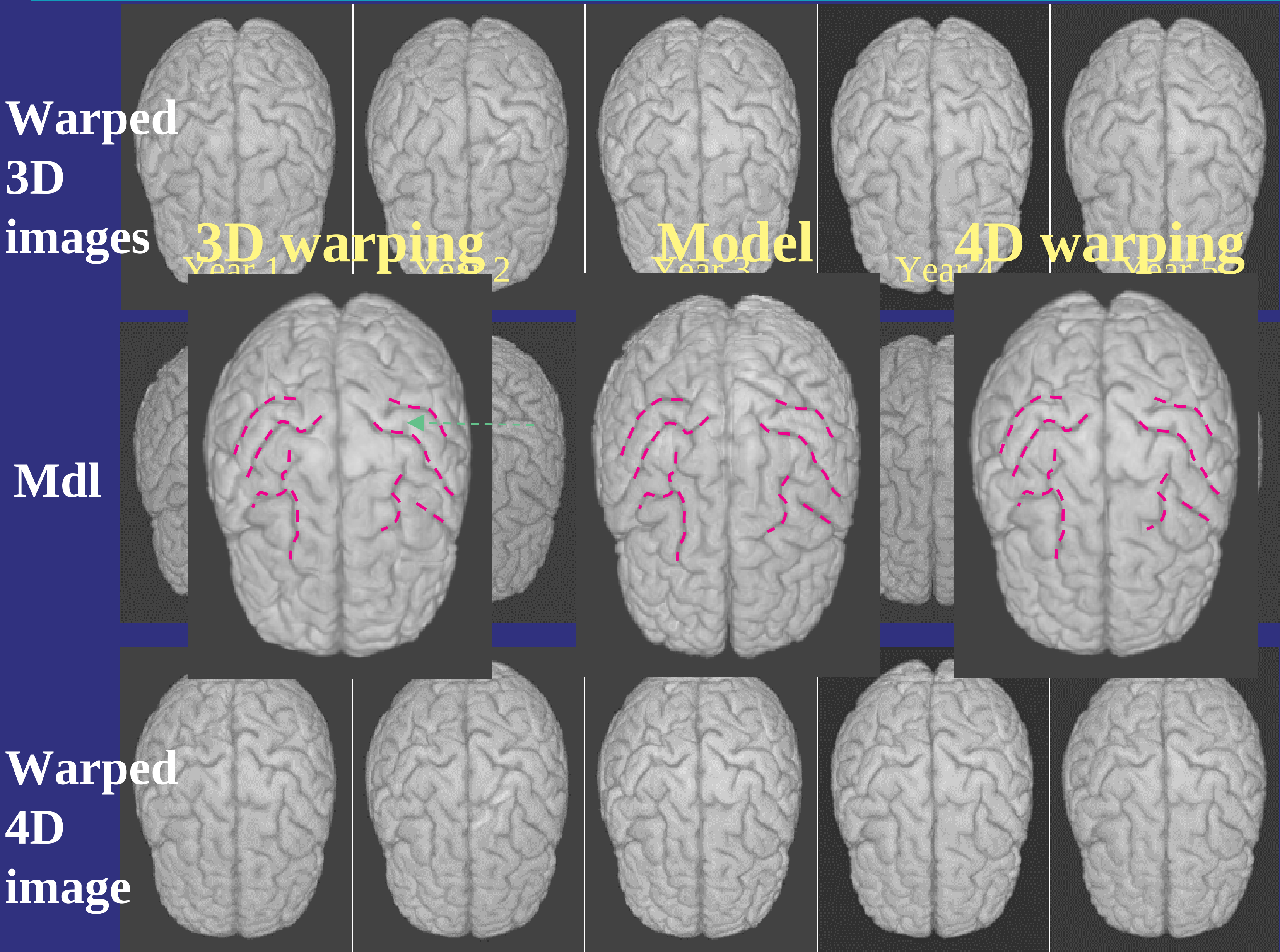
- **All temporal images of the same individual are simultaneously considered in image warping**



✓ Robust anatomical correspondence detection

✓ Smooth and temporaly consistent transformations

Warping consistence - comparison



Problems when tumors are present:

