Computational Functional Anatomy

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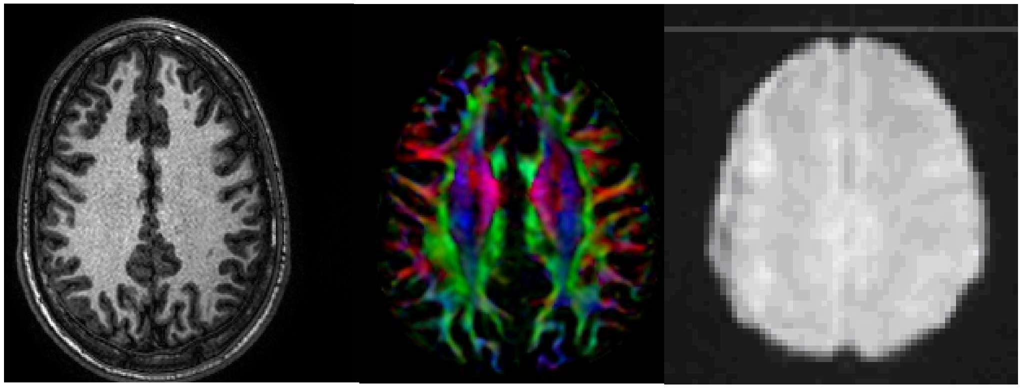
Division of Bioengineering

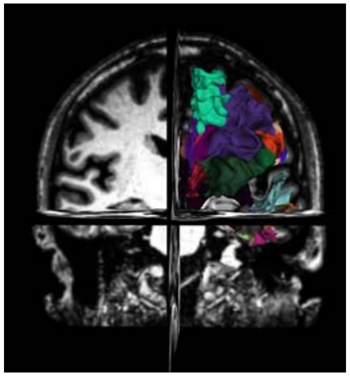
Computational Functional Anatomy (CFA) is the mathematical study of anatomical configurations and signals associated with anatomy and functions in anatomical coordinates.

1 MultiModal Images

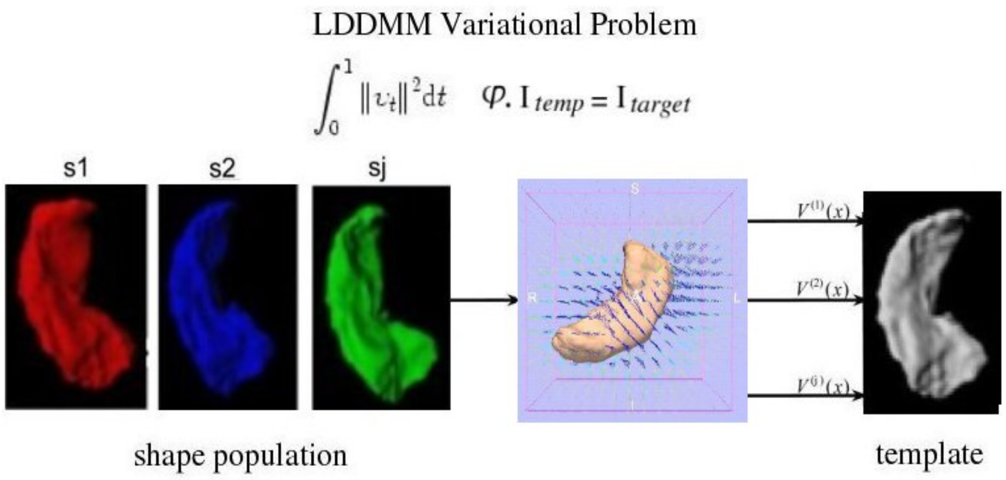
MRI DTI fMRI



2 Segmentation

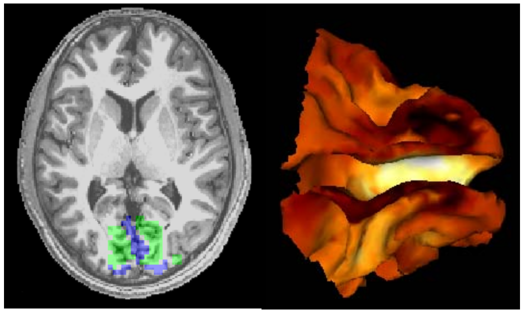


3 LDDMM Shape Analysis



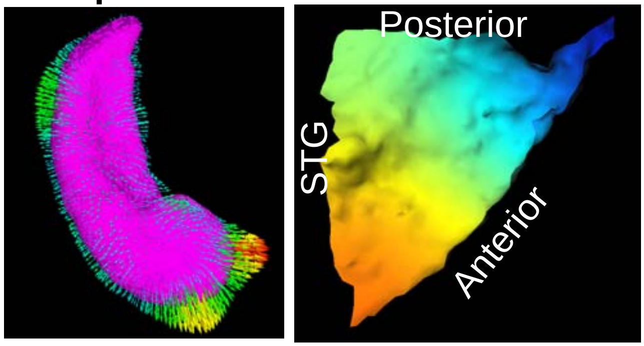
4 Functions in Anatomy

volume **surface**

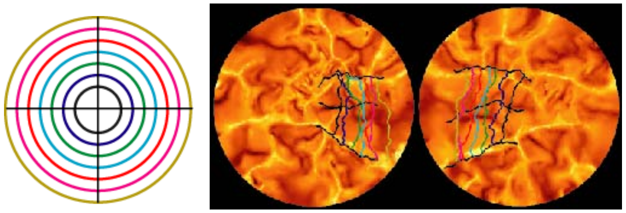


5 Statistical Analysis

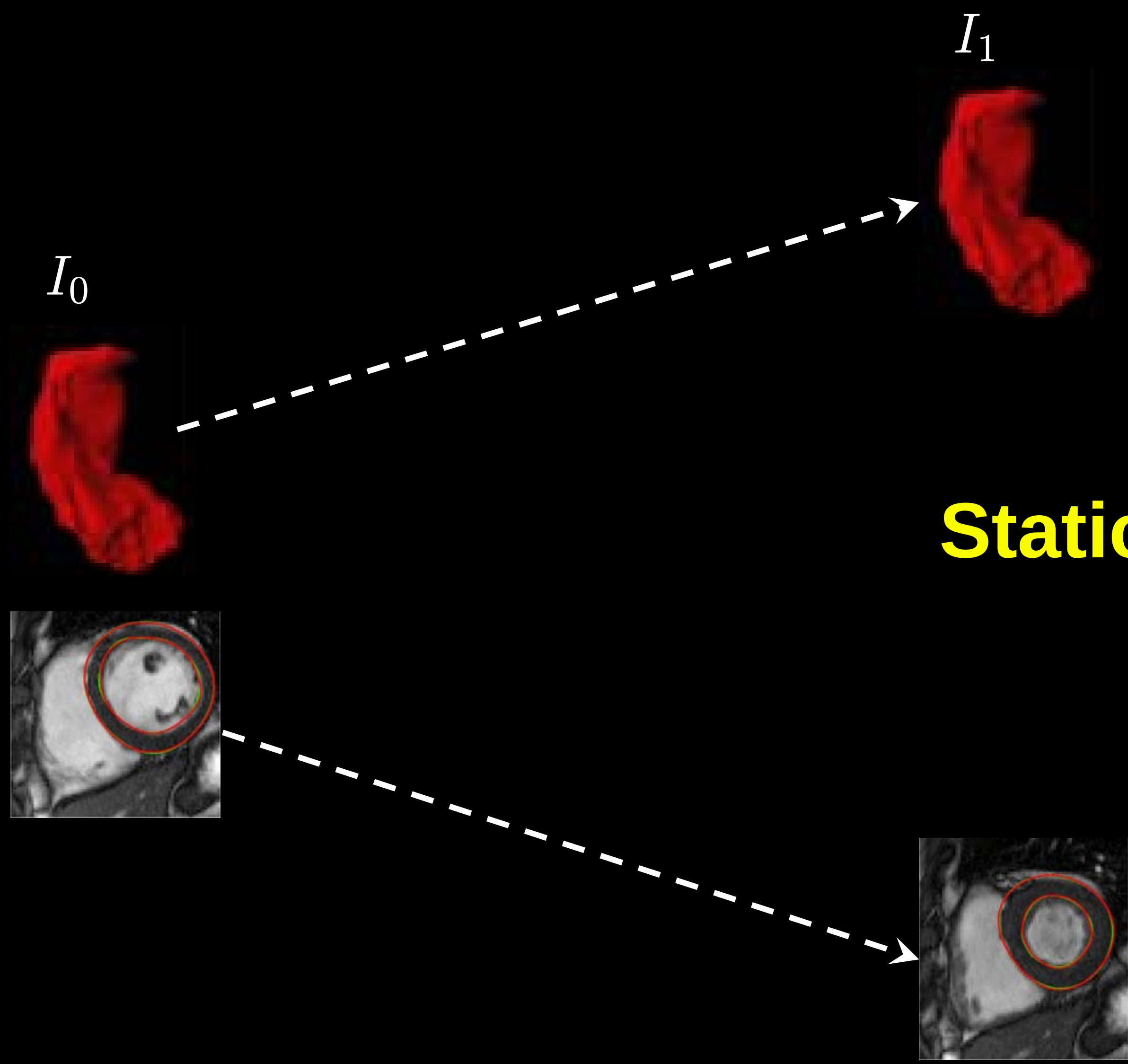
shape in AD **thickness in SCZ**



retinotopic mapping



Large Deformation Diffeomorphic Metric Mapping (LDDMM)

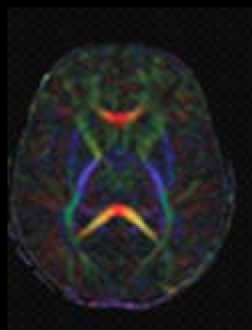


Static LDDMM

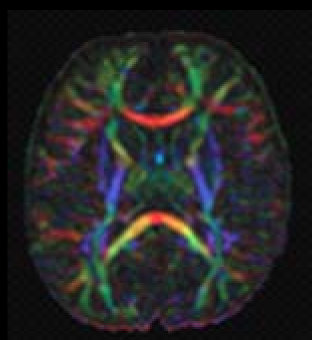
Tracking Growth, Atrophy, Dynamic Motion

Growth

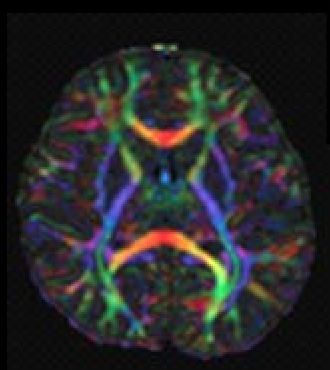
new born



6 months



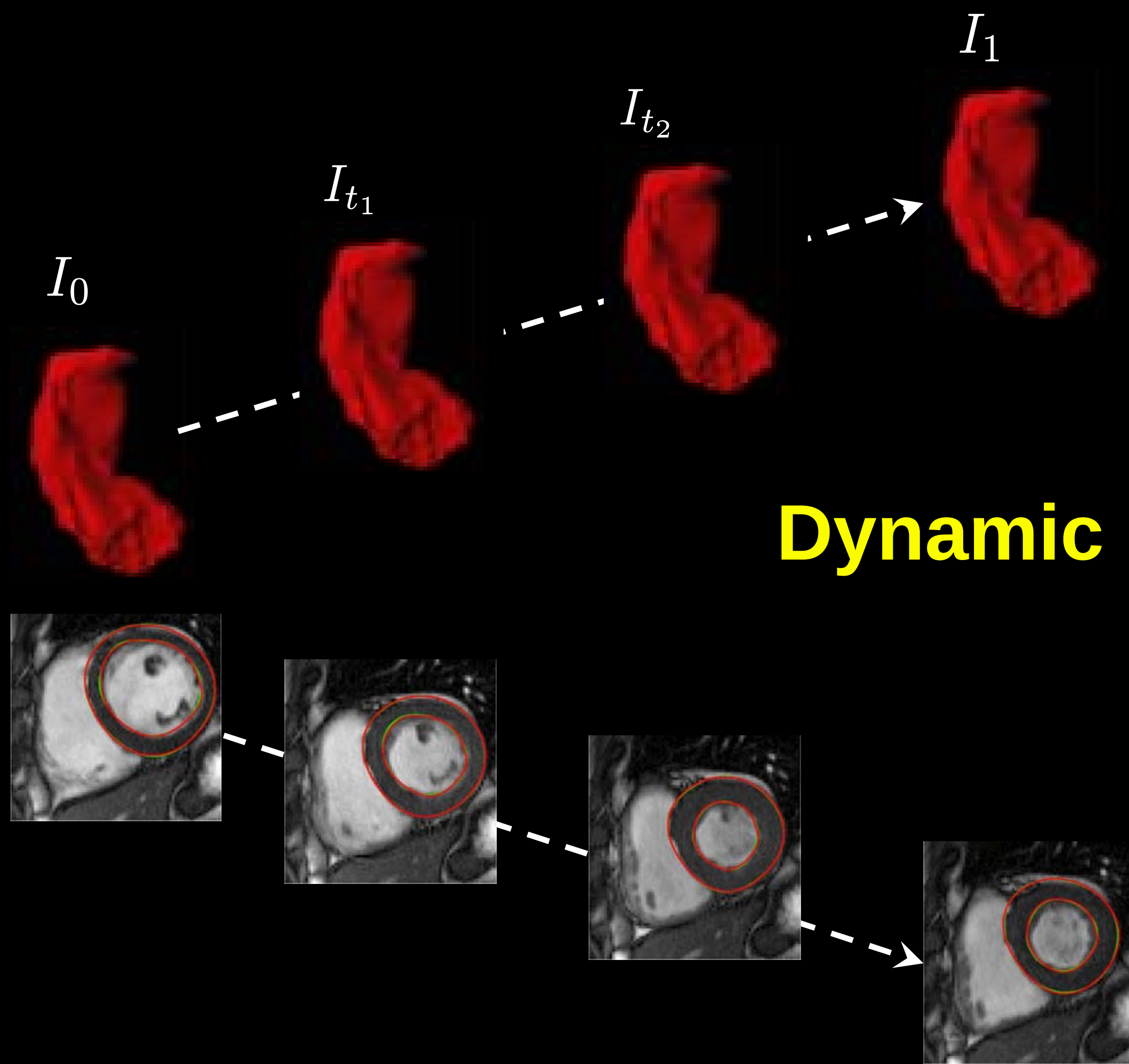
12 months



Atrophy

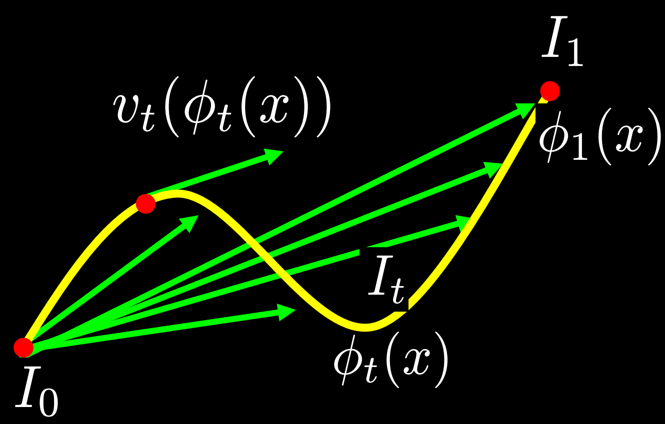
Dynamic Motion

Time Sequence Large Deformation Diffeomorphic Metric Mapping (TS-LDDMM)



Dynamic LDDMM

Time Sequence Large Deformation Diffeomorphic Metric Mapping (TS-LDDMM)



$$\dot{\phi}_t = v_t(\phi_t), \phi_0 = id$$

$$J(v_t) = \arg\min_{v_t : \dot{\phi}_t = v_t(\phi_t), \phi_0 = id} \int_0^1 \|v_t\|_V^2 dt + \int_0^1 E_t(\phi_t \cdot I_0, I_t) dt,$$

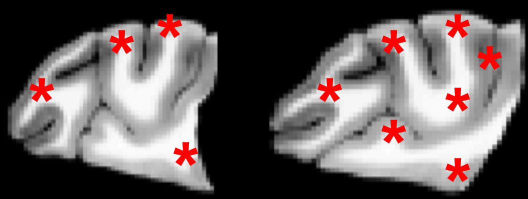
Equivalently,

$$J(m_t) = \arg\min_{m_t : \dot{\phi}_t = k_V m_t(\phi_t), \phi_0 = id} \int_0^1 < m_t, k_V m_t >_2 dt + \int_0^1 E_t(\phi_t \cdot I_0, I_t) dt,$$

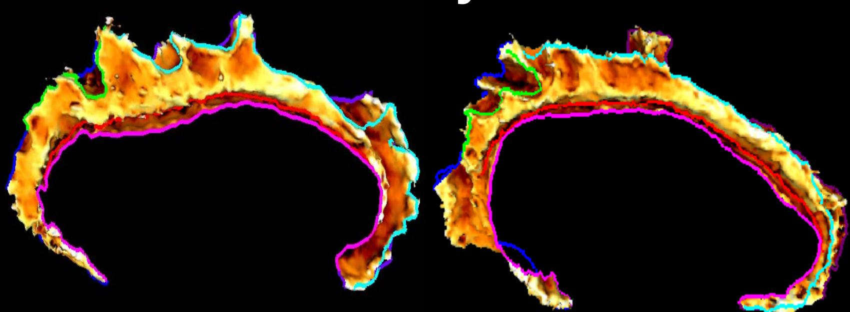
where m_t, termed as momentum, is defined by the kernel $k_V : v_t \to m_t = k_V^{-1} v_t$, a linear transformation of v_t.