• The anatomy is partially obscured by edema

• Extreme deformations make anatomical matching difficult

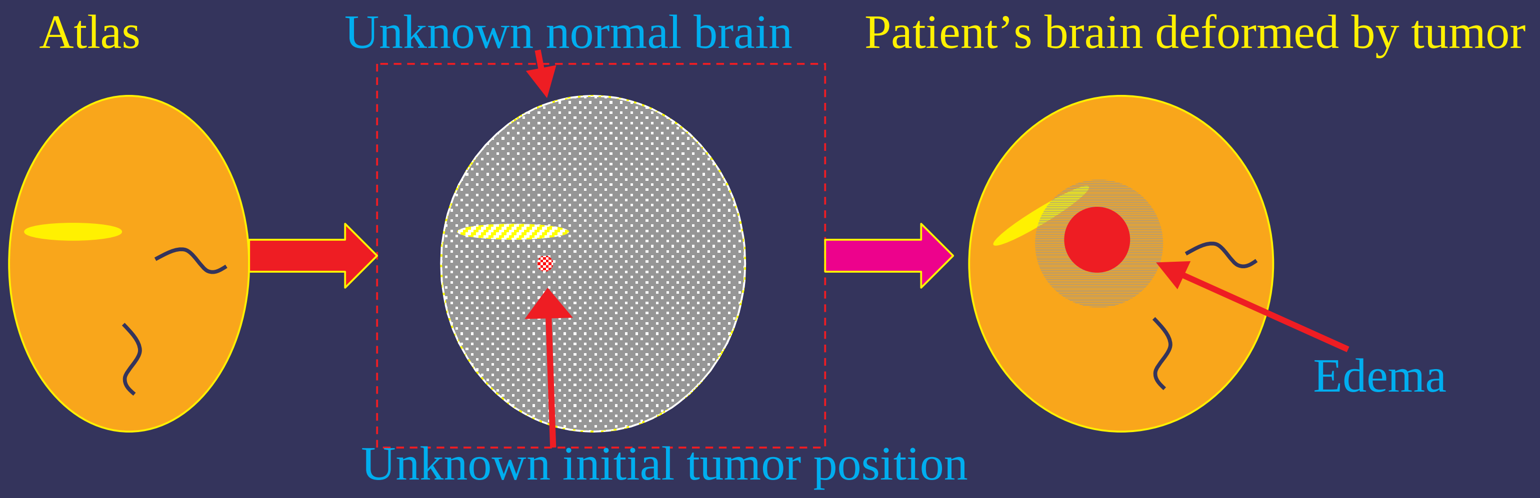
• Part of the tissue has died

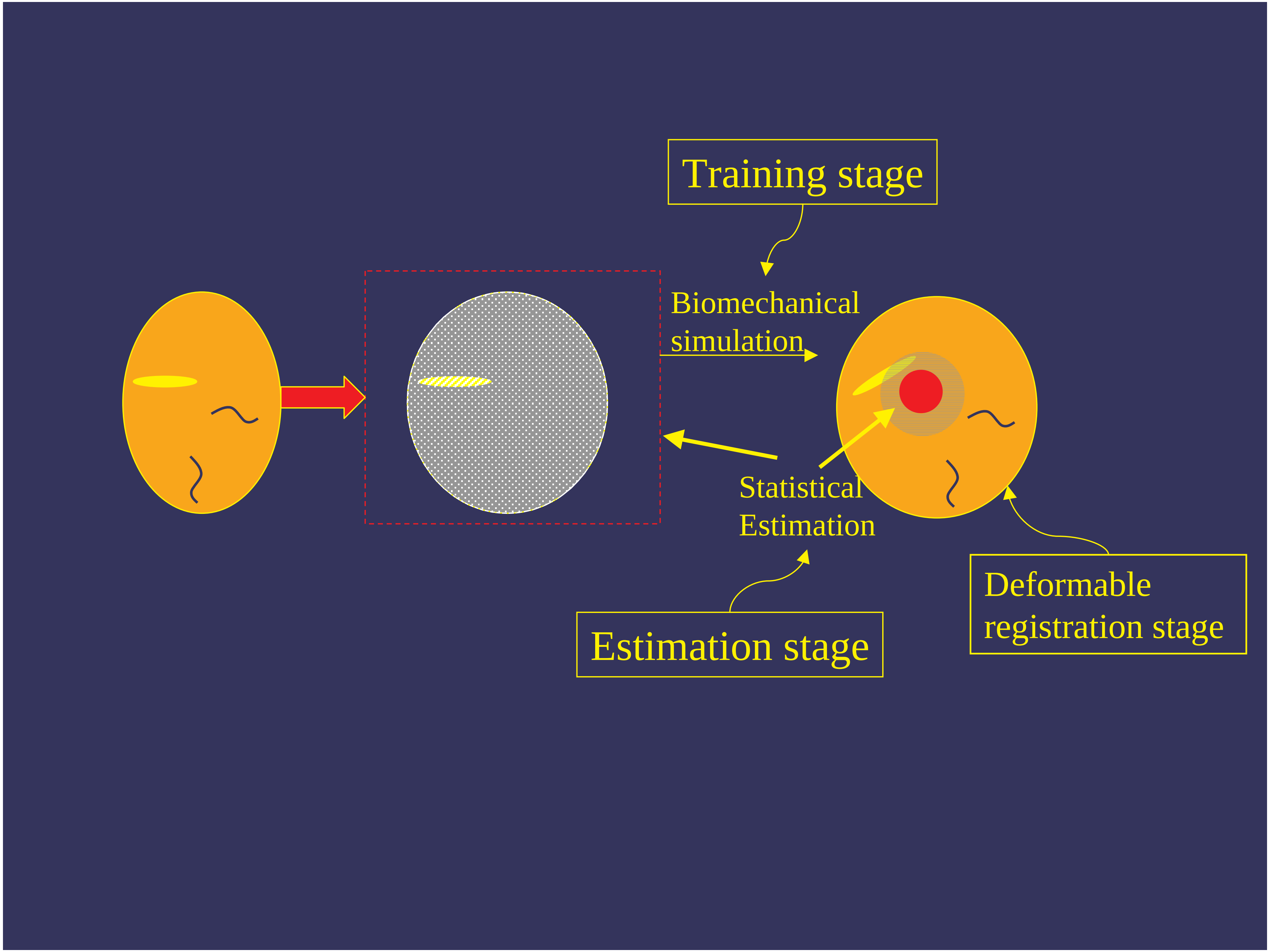
Need for

- Biomechanical models of soft tissue deformation
- Statistical models for estimation of obscured anatomy and for generation of atlas templates that look more like deformed anatomy

3. Deformable registration methods robust to deformations

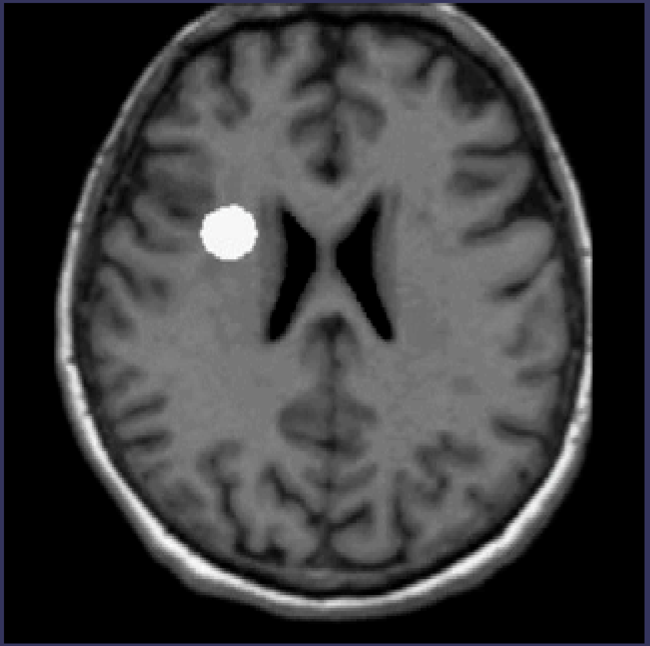
<u>Fundamental Limitation</u>: Estimating the inverse deformation field is a very ill-posed problem