Time Sequence Large Deformation Diffeomorphic Metric Mapping (TS-LDDMM)

Landmarks



Sulcal or Gyral Curves



Surfaces

$I_0 = x = \{x_i\}_{i=1}^{n}, \quad I_t = y_t = \{y_j(t)\}_{j=1}^{n_t}.$

Define the trajectory $x_t = \{x_i(t)\}_{i=1}^{n} = \{\phi_t(x_i)\}_{i=1}^{n}.$

The momentum, m_t, takes the singular form

$$m_t = \sum_{i=1}^{n} \alpha_i(t) \otimes \delta_{x_i(t)},$$

where $\alpha_i(t)$ is the momentum vector of the i^{th} point at time t.

TS-LDDMM:

$$J(m_t) = \underset{m_t : \dot{\phi}_t = k_V m_t(\phi_t), \phi_0 = id}{\arg\min} \int_0^1 < m_t, k_V m_t >_2 dt + \int_0^1 E_t(\phi_t(x), y_t) dt$$

Point-based TS-LDDMM:

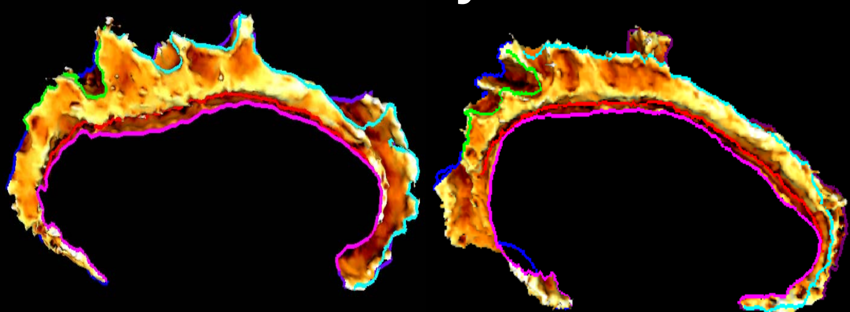
$$J(\alpha_t) = \underset{\alpha_t : \dot{\phi}_t = k_V \alpha_t(\phi_t), \phi_0 = id}{\arg\min} \int_0^1 \sum_{i=1}^{n} \sum_{j=1}^{n} [k_V(x_i(t), x_j(t)) \alpha_j(t)] \cdot \alpha_i(t) dt + \int_0^1 E_t(\phi_t(x), y_t) dt$$

Qiu, A. et. al. NeuroImage, special issue

Time Sequence Large Deformation Diffeomorphic Metric Mapping (TS-LDDMM)

Landmarks

Sulcal or Gyral Curves



Surfaces

Unlabeled landmarks, curves, and surfaces are represented as discrete measures in the form:

$$\mu_x = \sum_{i=1}^{n} \omega_i \otimes \delta_{x_i},$$

with the norm $\|\mu_x\|_{W^*}^2 = \sum_{i=1}^{n}\sum_{j=1}^{n}[k_W(x_i, x_j)\omega_j]\cdot\omega_i.$

The action of ϕ_t on the discrete measure μ_x is given as

$$\phi_t \cdot \mu_x = \sum_{i=1}^{n} \omega_i \otimes \delta_{\phi_t(x_i)}.$$

With $\mu_x = \sum_{i=1}^{n} \omega_i \otimes \delta_{x_i}$ and $\mu_{y_t} = \sum_{j=1}^{n_t} \tilde{\omega}_j \otimes \delta_{y_j(t)}$,

$$E_t(\phi_t(x), y_t) = \left\|\phi_t \cdot \mu_x - \mu_{y_t}\right\|_{W^*}^2$$

$$= \sum_{i=1}^{n}\sum_{j=1}^{n}[k_W(x_i(t), x_j(t))\omega_j]\cdot\omega_i$$

$$-2\sum_{i=1}^{n}\sum_{j=1}^{n_t}[k_W(x_i(t), y_j(t))\tilde{\omega}_j]\cdot\omega_i + \sum_{i=1}^{n_t}\sum_{j=1}^{n_t}[k_W(y_i(t), y_j(t))\tilde{\omega}_j]\cdot\tilde{\omega}_i$$

Euler-Lagrange Equation for Point-Based TS-LDDMM

The point-based TS-LDDMM:

$$J(\alpha_t) = \arg\min_{\alpha_t:\dot{\phi}_t = k_V \alpha_t(\phi_t), \phi_0 = id} \int_0^1 \sum_{i=1}^{n} \sum_{j=1}^{n} [k_V(x_i(t), x_j(t))\alpha_j(t)] \cdot \alpha_i(t) dt + \int_0^1 E_t(\phi_t(x), y_t) dt.$$

Its Euler-Lagrange Equation:

$$\frac{d\alpha_i(t)}{dt} = -\sum_{j=1}^{n} \alpha_i(t) \cdot [\alpha_j(t) \nabla_1 k_V(x_i(t), x_j(t))] + \frac{1}{2} \nabla_{x_i(t)} E_t(\phi_t(x), y_t).$$

Let's review *static* point-based LDDMM:

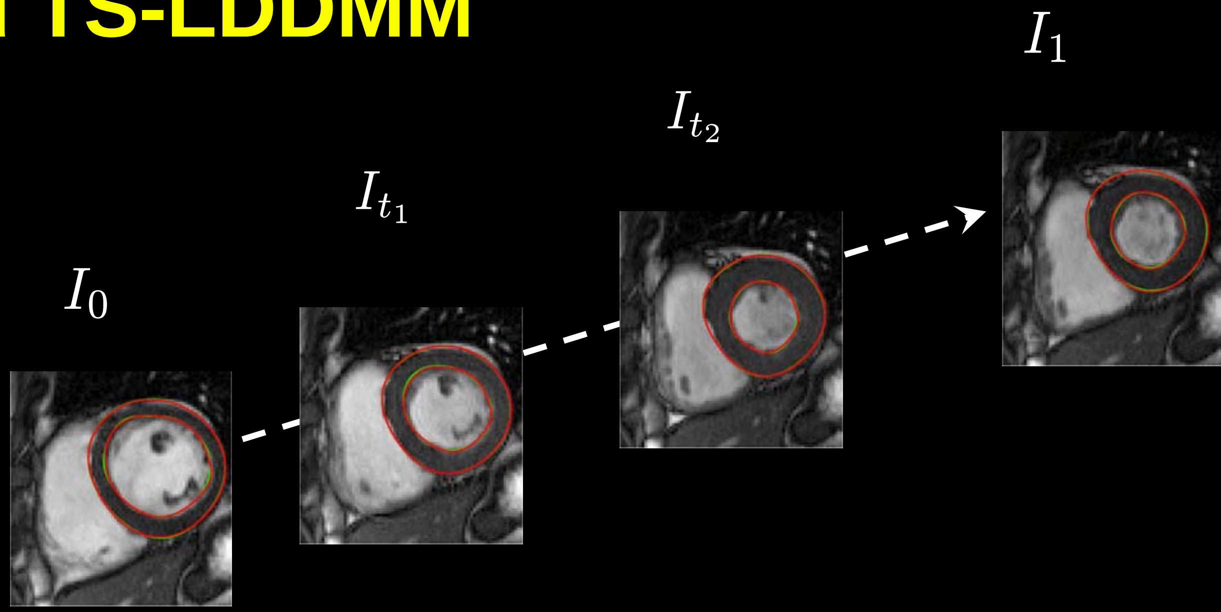
$$J(\alpha_t) = \arg\min_{\alpha_t:\dot{\phi}_t = k_V \alpha_t(\phi_t), \phi_0 = id} \int_0^1 \sum_{i=1}^{n} \sum_{j=1}^{n} [k_V(x_i(t), x_j(t))\alpha_j(t)] \cdot \alpha_i(t) dt + E_1(\phi_1(x), y),$$

with its Euler-Lagrange Equation

$$\frac{d\alpha_i(t)}{dt} = -\sum_{j=1}^{n} \alpha_i(t) \cdot [\alpha_j(t) \nabla_1 k_V(x_i(t), x_j(t))].$$

Flow Equation: $\frac{dx_i(t)}{dt} = \sum_{j=1}^{n} k_V(x_i(t), x_j(t))\alpha_j(t).$

Sampled TS-LDDMM



The optimal flow connecting the observables $y_{t_k}, k = 1,2,\cdots N$, given by

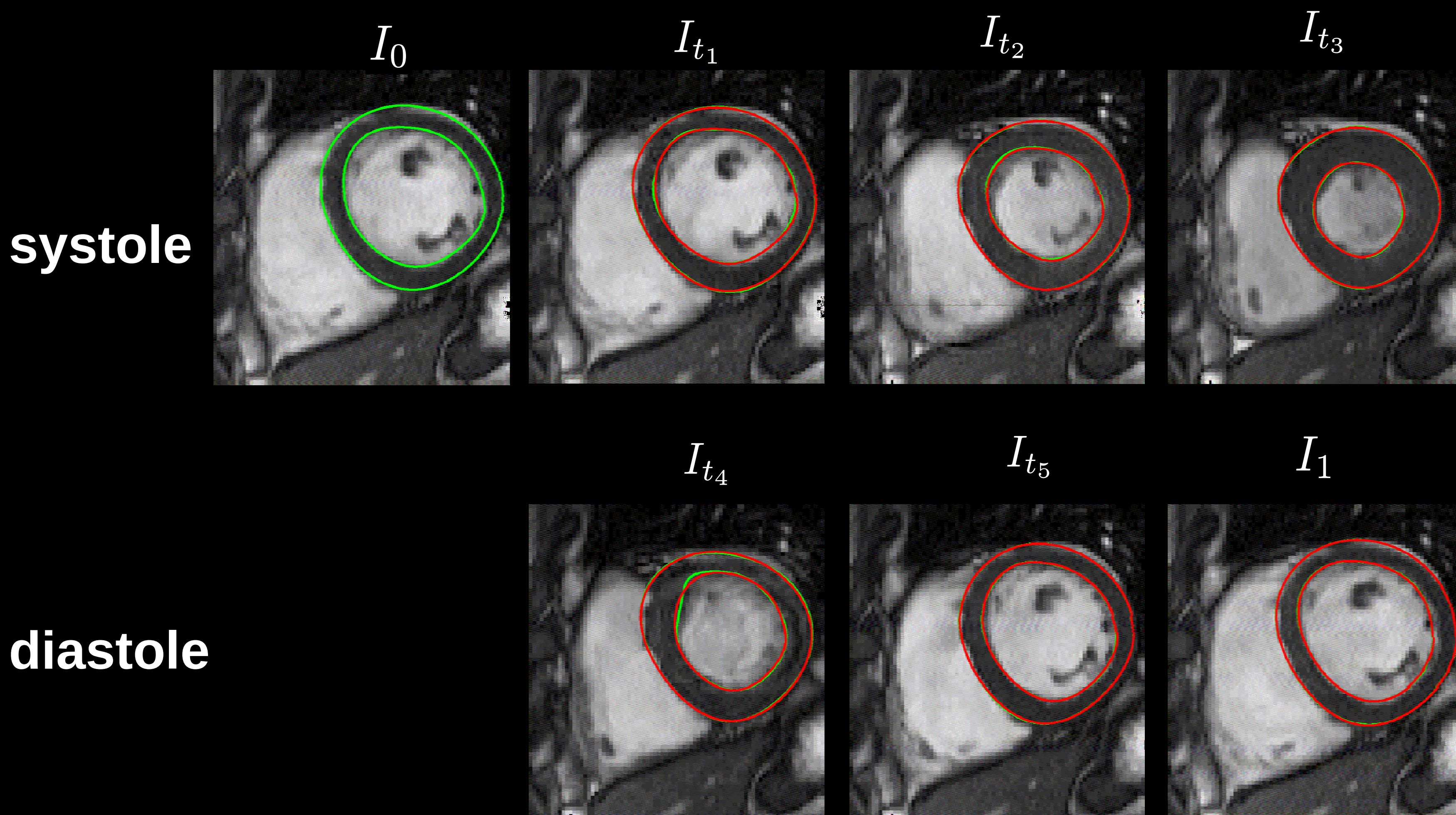
$$J(\alpha_t) = \underset{\alpha_t : \dot{\phi}_t = k_V \alpha_t(\phi_t), \phi_0 = id}{\arg\min} \int_0^1 \sum_{i=1}^n \sum_{j=1}^n [k_V(x_i(t), x_j(t))\alpha_j(t)] \cdot \alpha_i(t) dt + \sum_{k=1}^N E_{t_k}(\phi_{t_k}(x), y_{t_k}).$$

satisfies Euler-Lagrange optimality conditions for the point-based TS-LDDMM given by

$$\frac{d\alpha_i(t)}{dt} = -\sum_{j=1}^n \alpha_i(t) \cdot [\alpha_j(t) \nabla_1 k_V(x_i(t), x_j(t))], \quad t \in (t_{k-1}, t_k), k = 1,2,\cdots N,$$

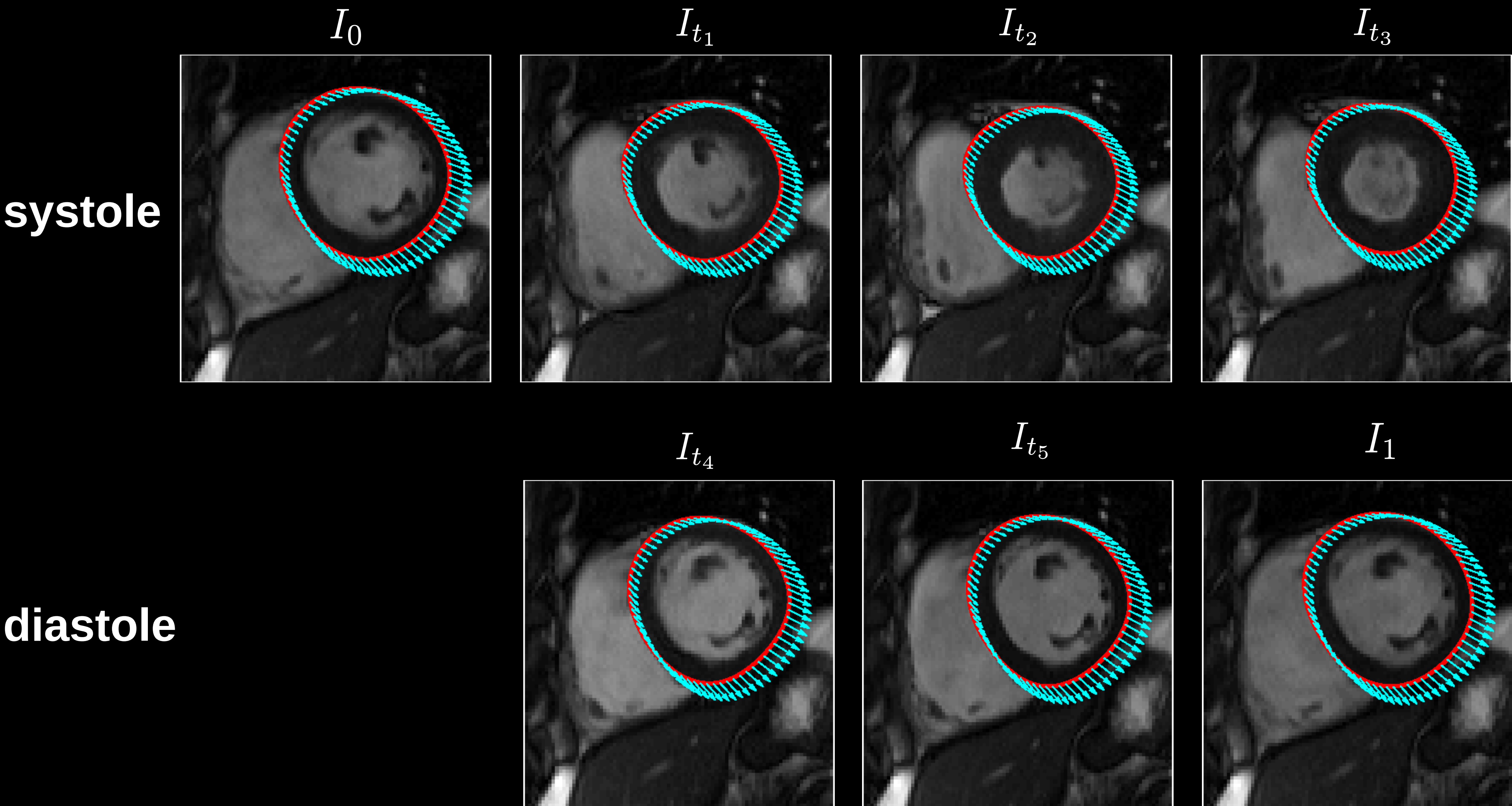
with jumps at observation times defined as $\alpha_1 = \nabla_{x_1} E_1 / 2$, and $\alpha_{t_k^+} - \alpha_{t_k^-} = \nabla_{x_{t_k}} E_{t_k} / 2$.