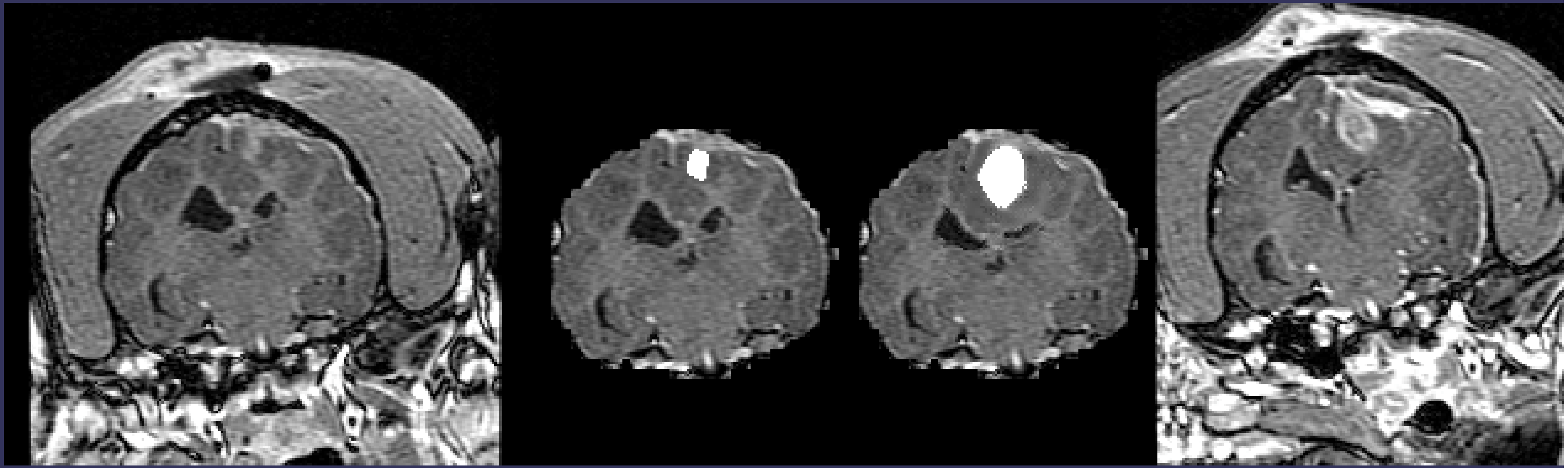




Training stage
Biomechanical
simulation
Statistical
Estimation
Estimation stage
Deformable
registration stage

Biomechanical Modeling





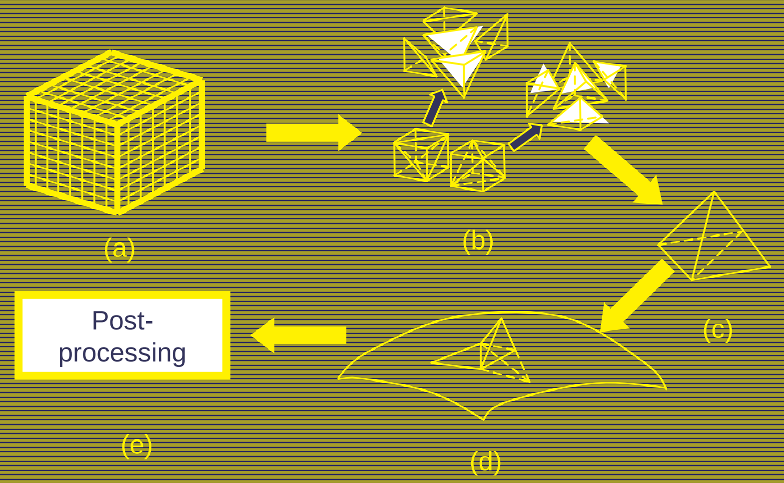
Biomechanical Modeling

Motivation

Generate biomechanical simulations of deformations of interest for the purpose of training statistical models used to predict those deformations.