TS-LDDMM for Curves



TS-LDDMM for Curves

$$\text{Momentum Vectors}: \quad \alpha_i(t)$$



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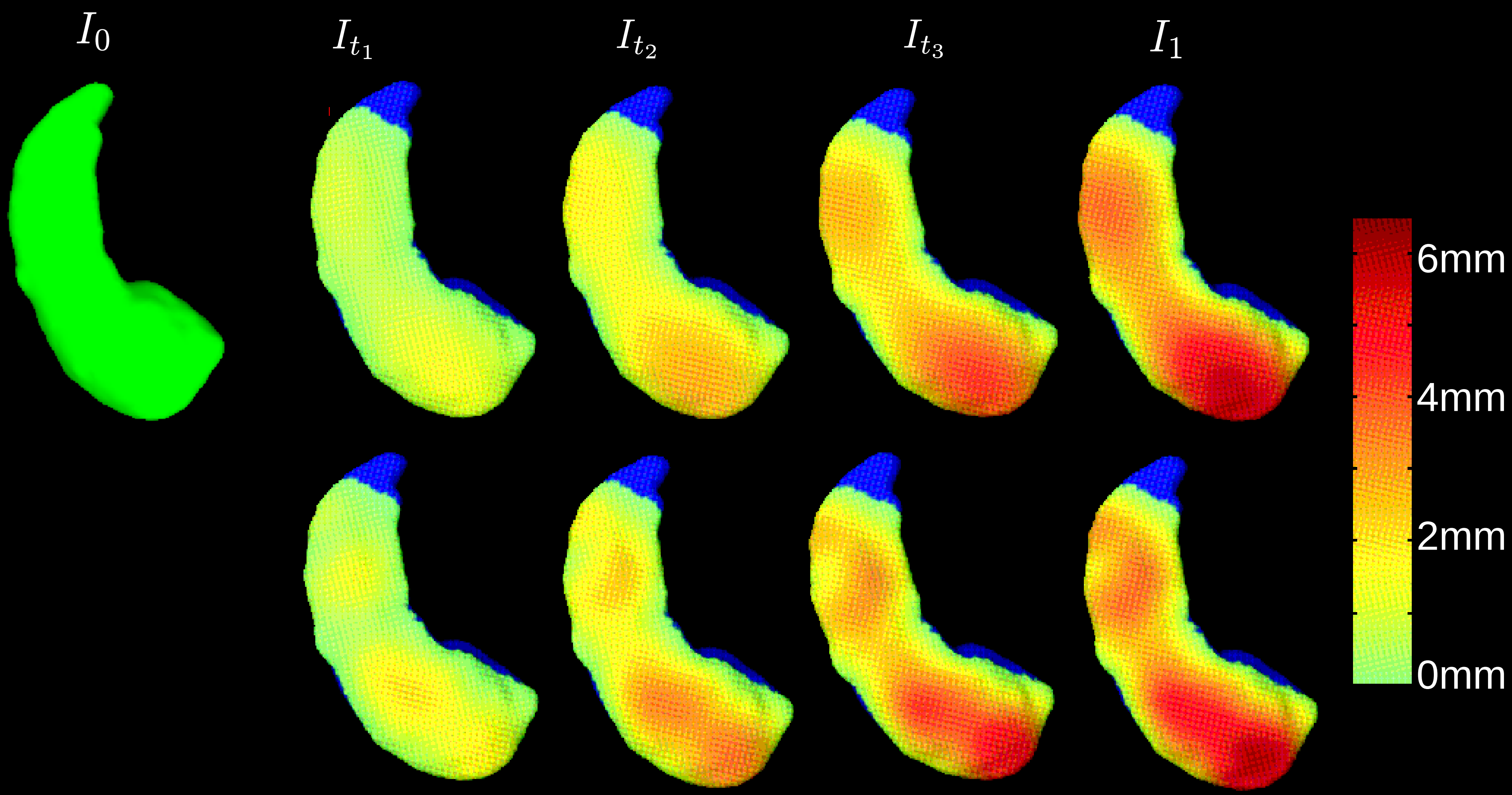
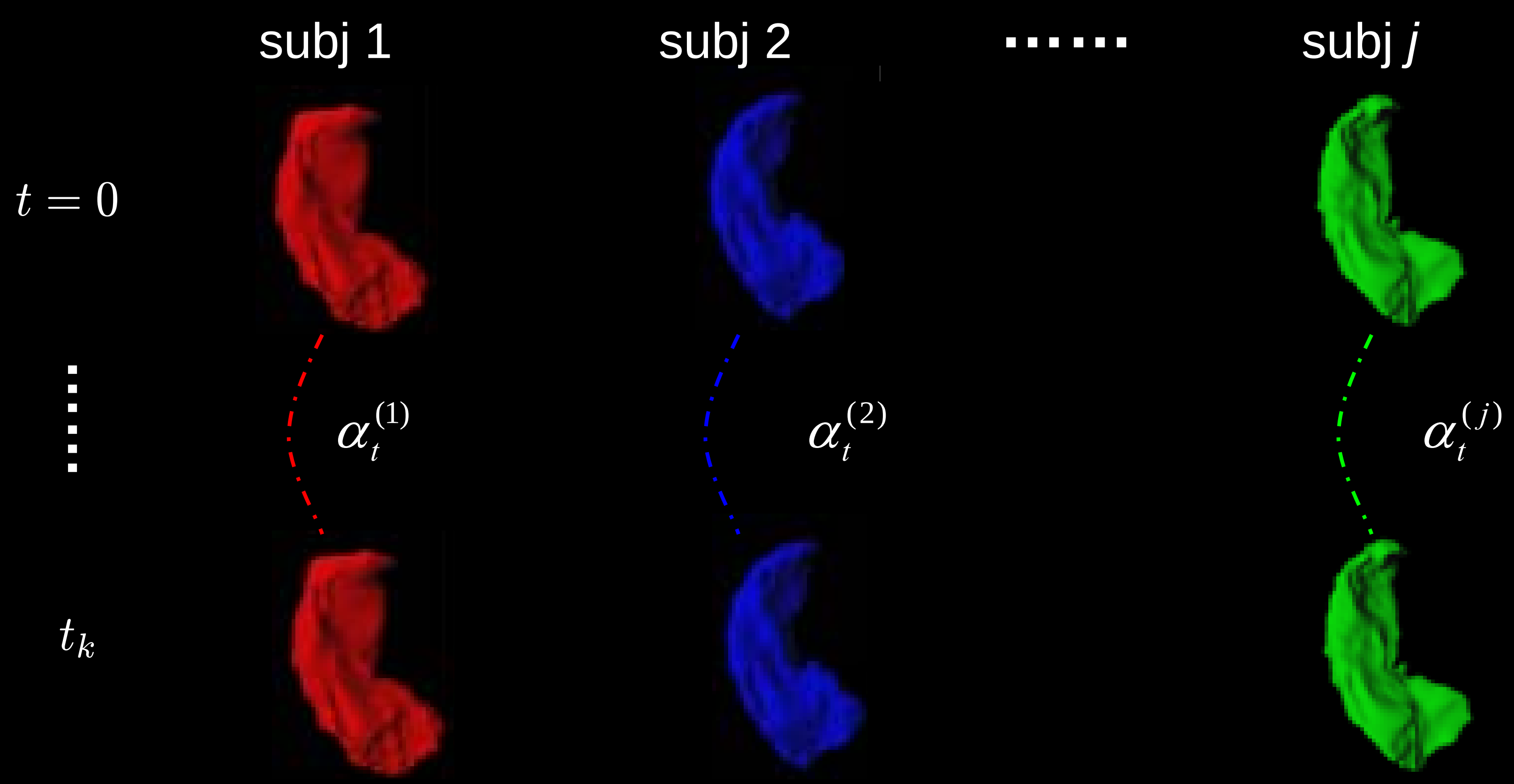
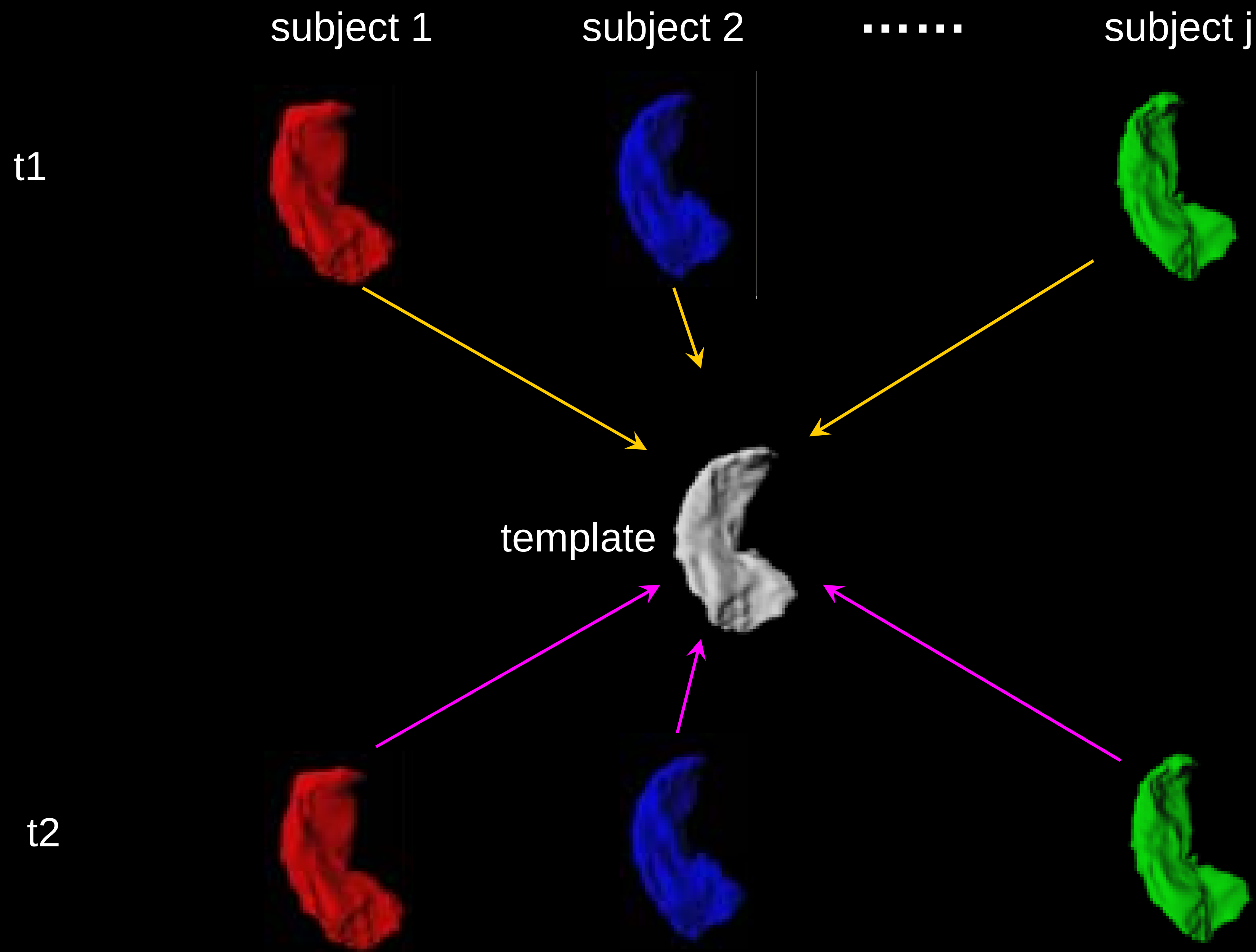
TS-LDDMM for Surfaces



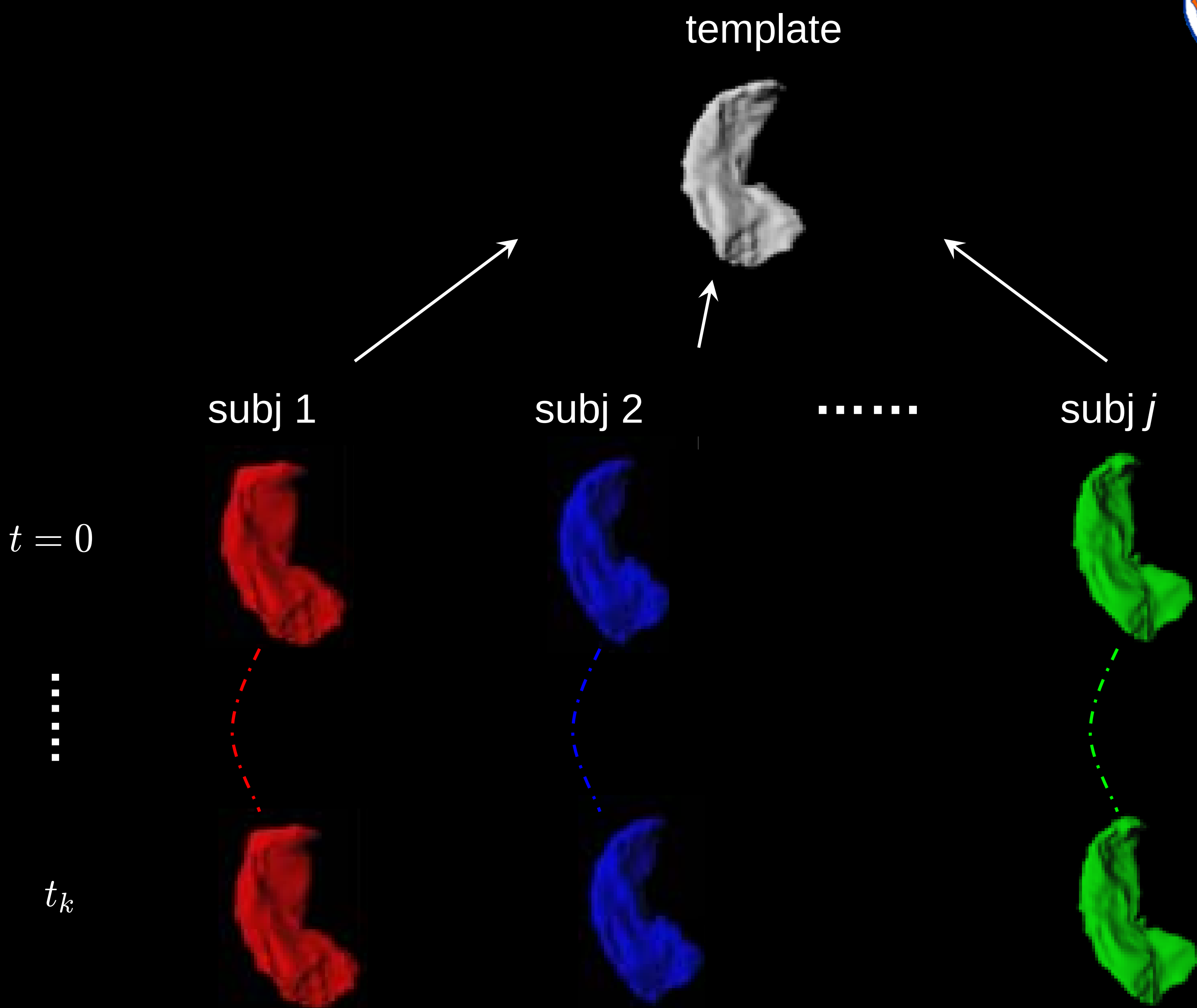
Inference on Growth, Atrophy, Dynamic Motion



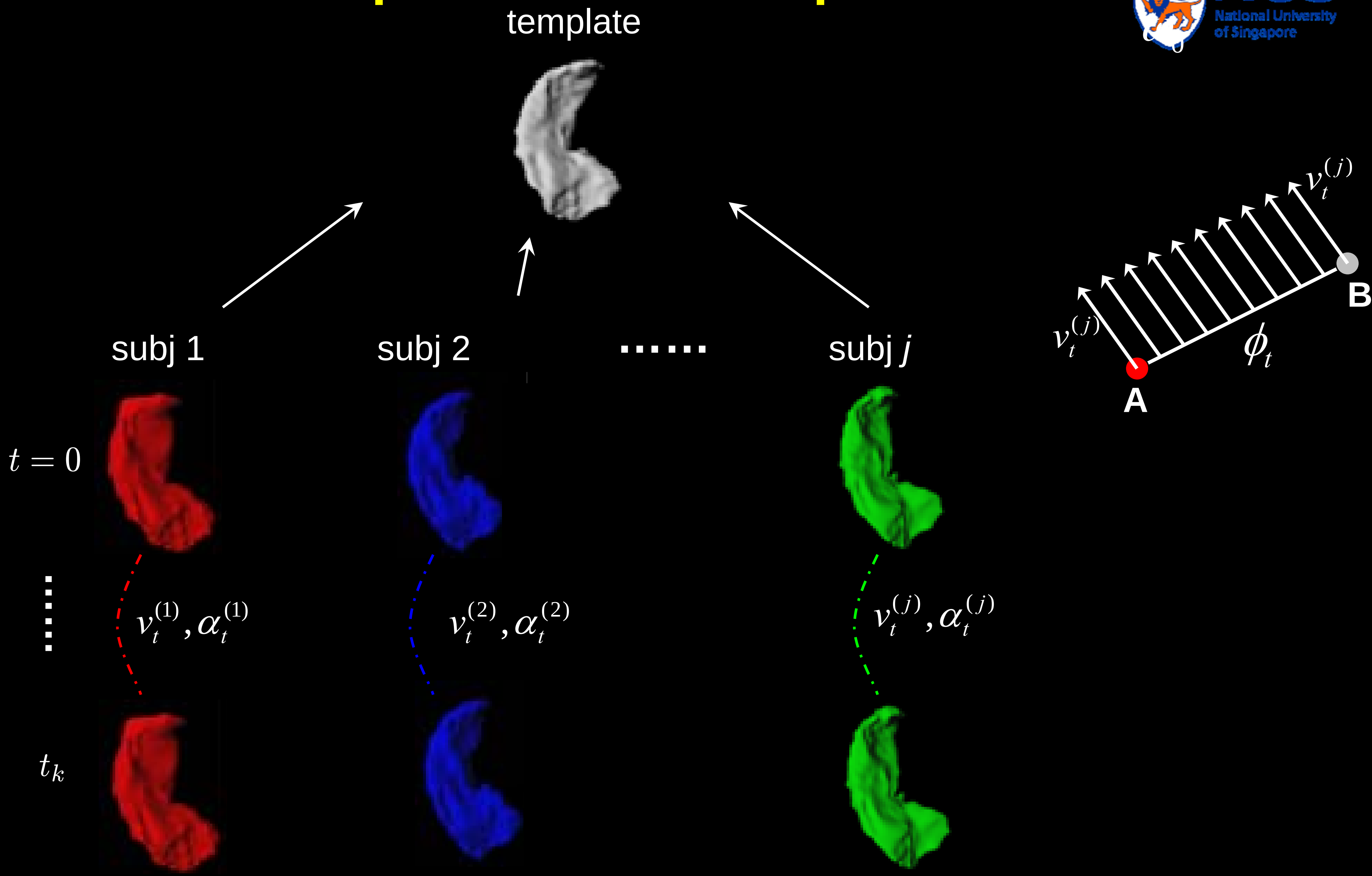
General Approach (1)