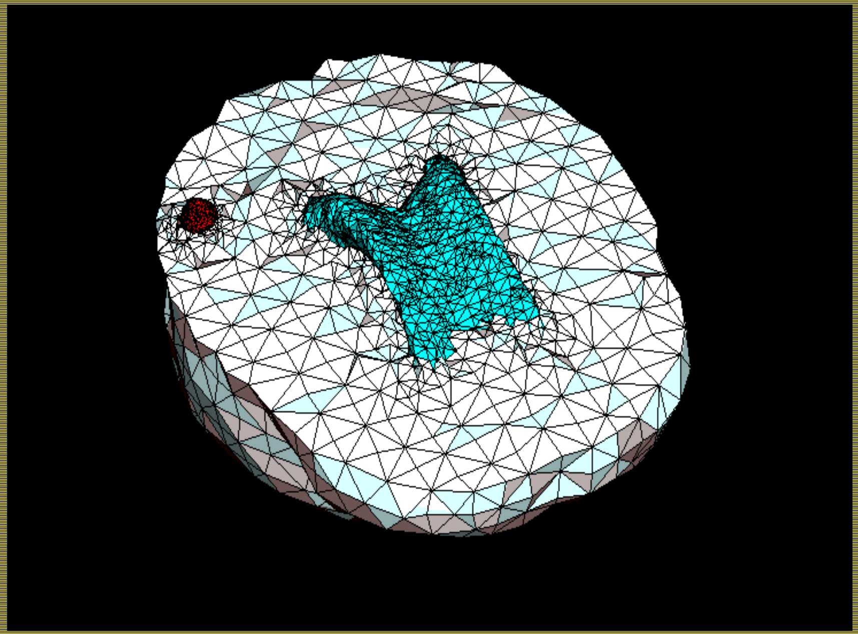
Approach

Automatically construct biomechanical models from segmented scans

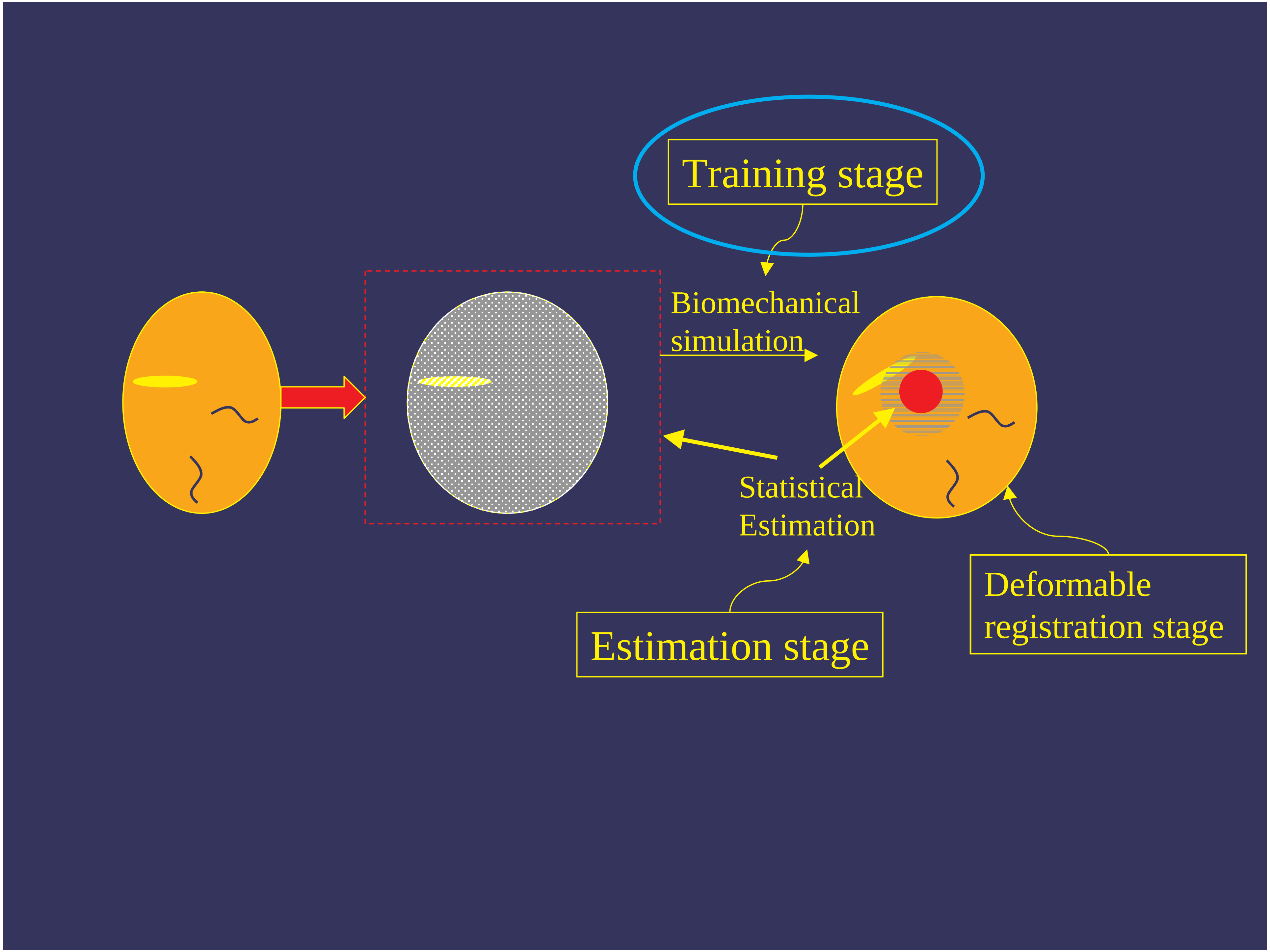


(a) A regular grid of small cubes is cast over the segmented volume. (b) Cubes are tesselated into tetrahedra. (c) Mesh refinement by subdivision of tetrahedra using edge split and LEPP. (d) Making the mesh conform to the geometry of the segmented volume. (e) Post-processing for improvement of quality of elements for FE analysis.

Use Finite Element Analysis (FEA) to simulate deformation based on realistic tissue properties and boundary conditions



A mechanical FEA simulation of growth of a tumor using a mesh generated from a normal brain scan.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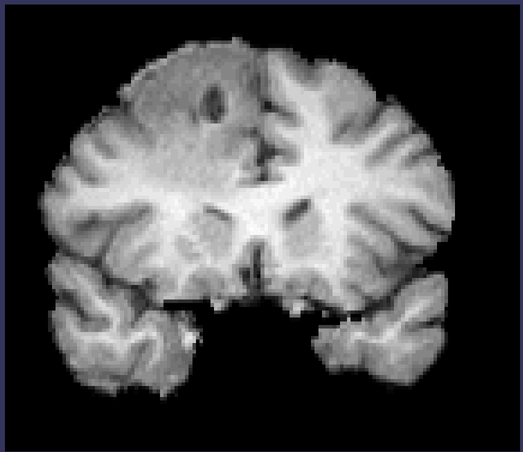
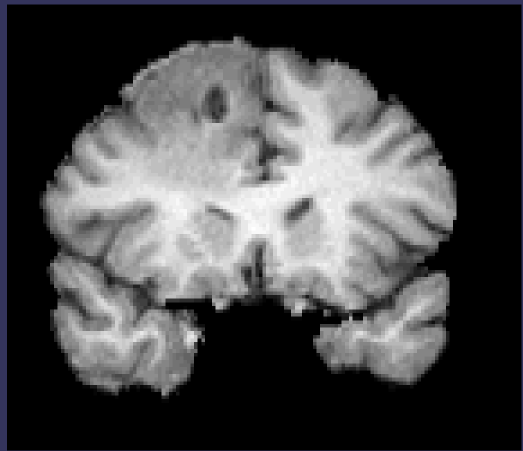
Deformable registration of tumor-occluded brain images