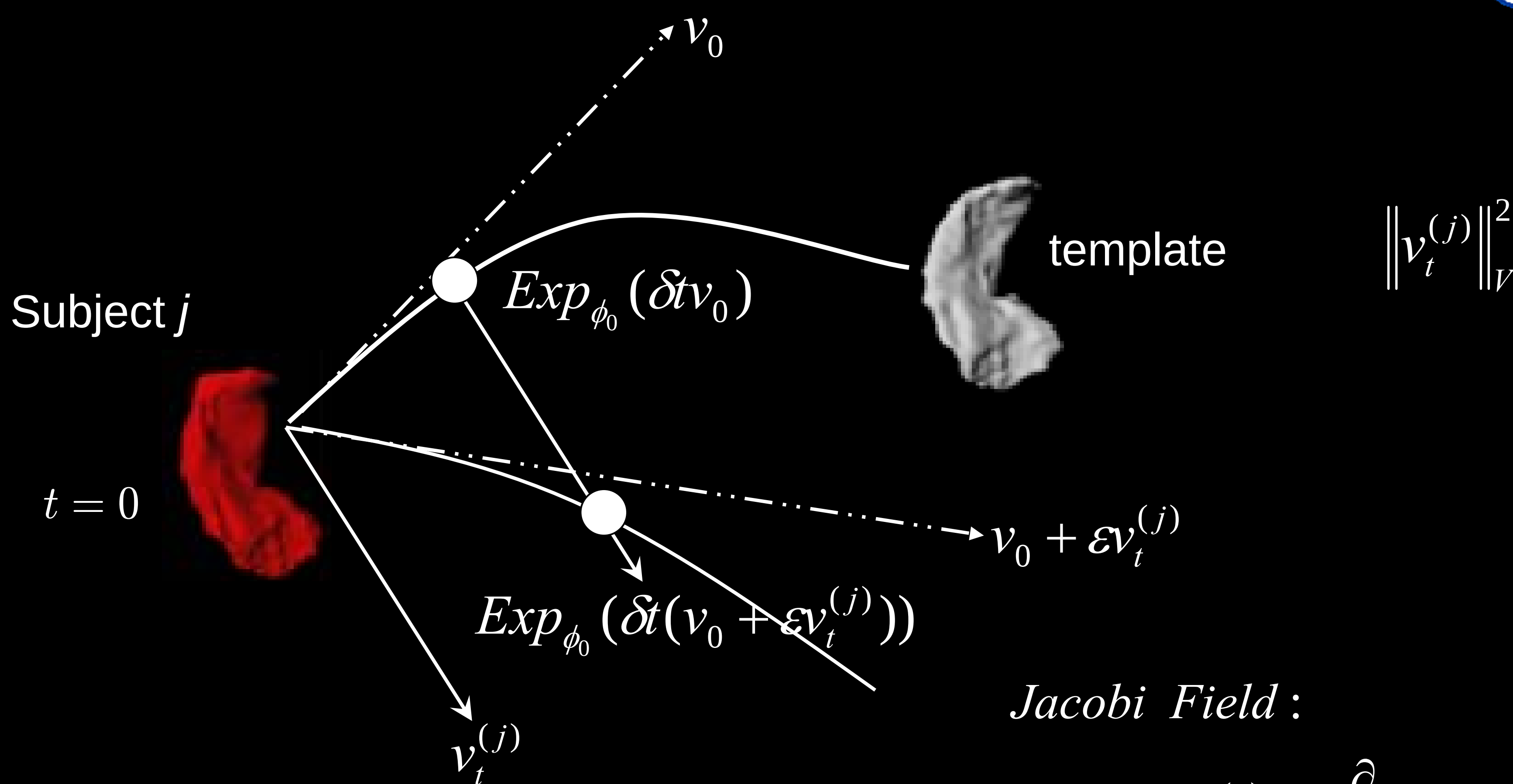
General Approach (2)



Parallel Transport in Diffeomorphisms



Parallel Transport in Diffeomorphisms



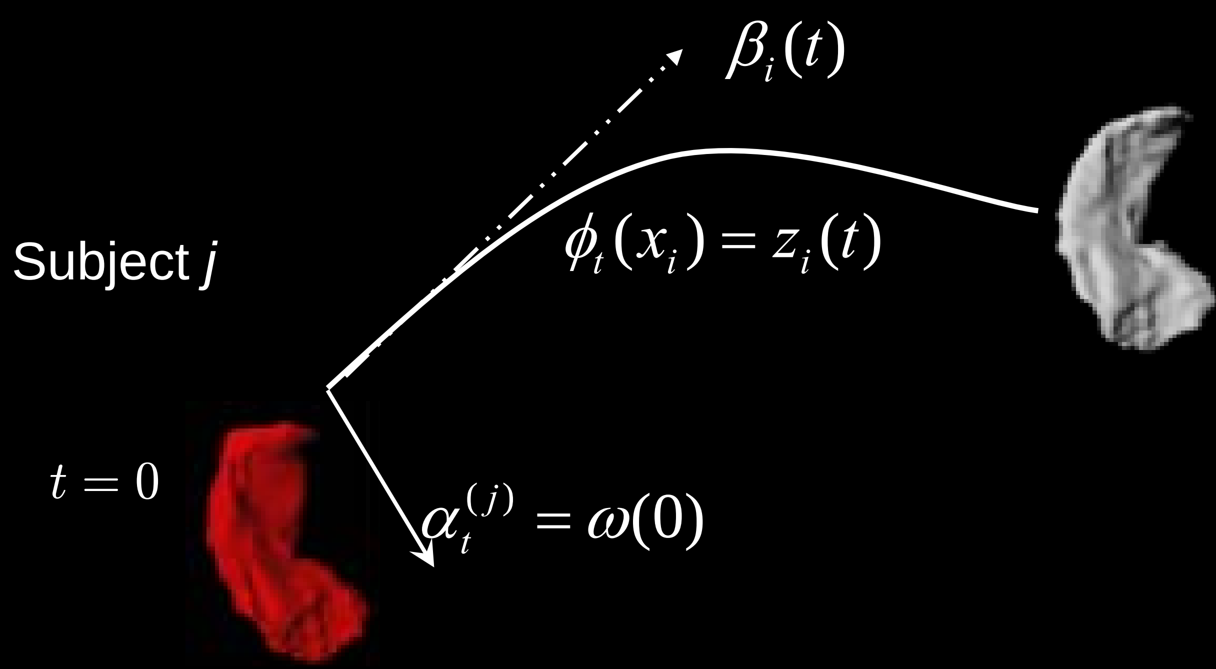
$Jacobi\ \ Field:$

$$J_{\phi_t}(\delta t, v_t, v_{t_k}^{(j)}) = \frac{\partial}{\partial \varepsilon} Exp_{\phi_t}(\delta t(v_t + \varepsilon v_t^{(j)}))$$

$$v_t^{(j)} = \frac{J_{\phi_t}(\delta t, v_t, v_t^{(j)})}{\delta t}$$

$$k_V \alpha_t^{(j)} = v_t^{(j)}$$

Parallel Transport in Diffeomorphisms

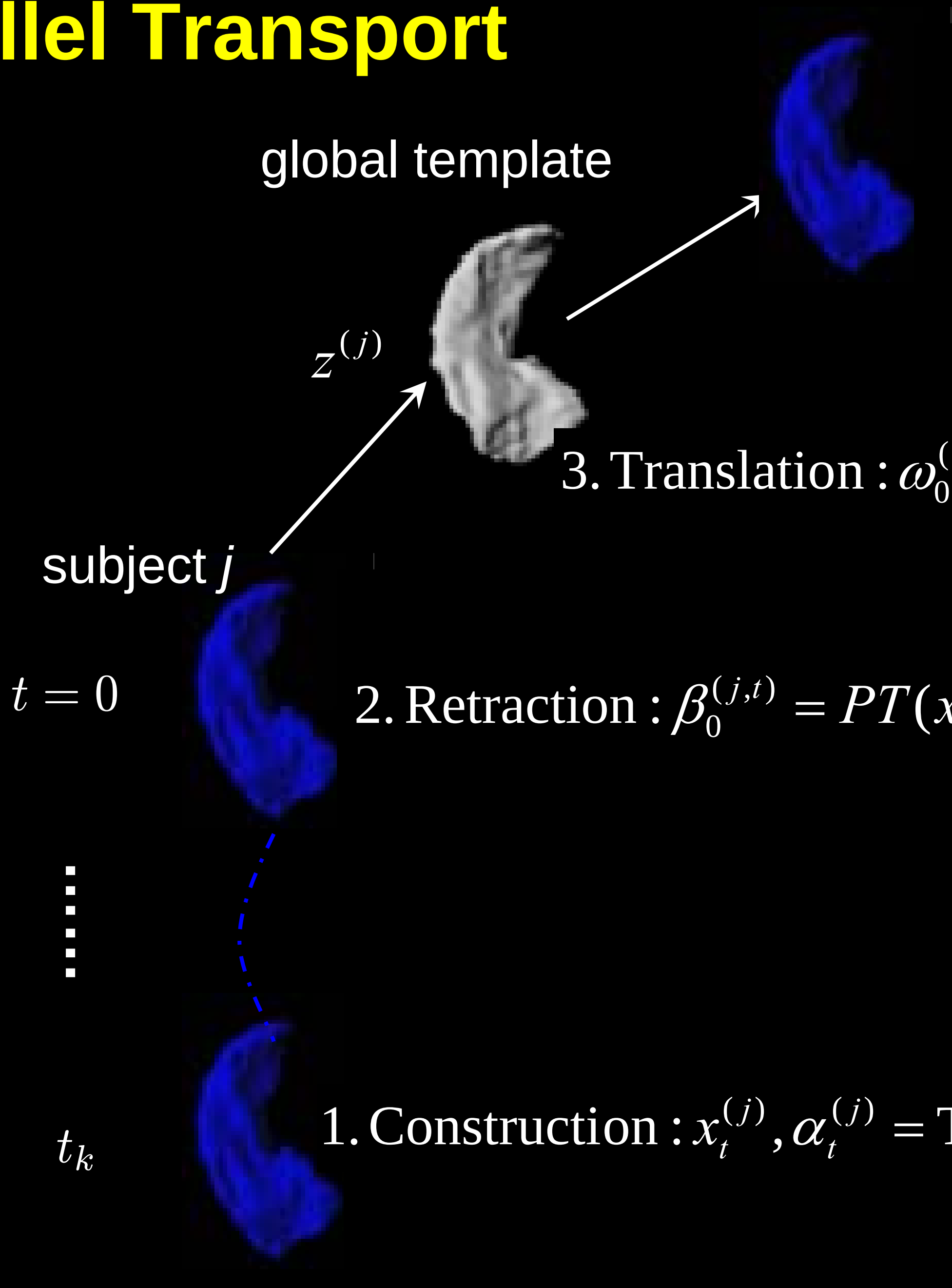


$$\sum_{j=1}^{n} k_V(z_i(t), z_j(t))\Big(\frac{d\omega_j(t)}{dt} + \sum_{l=1}^{n} \nabla_1 k_V(z_j(t), z_l(t))(\beta_j(t)\cdot\omega_l(t) + \omega_j(t)\cdot\beta_l(t))\Big)$$

$$= \sum_{j=1}^{n} \nabla_1 k_V(z_i(t), z_j(t)) \cdot \Big((\sum_{l=1}^{n} k_V(z_i(t), z_l(t))\omega_l(t) - \sum_{l=1}^{n} k_V(z_j(t), z_l(t))\omega_l(t))\beta_j(t)$$

$$-(\sum_{l=1}^{n} k_V(z_i(t), z_l(t))\beta_l(t) - \sum_{l=1}^{n} k_V(z_j(t), z_l(t))\beta_l(t))\omega_j(t)\Big) \ .$$

Integration of TS-LDDMM and Parallel Transport



4. Extension : $\frac{dy_t^{(j)}}{dt} = k_V(y_t, y_t)\omega_t^{(j,t)}$

when $\omega_t^{(j,t)} = PT(y^{(j)}, 0, \omega_0^{(j,t)}, t)$

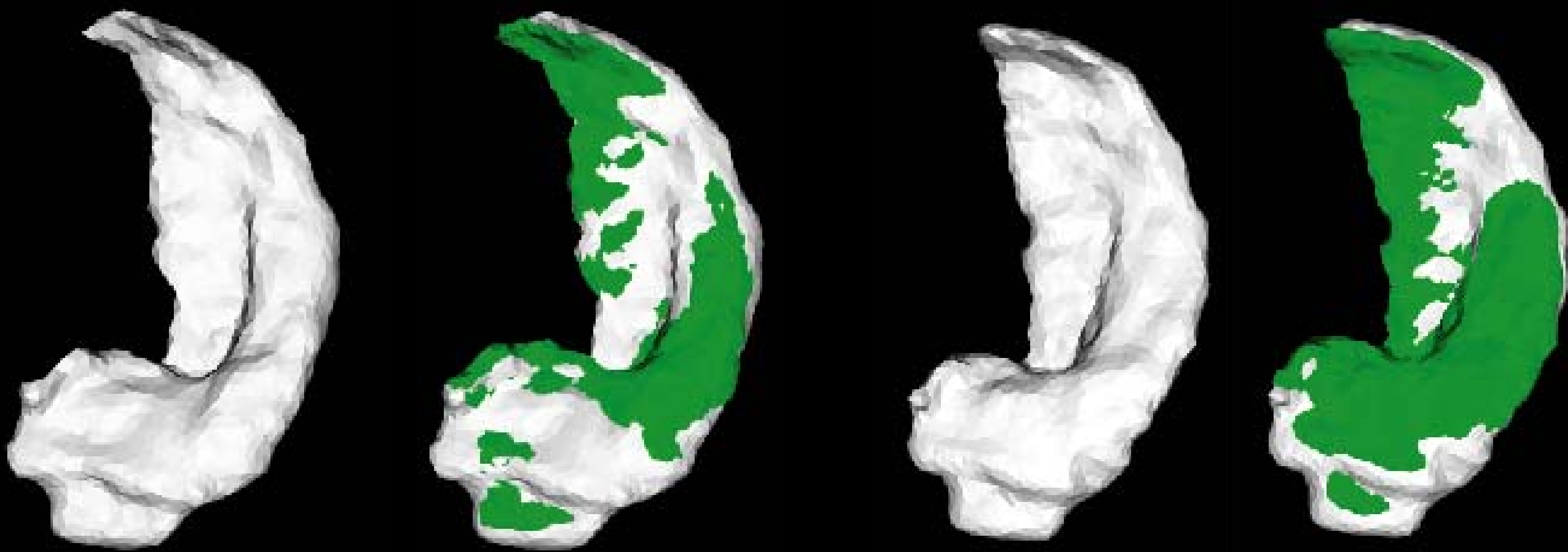
3. Translation : $\omega_0^{(j,t)} = PT(z^{(j)}, 0, \beta_0^{(j,t)}, 1)$

2. Retraction : $\beta_0^{(j,t)} = PT(x_t^{(j)}, t, \alpha_t^{(j)}, 0)$

1. Construction : $x_t^{(j)}, \alpha_t^{(j)} = \text{TS-LDDMM}(x, y_t)$

Example of Parallel Transport

baseline | t | global template | in global template



Time-Dependent Pattern of Hippocampal Surface Deformation Distinguishes Healthy Aging and Alzheimer's Disease

Objective: distinguish the Time-Dependent Pattern of Hippocampal Surface Deformation due to Healthy Aging and Alzheimer's Disease