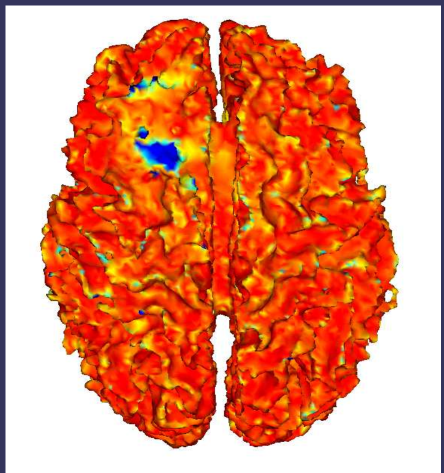


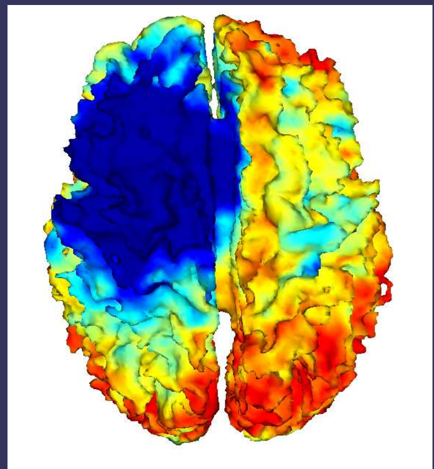
Original sequence:
5 scans, total 2 years apart