Subjects: 26 Healthy Comparison Controls

18 Patients with very mild AD, scored as CDR0.5

9 Converters

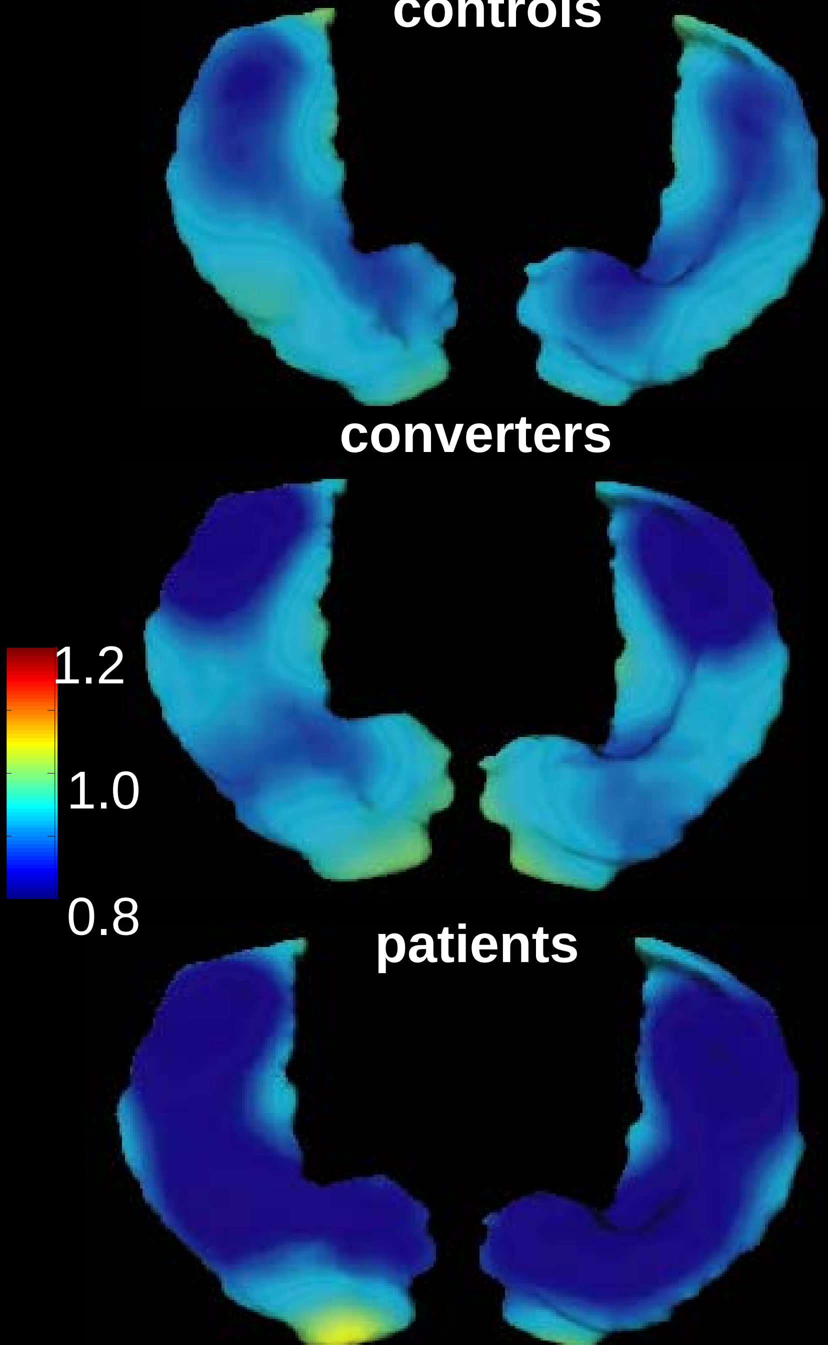
Acquisition: 1.5T Magnetom SP-4000, MPRAGE, TR = 10 ms, TE = 4 ms, Resolution: 1X1X1mm, acquired at WUSTL

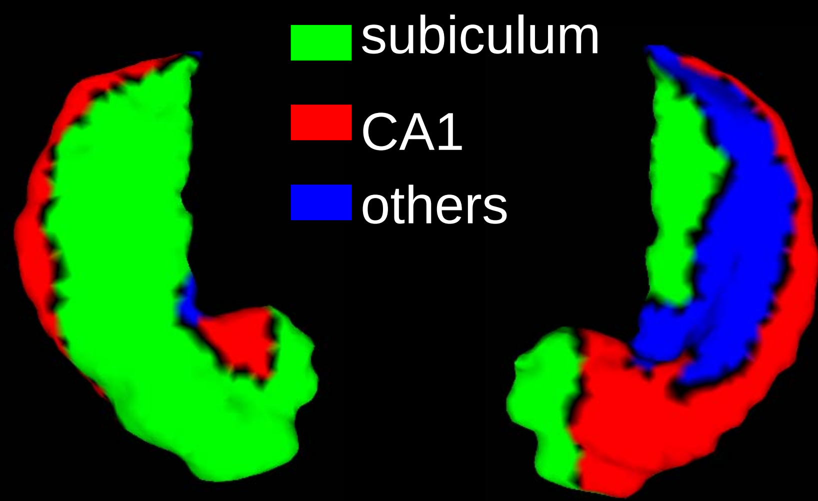
Process: hippocampus delineation at WUSTL

shape deformation between baseline and follow-up within each subject

statistical testing in each subfield of the hippocampus

Mean Jacobian Determinant





Average Jacobian within Subfields

	subiculum	CA1	others
control	0.924	0.917	0.894
converter	0.917	0.899	0.874
patient	0.867	0.874	0.817

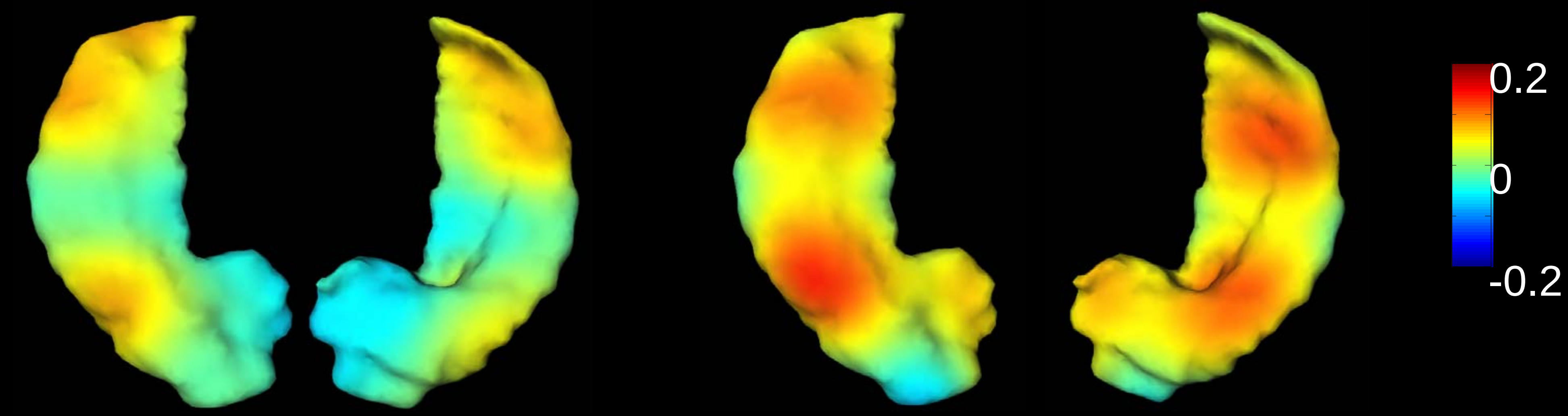
Shape Analysis in the Global Template

Random Field Model:

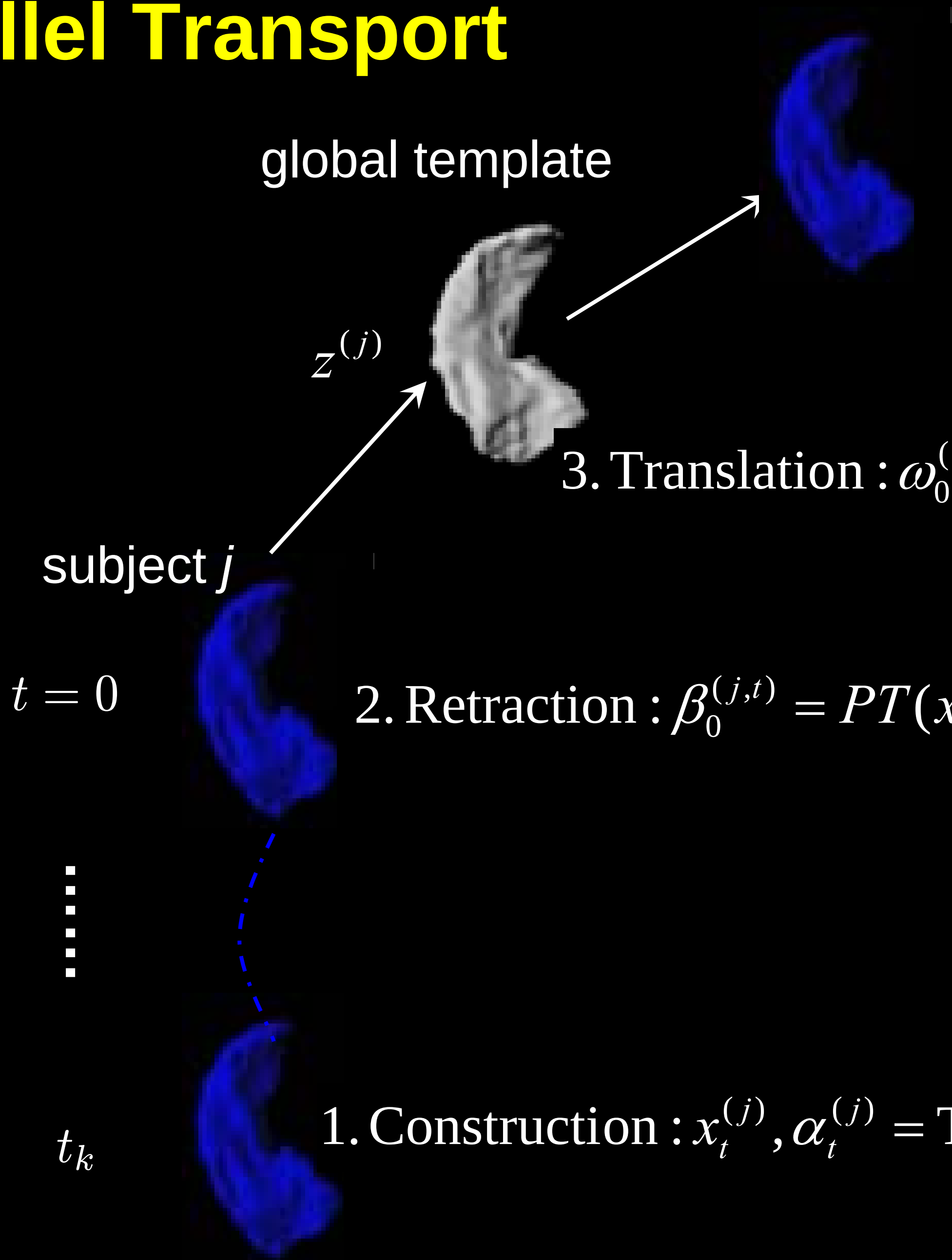
$$F(x) = \sum_{i=1}^{m} F_i \psi_i(x), x \in M^{template}$$

Difference
between controls and converters

Difference
between controls and AD patients



Integration of TS-LDDMM and Parallel Transport



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when $\omega_t^{(j,t)} = PT(y^{(j)}, 0, \omega_0^{(j,t)}, t)$

3. Translation : $\omega_0^{(j,t)} = PT(z^{(j)}, 0, \beta_0^{(j,t)}, 1)$

2. Retraction : $\beta_0^{(j,t)} = PT(x_t^{(j)}, t, \alpha_t^{(j)}, 0)$

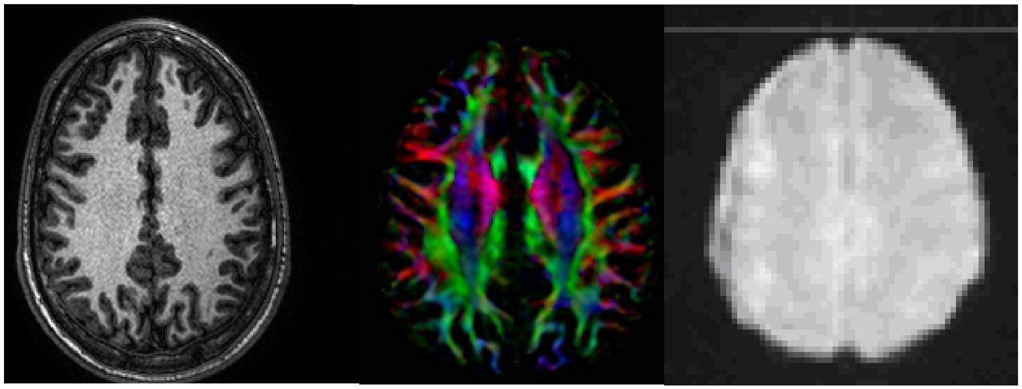
1. Construction : $x_t^{(j)}, \alpha_t^{(j)} = \text{TS-LDDMM}(x, y_t)$

National University of Singapore

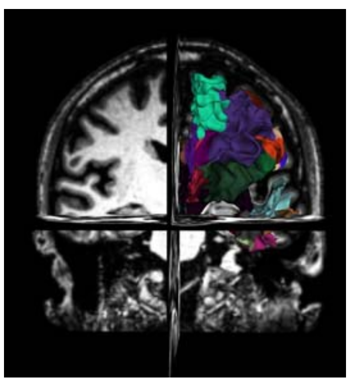
Computational Functional Anatomy (CFA) is the mathematical study of anatomical configurations and signals associated with anatomy and functions in anatomical coordinates.

1 MultiModal Images

MRI DTI fMRI



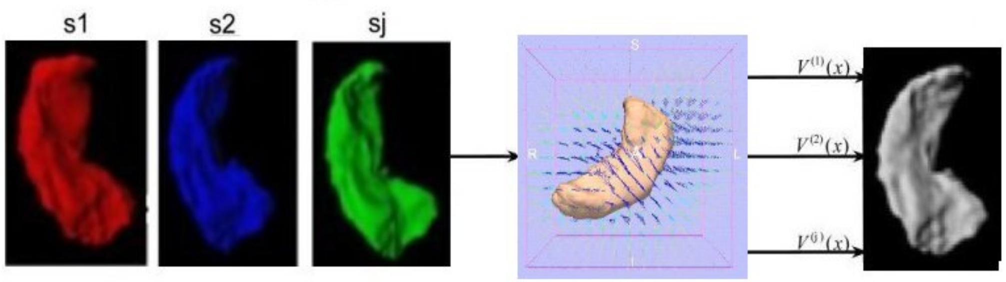
2 Segmentation



3 LDDMM Shape Analysis

LDDMM Variational Problem

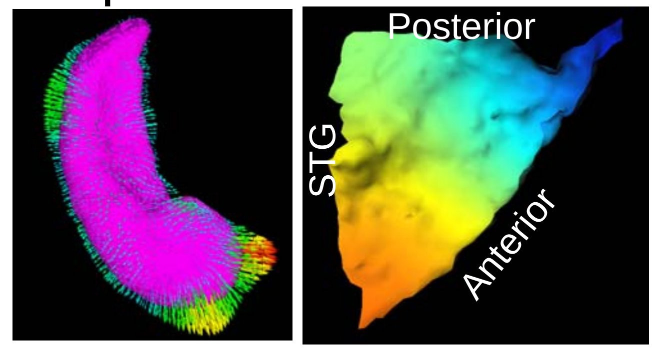
$$\int_0^1 \|v_t\|^2 dt \quad \varphi . I_{temp} = I_{target}$$