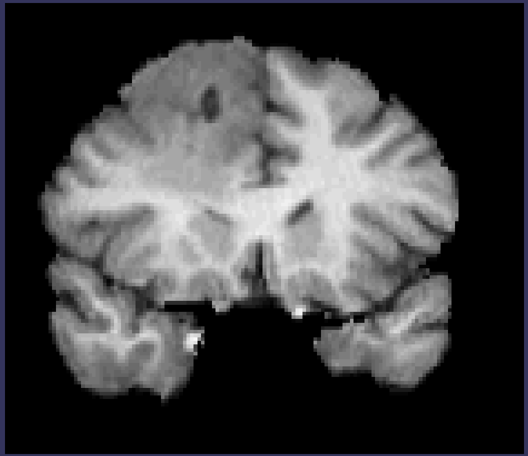
Result of image warping

Confidence of matching map

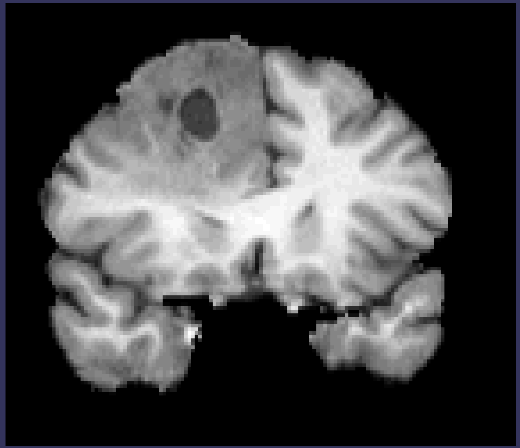




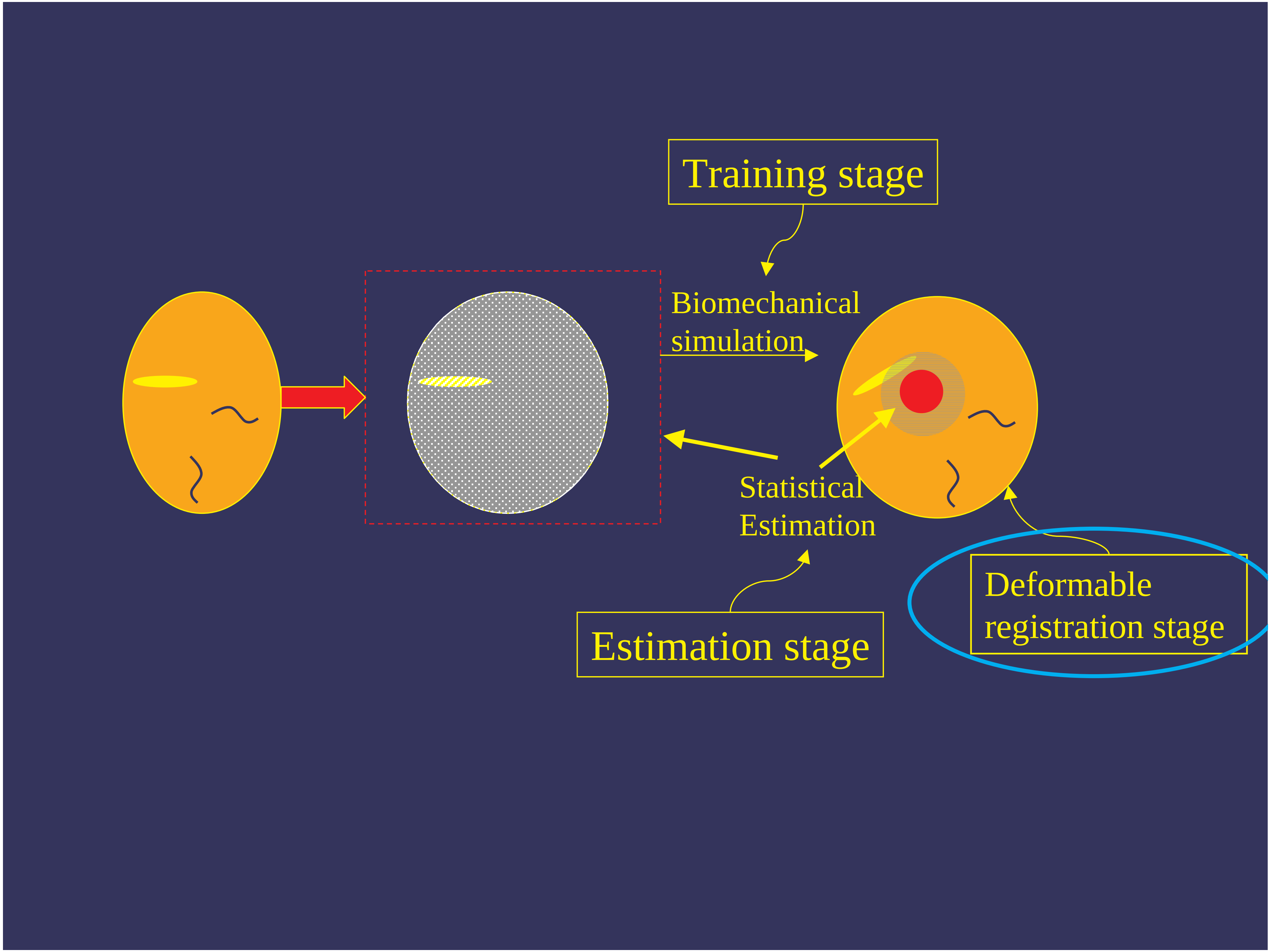
Magnitude of deformation



Overlay of 2nd
time-point:
warped original +
2nd scan



Overlay of 5th
time-point:
warped original +
5th scan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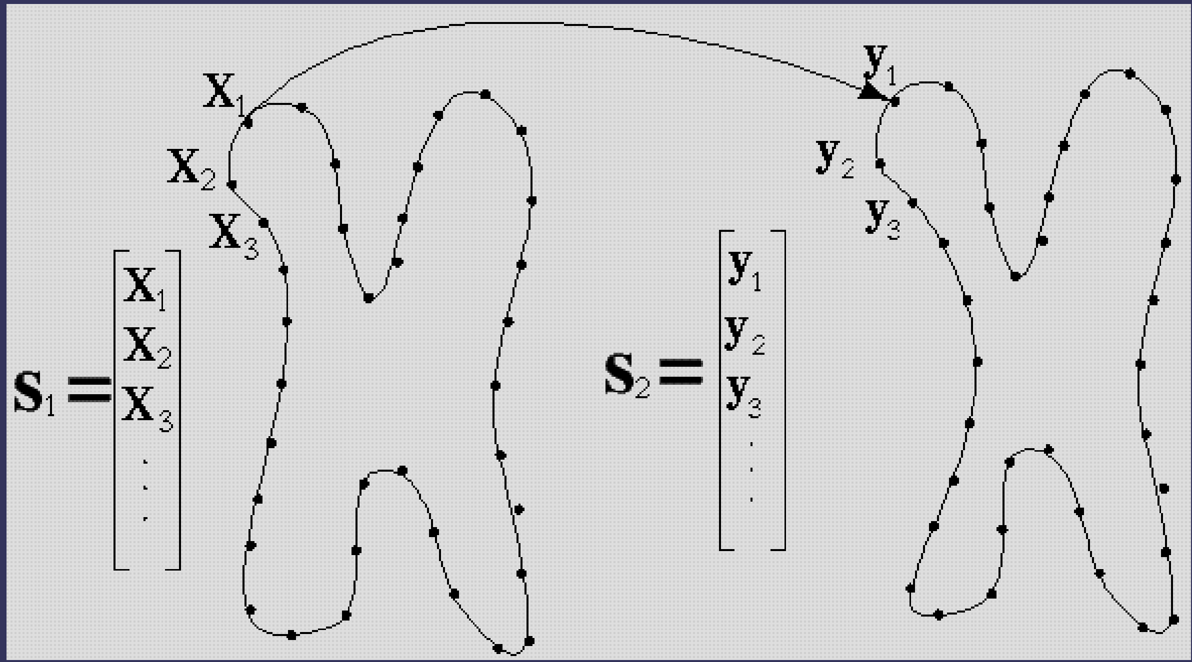
We will generate training samples, using tumor growth simulation



$$s = [\, s_1 \,, s_2]$$

- Perform a number of forward biomechanical simulations
- Estimate joint pdf

2) **MAP** estimation framework:

$$\underset{\mathbf{s}_1,\mathbf{s}_2}{\text{maximize}}\, f(\mathbf{s}_1,\mathbf{s}_2|\mathbf{n}_2;\hat{\mathbf{t}},\hat{g}) \Leftrightarrow \underset{\mathbf{s}_1,\mathbf{s}_2}{\text{maximize}}\, f(\mathbf{n}_2|\mathbf{s}_1,\mathbf{s}_2)f(\mathbf{s}_1,\mathbf{s}_2;\hat{\mathbf{t}},\hat{g})$$