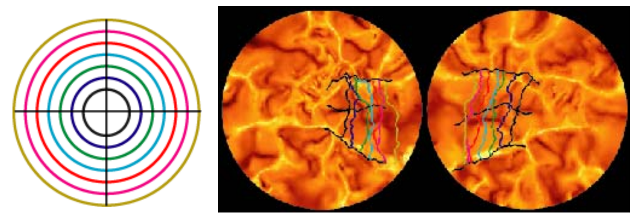
shape population template

5 Statistical Analysis

shape in AD thickness in SCZ

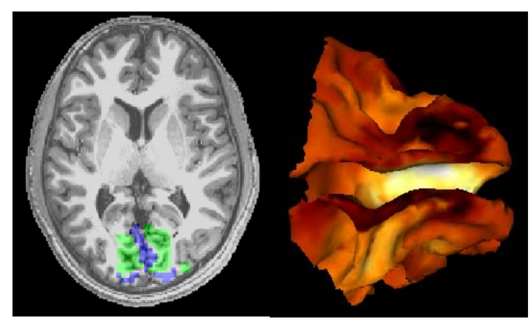


retinotopic mapping



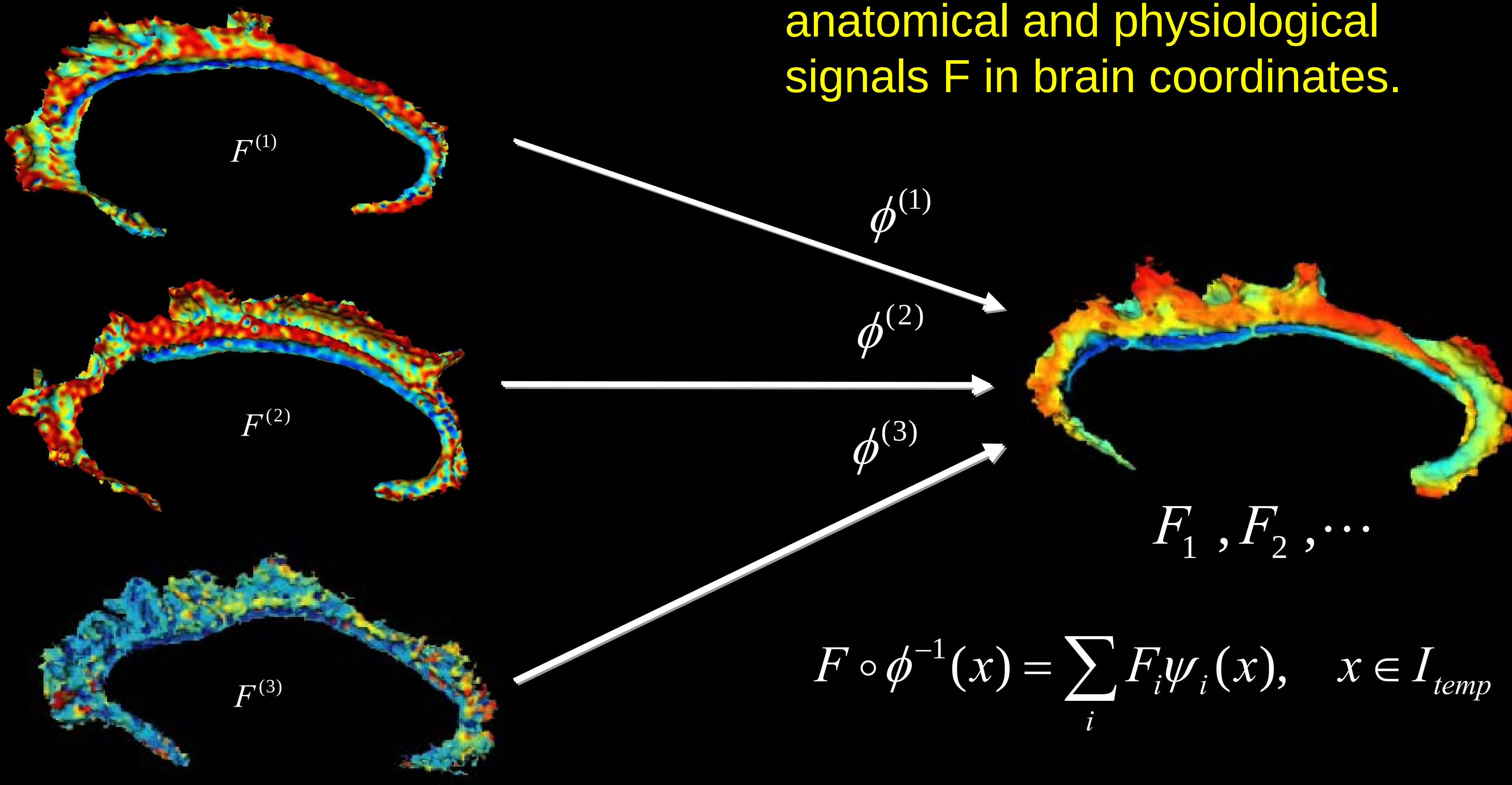
4 Functions in Anatomy

volume surface



Extrinsic Analysis on Functions

Statistical Method: Characterize anatomical and physiological signals F in brain coordinates.



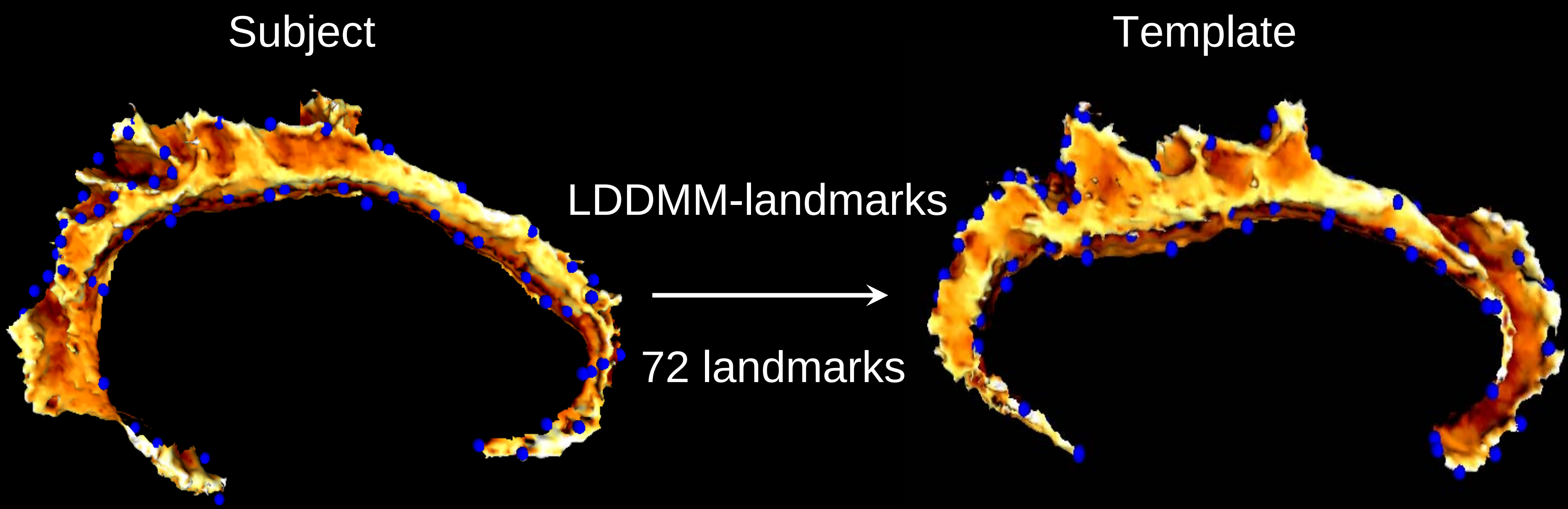
$$F \circ \phi^{-1}(x) = \sum_i F_i \psi_i(x), \quad x \in I_{temp}$$

Combining Anatomical Manifold Information via LDDMM for Studying Cortical Thinning of the Cingulate Gyrus in Schizophrenia

WUSTL: Csernansky, Wang

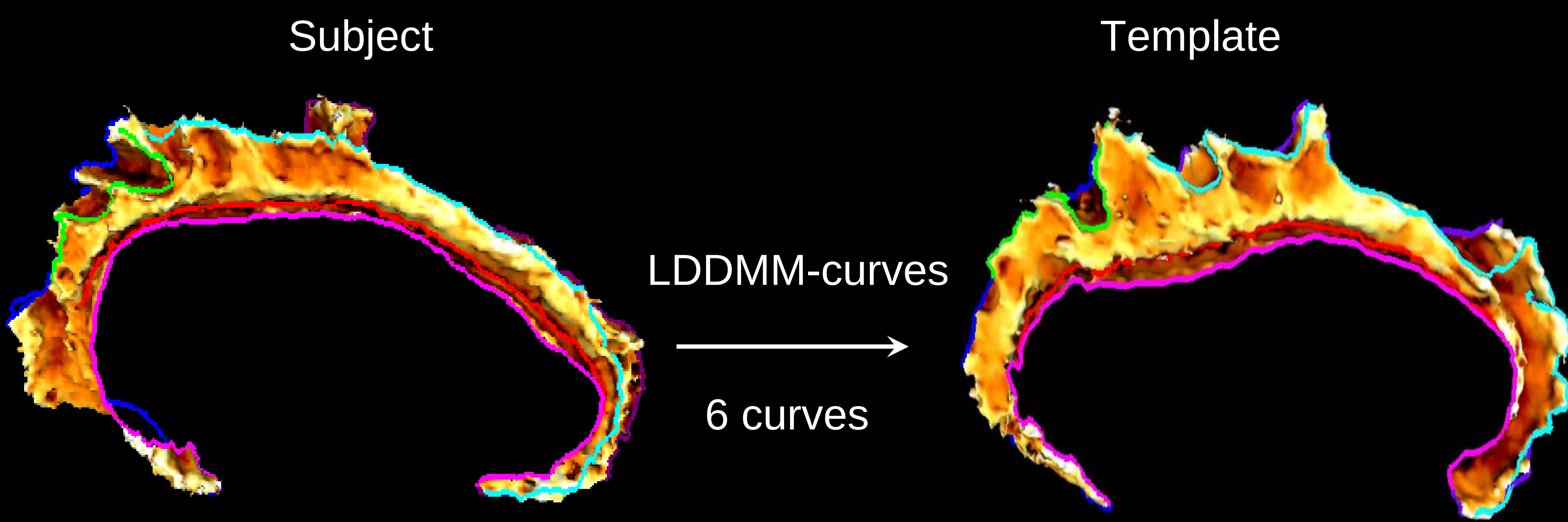
Objective: cortical variation of the cingulate gyrus in schizophrenia
Subjects: 49 schizophrenia subjects
64 healthy comparison controls
Acquisition: 1.5T Siemens, FLASH, TR = 20ms, TE = 5.4ms,
Resolution 1X1X1mm, acquired at WUSTL

LDDMM Landmark Mapping



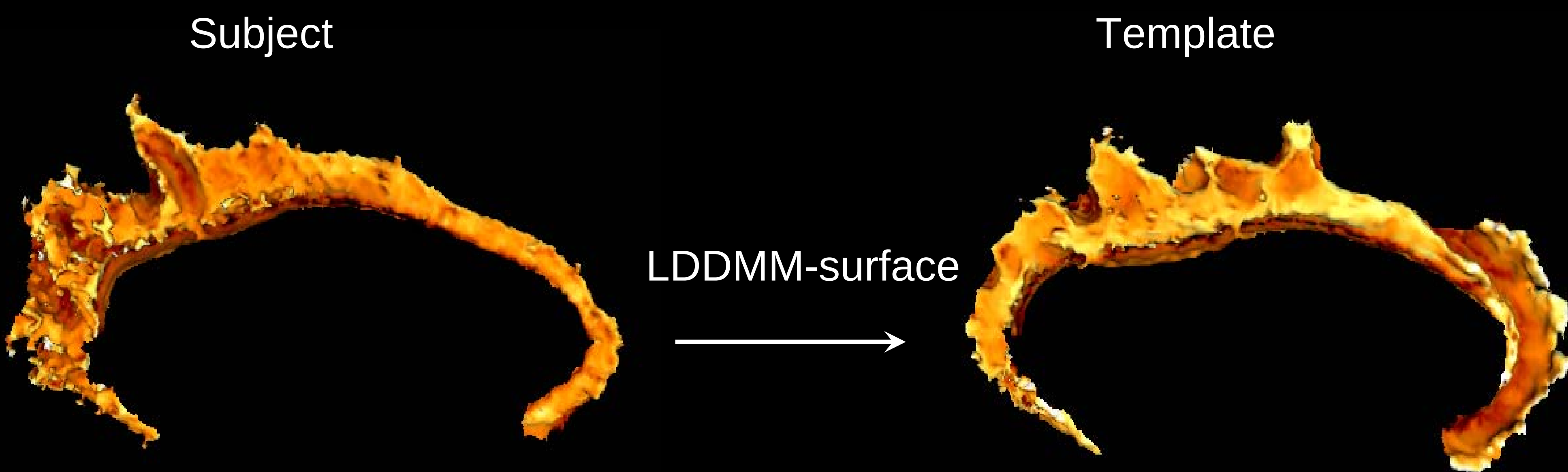
$$F \circ \phi^{-1}(x) = \sum_i F_i^L \psi_i(x), \quad x \in I_{temp}$$

LDDMM Curve Mapping



$$F \circ \phi^{-1}(x) = \sum_i F_i^C \psi_i(x), \quad x \in I_{temp}$$

LDDMM Surface Mapping

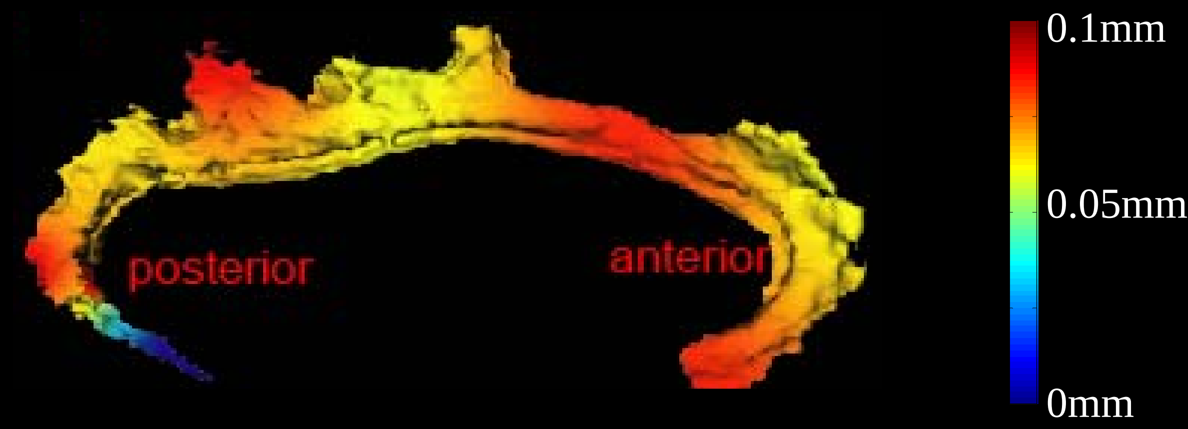


$$F \circ \phi^{-1}(x) = \sum_i F_i^S \psi_i(x), \quad x \in I_{temp}$$

Cortical Thinning of the Cingulate Gyrus in Schizophrenia

$$F \circ \phi^{-1}(x) = \sum_i F_i \psi_i(x), \quad x \in I_{temp} \rightarrow F_i^L, F_i^C, F_i^S$$

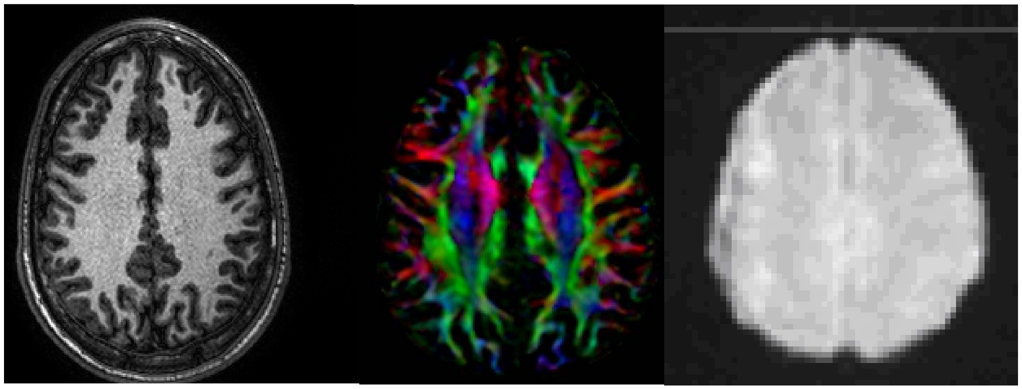
$$F_i^{\phi} = \overline{F}_i + \varepsilon_i, \quad \varepsilon_i \sim N(0, \sigma_i^2), \overline{F}_i \sim N(0, \sigma_{F_i}^2)$$



Combining landmark, curve, surface LDDMM mappings provided reliable statistical results and eliminated ambiguous results due to surface mismatches.

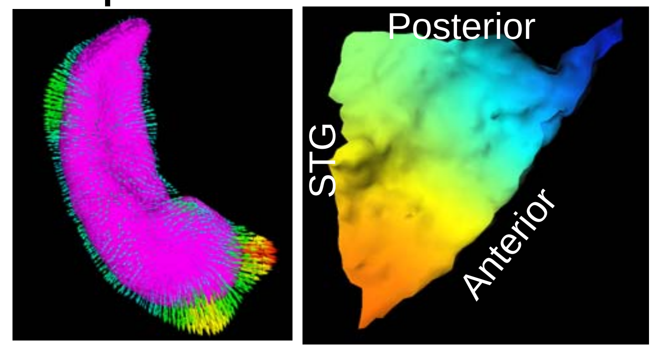
Computational Functional Anatomy (CFA) is the mathematical study of anatomical configurations and signals associated with anatomy and functions in anatomical coordinates.