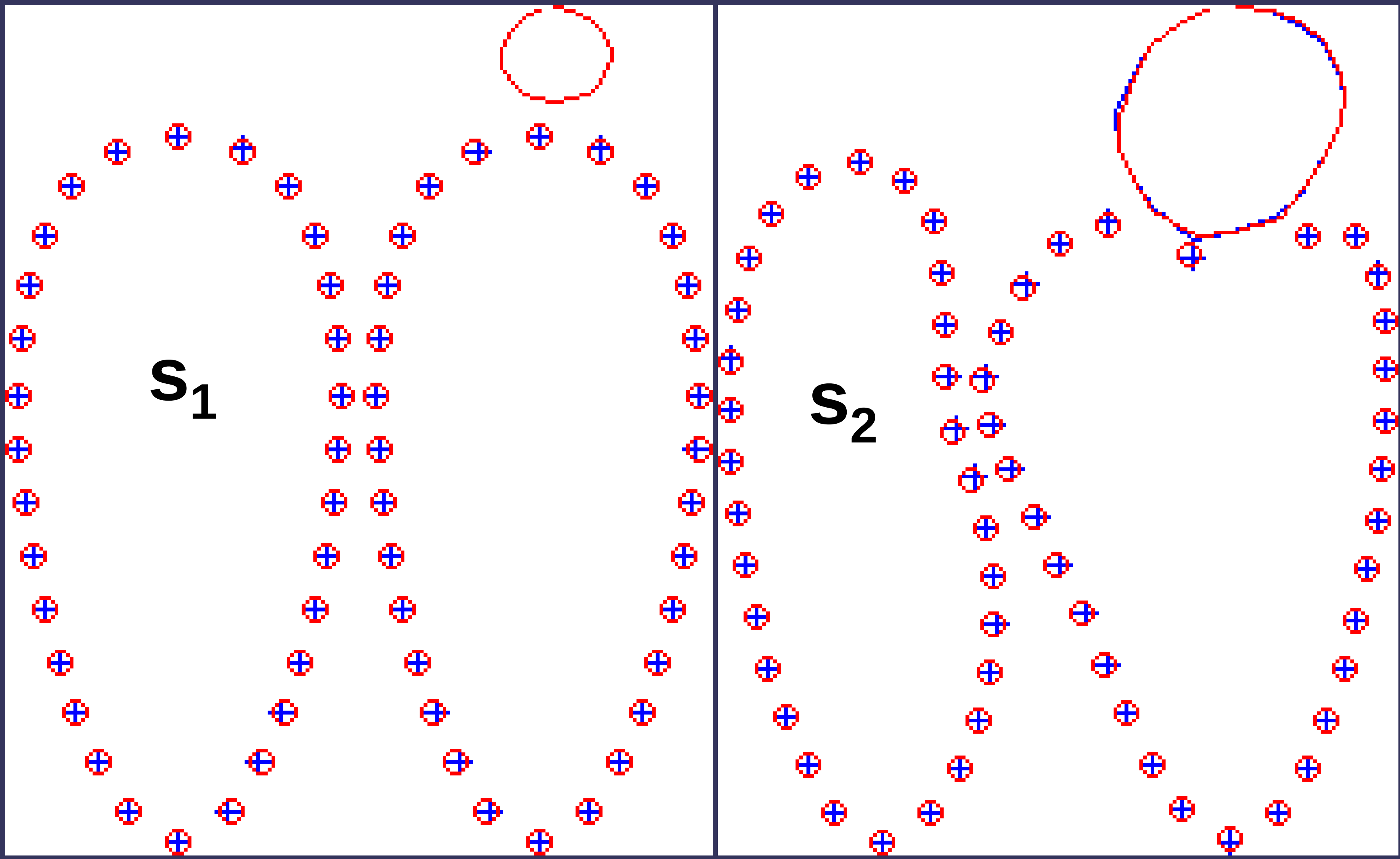
$$\Updownarrow$$

$$\underset{\mathbf{s}_1,\mathbf{s}_2}{\text{maximize}}\, f(\mathbf{n}_2|\mathbf{s}_2)f(\mathbf{s}_1,\mathbf{s}_2;\hat{\mathbf{t}},\hat{g})$$

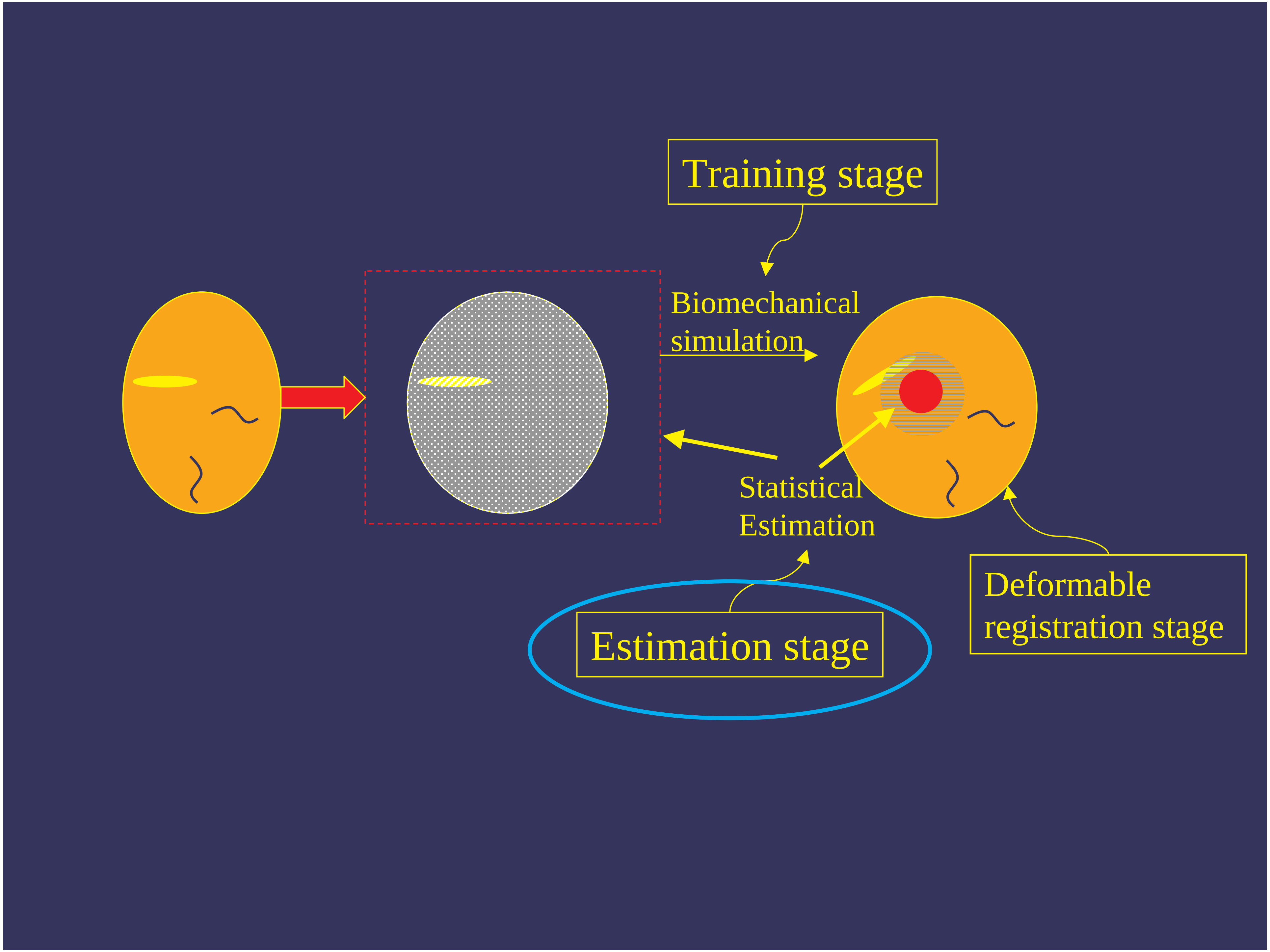
$$\mathbf{s} = [\mathbf{s}_1,\mathbf{s}_2] = \mu_s + \sum_{i=1}^{K}\alpha_i\mathbf{v}_i$$

$$\underset{\alpha_1,\ldots,\alpha_K}{\text{minimize}}\, h(\alpha_1,\ldots,\alpha_K,\mathbf{n}_2) + A\sum_{i=1}^{K}\lambda_i^{-1}\alpha_i^2$$

$$h(\alpha_1,\ldots,\alpha_K,\mathbf{n}_2) = \frac{1}{\sigma^2}\left\|\mu_2 + \sum_{i=1}^{K}\alpha_i\mathbf{v}_i^2 - \mathbf{n}_2\right\|^2$$



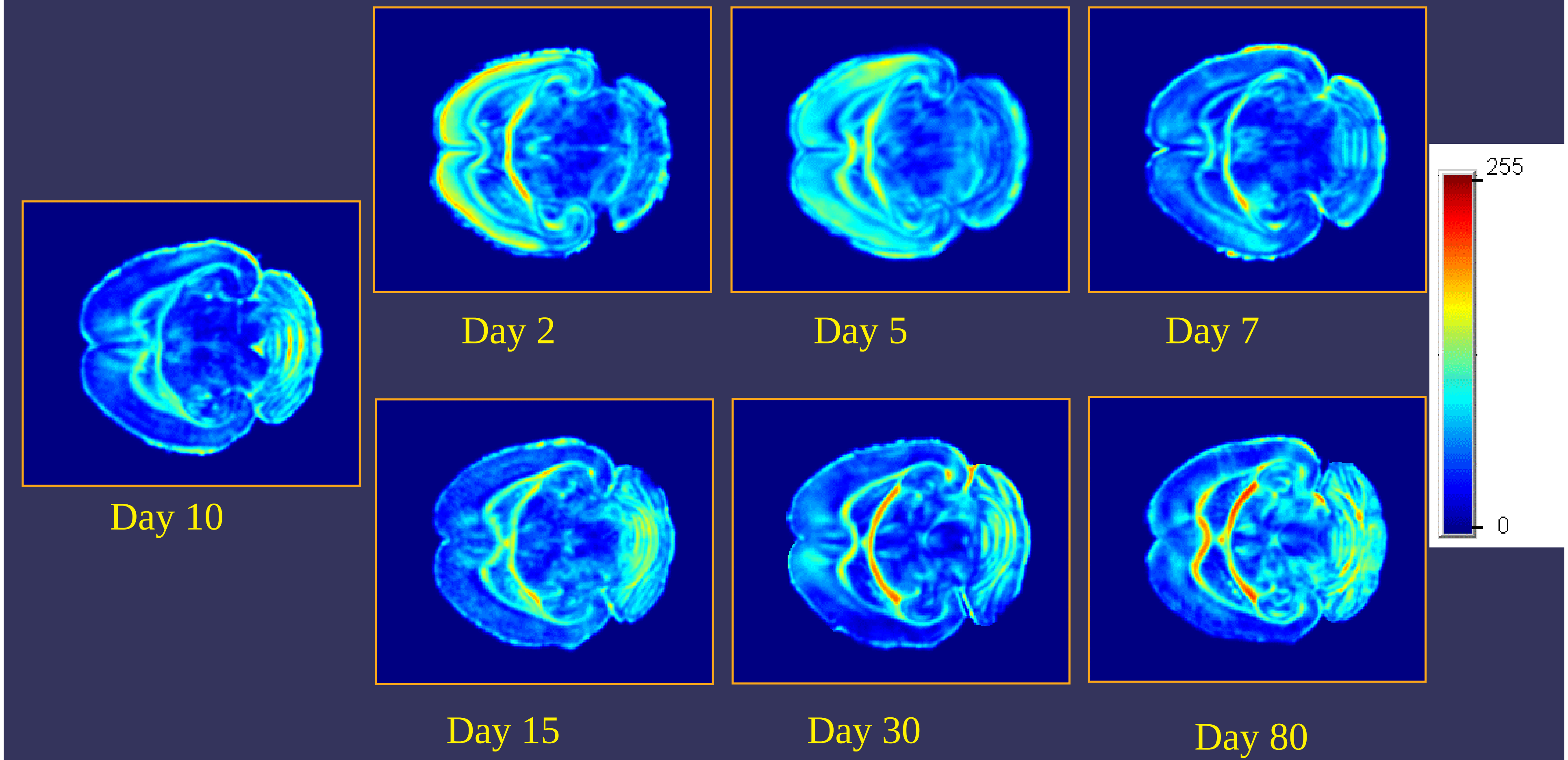
IEEE Trans. on Med. Imaging, 20(8):836-843, 2001


Training stage
Biomechanical simulation
Statistical Estimation
Estimation stage
Deformable registration stage

Thank you

…after nonlinear warping to the template (Day 10)

Voxel-based or multi-variate analysis of FA changes



Results – from 9 BLSA subjects

Manual expert: 5.5%
4D HAMMER: 5.7%
3D HAMMER: 2.1%