1 MultiModal Images

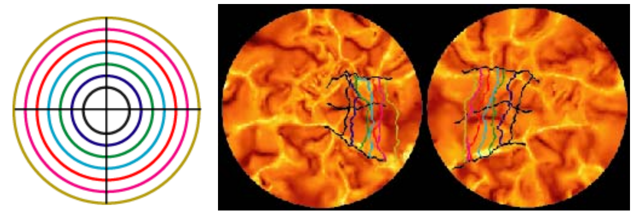


5 Statistical Analysis

shape in AD **thickness in SCZ**



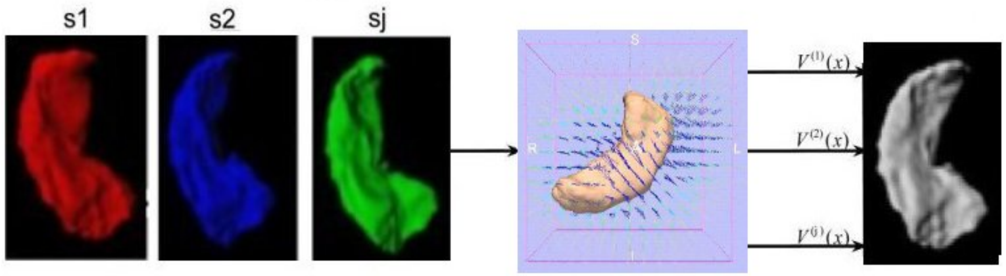
retinotopic mapping



3 LDDMM Shape Analysis

LDDMM Variational Problem

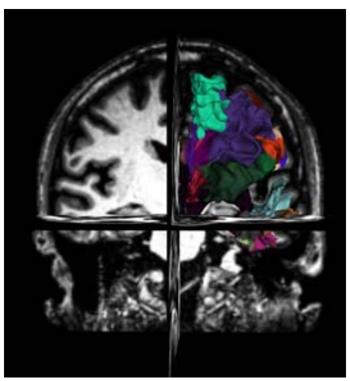
$$\int_0^1 \|v_t\|^2 dt \quad \varphi . I_{temp} = I_{target}$$



shape population

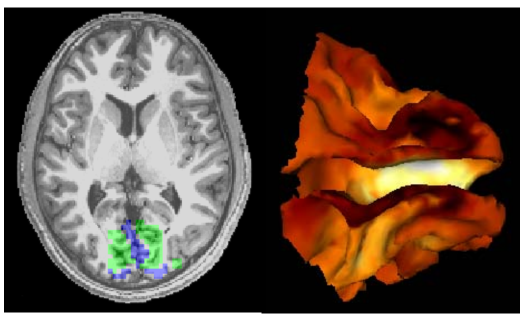
template

2 Segmentation



4 Functions in Anatomy

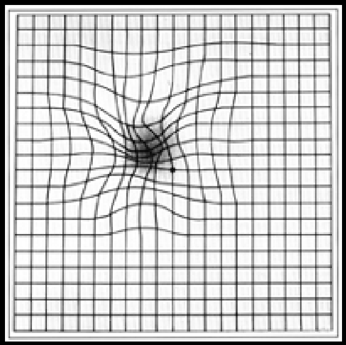
volume **surface**



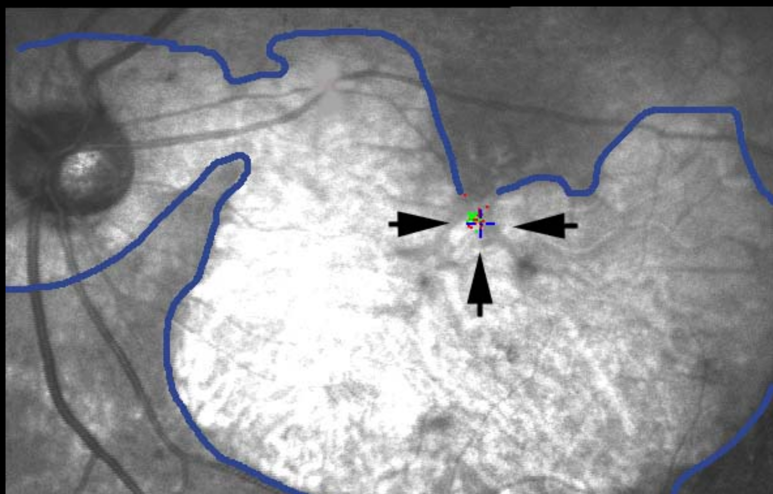
Retinotopic Mapping in Human Primary Visual Cortex

(JHU: Yantis)

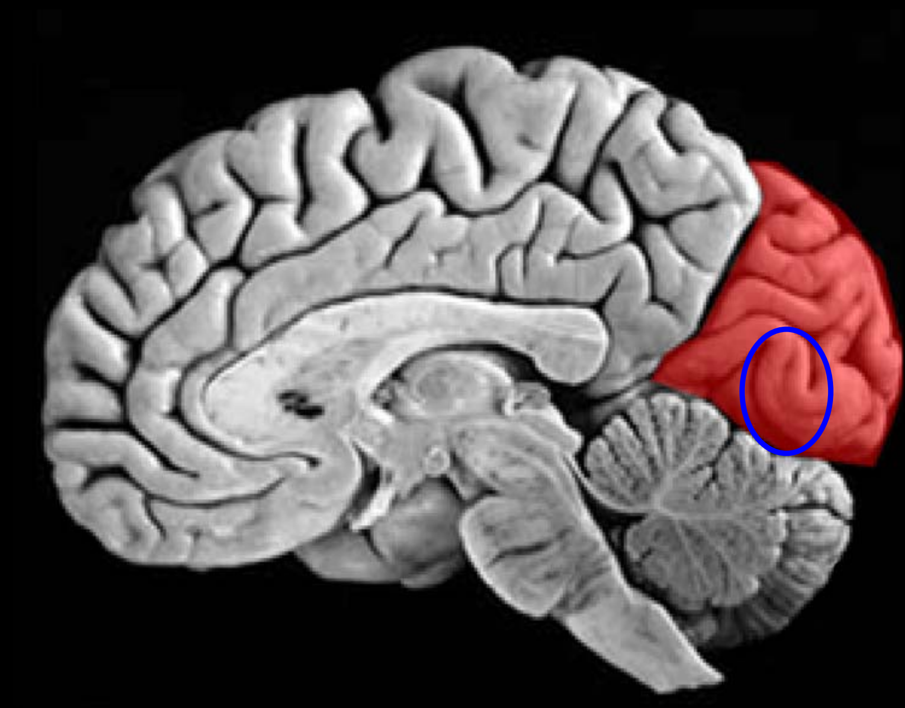
Age-Related Macular Degeneration;



Visual Cortex Reorganization?



Retinal Scotoma due to Age-Related Macular Degeneration: This image was taken by Dr. Janet Sunness with a **scanning laser ophthalmoscope** at the Wilmer Eye Institute, Johns Hopkins University School of Medicine. Arrows point to the fovea, and the outlined area indicates damaged retina.

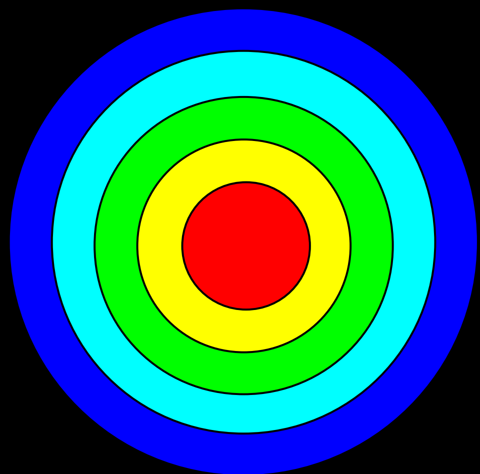


Retinal Lesion Projection Zones

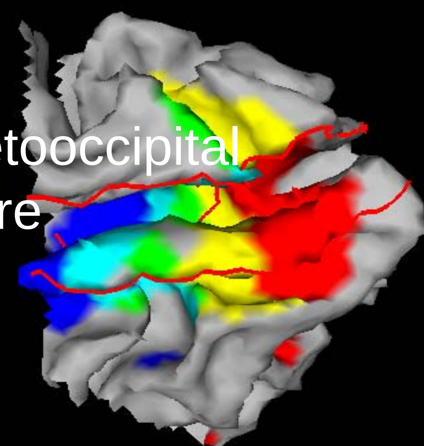
Retinotopic Mapping

- **Retinotopic Eccentricity Mapping**

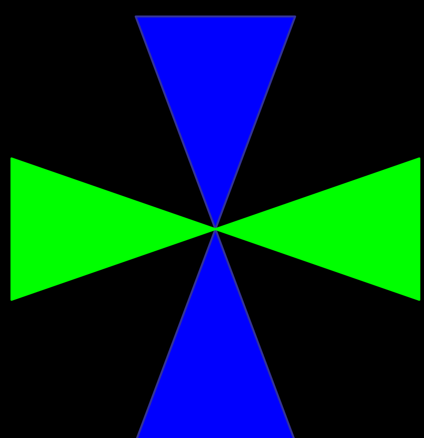
Visual Field

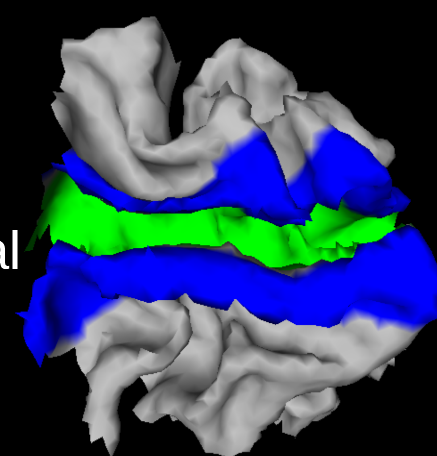


Visual Cortex



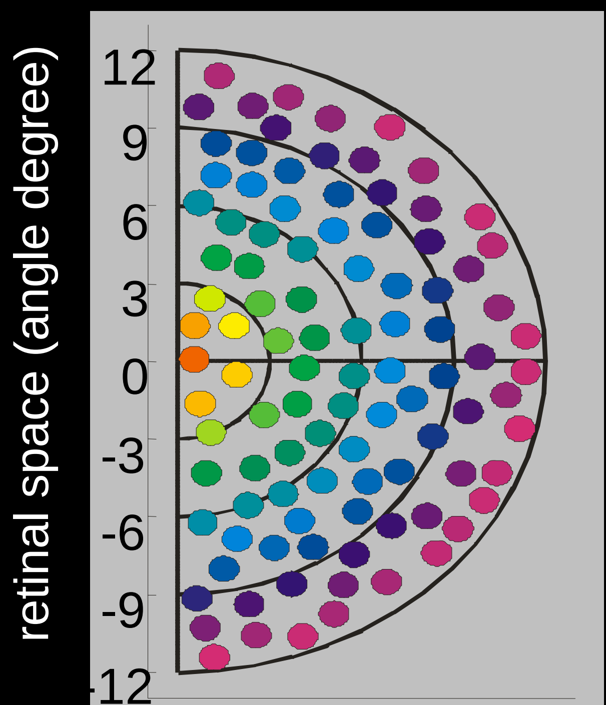
- **Retinotopic Polar Angle Mapping**



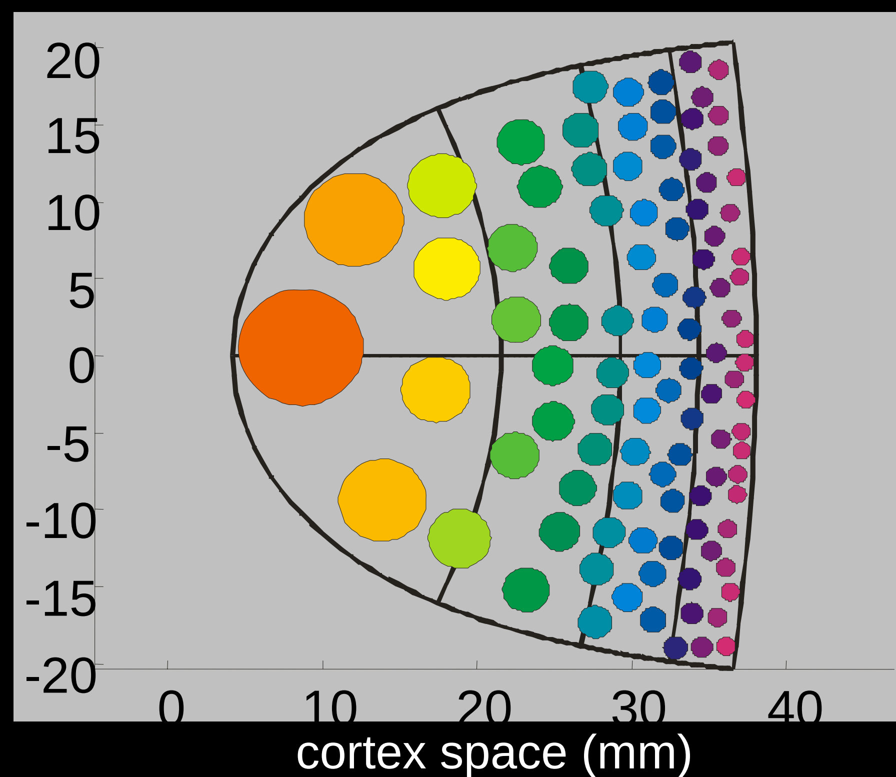


Linear Cortical Magnification

Retinal Area

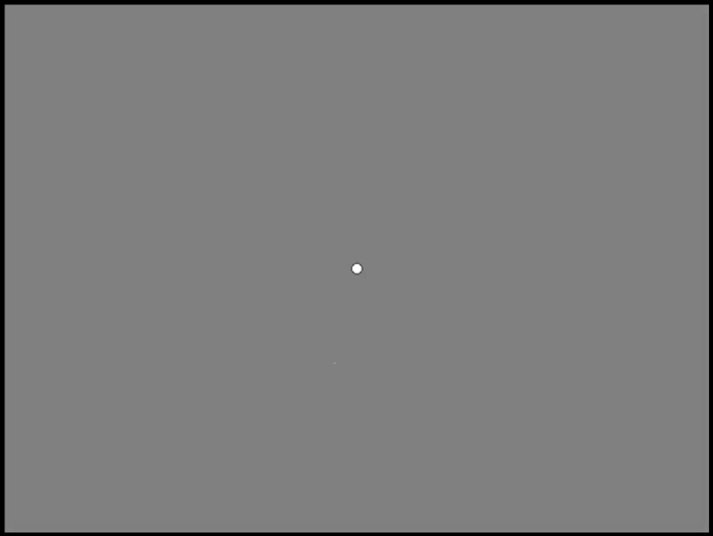


Cortical Area

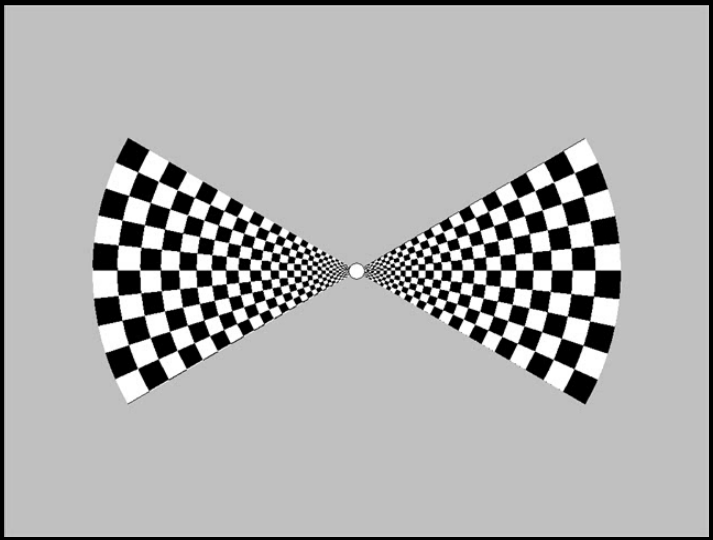


Experimental Design

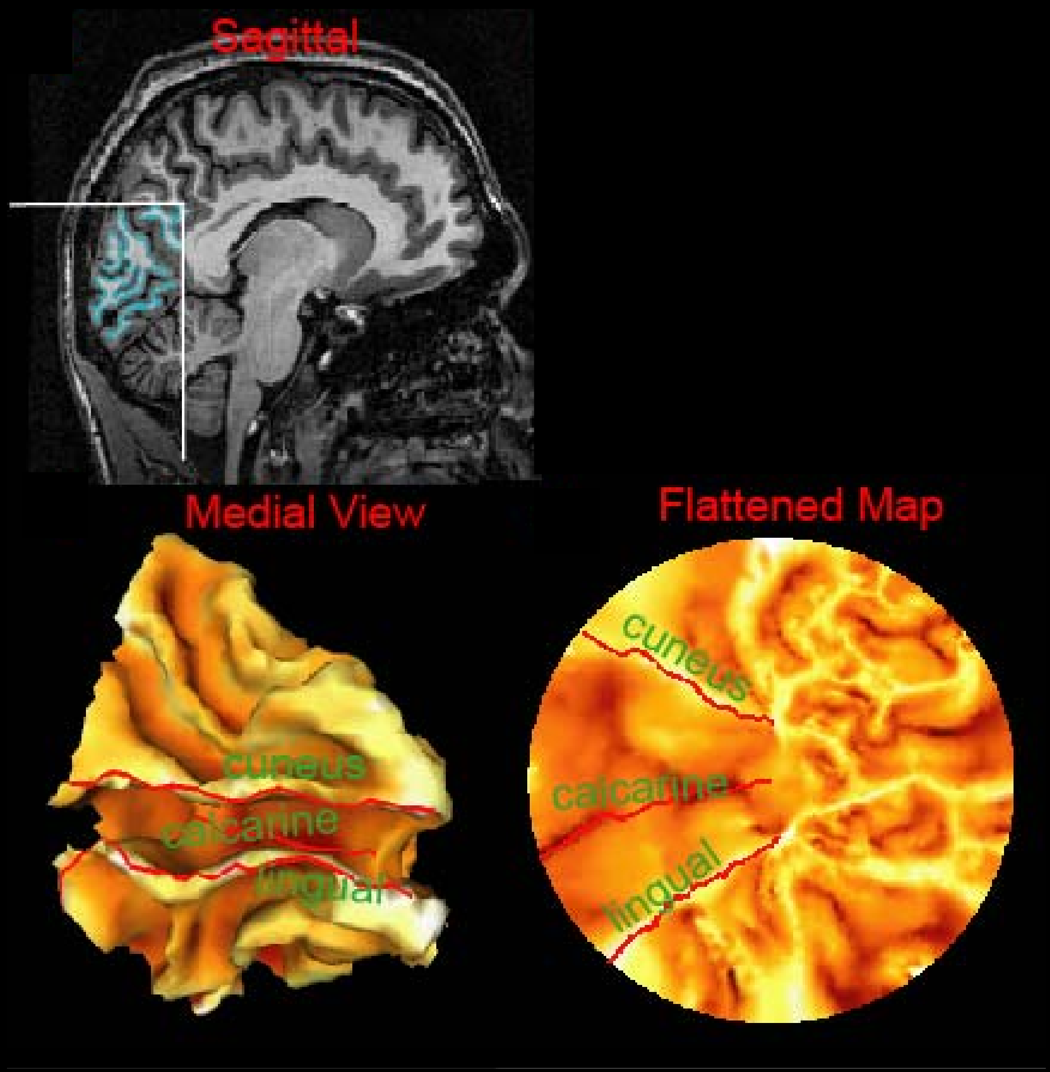
Stationary Contrast-Reversing Rings



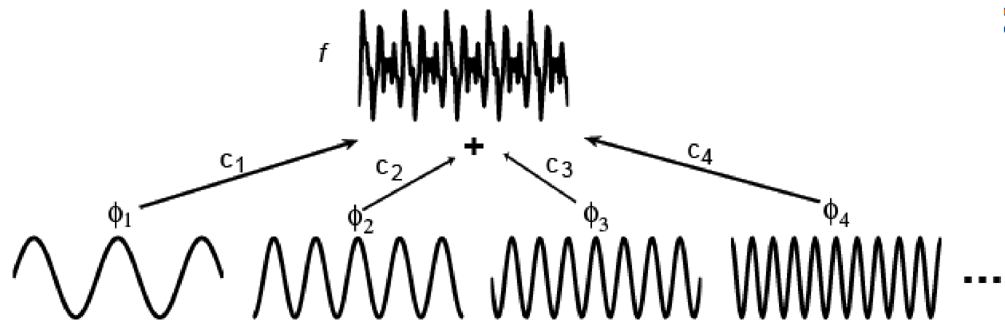
Polar Wedge Stimuli:



Anatomical MRI Analysis



Spatial Smoothing fMRI in Neocortex

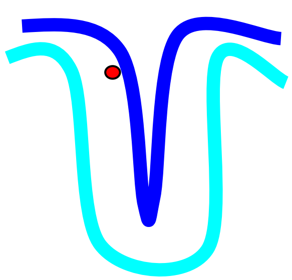


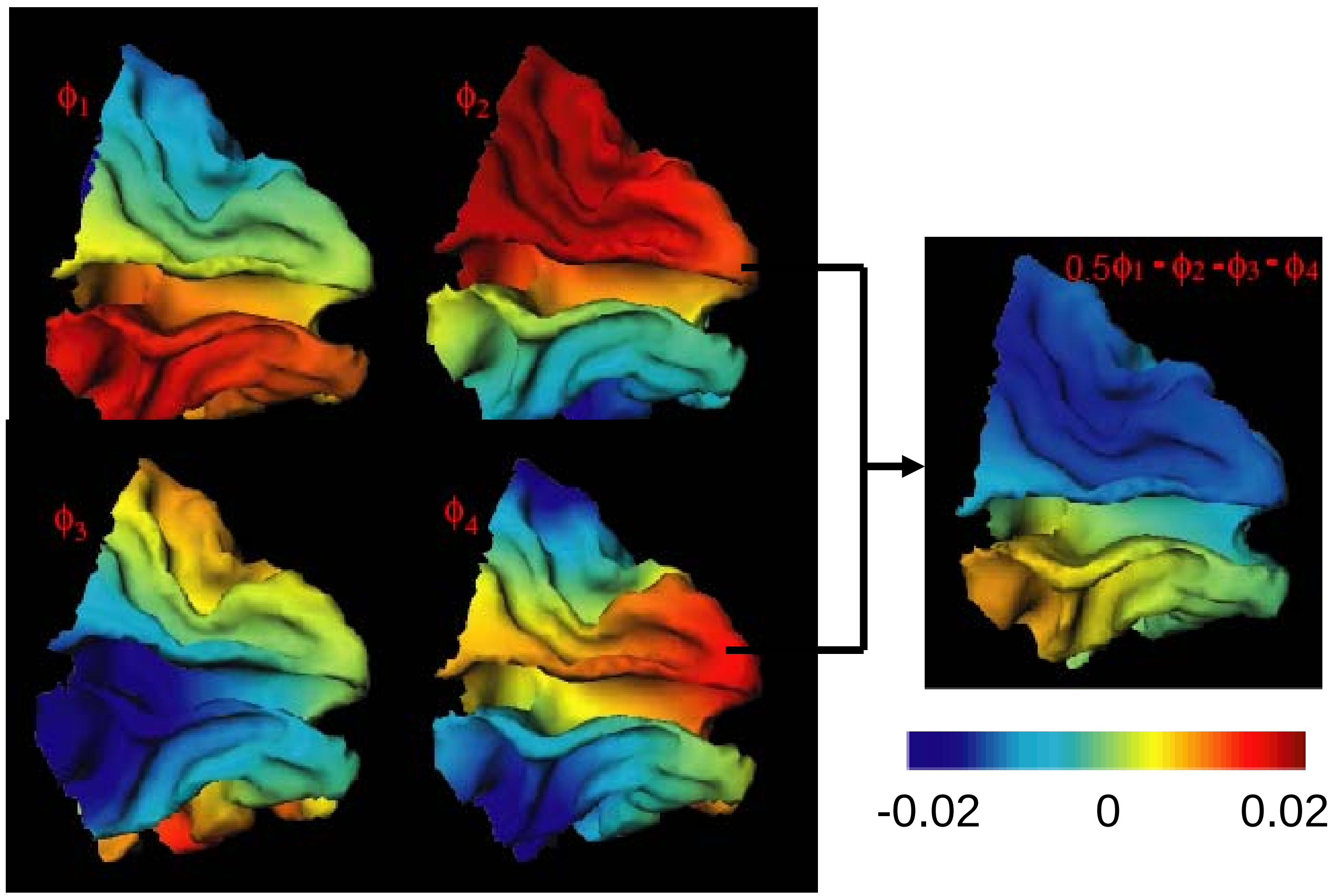
Laplace-Beltrami Bases:

$$\Delta\psi(u) + \lambda\psi(u) = 0 \text{ in } M,$$

$$\int_M |\psi(u)|^2 dM = 1,$$

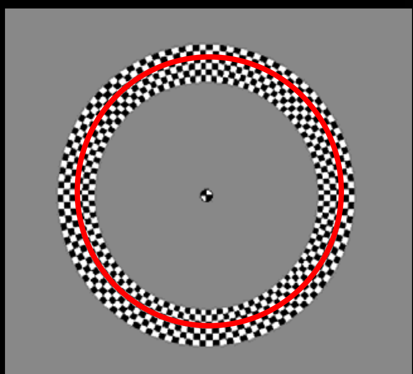
$$\left\langle \nabla \psi(u), \vec{n} \right\rangle \Big|_{\partial M} = 0.$$

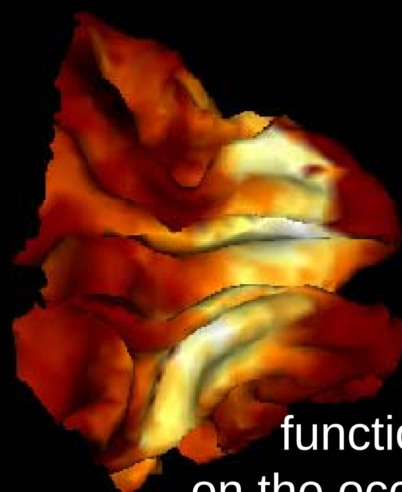


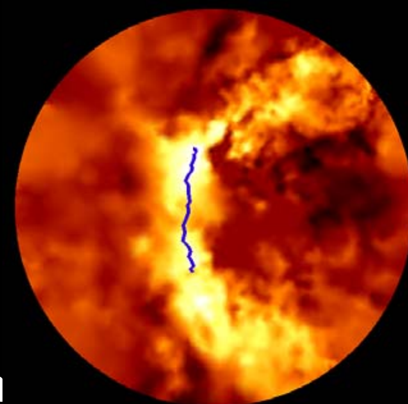


Cortical Function and Structure: Primary Visual Cortex Retinotopic Mapping

ring stimulus

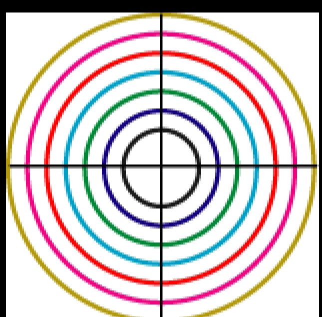


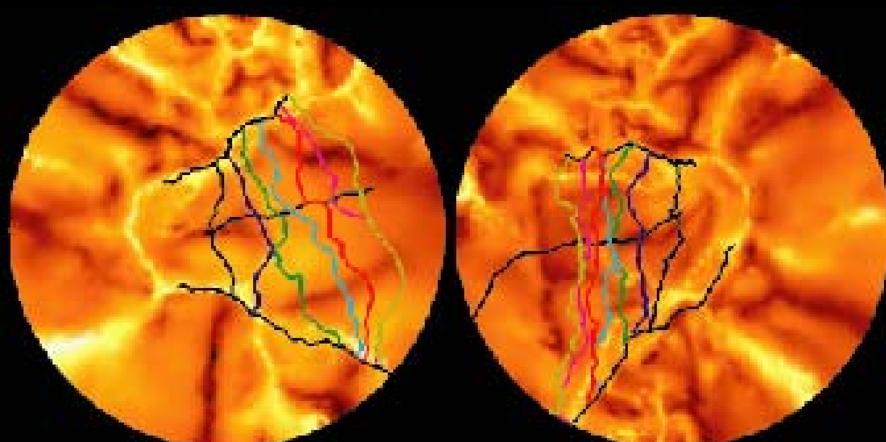




function
on the occipital surface

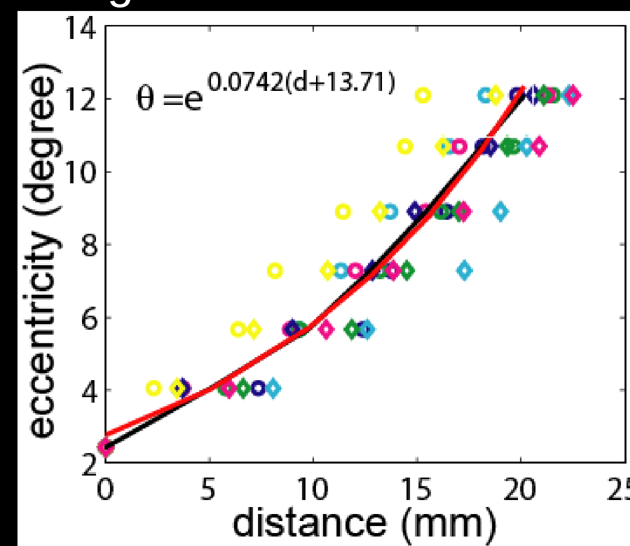
retinotopic stimuli



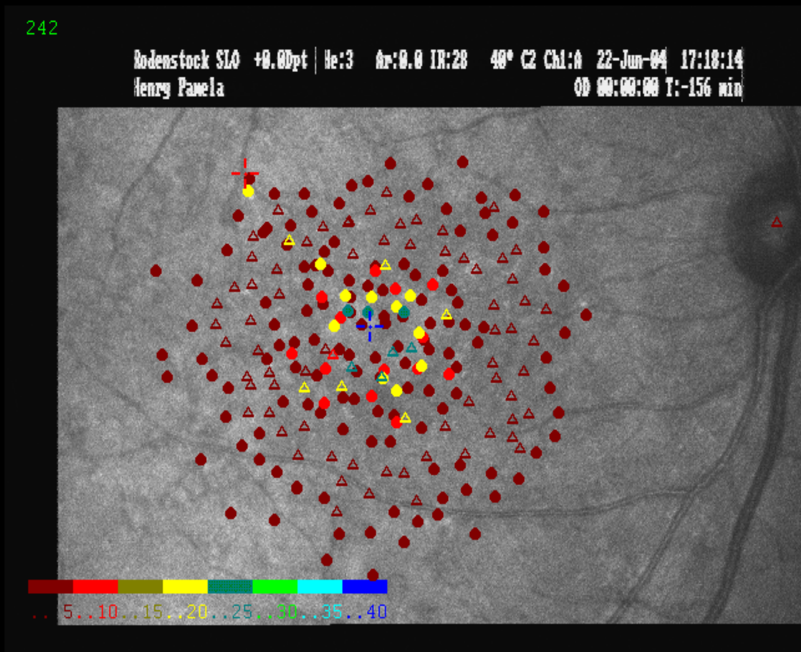


retinotopic maps in the
primary visual cortex

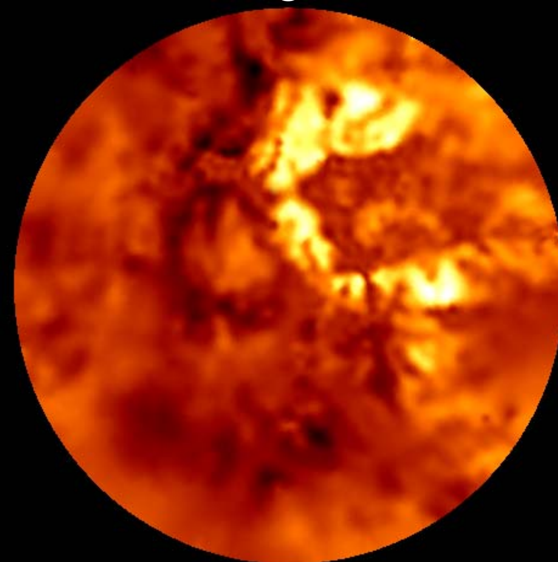
linear cortical
magnification estimation



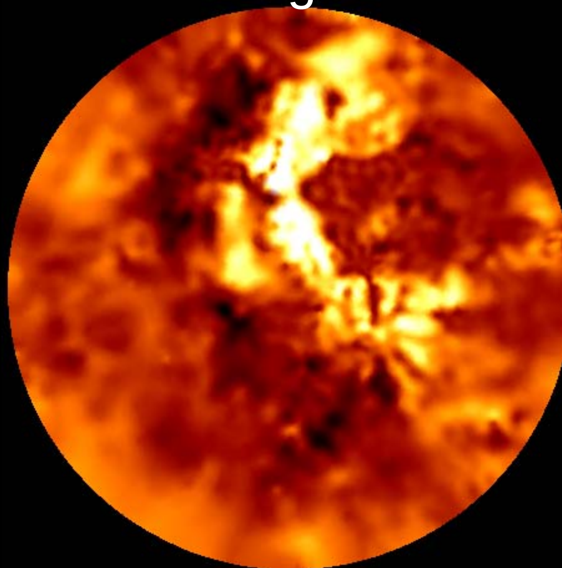
Patient Example



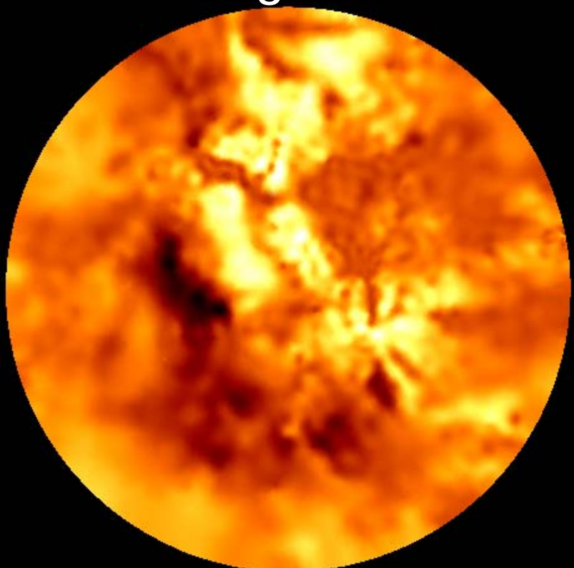
ring 1



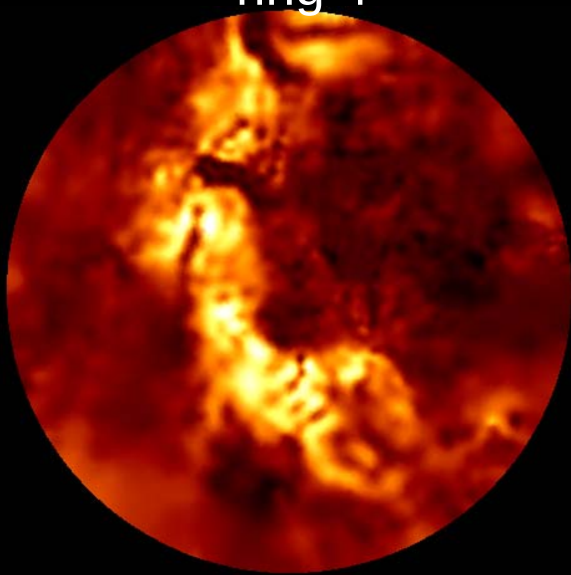
ring 2



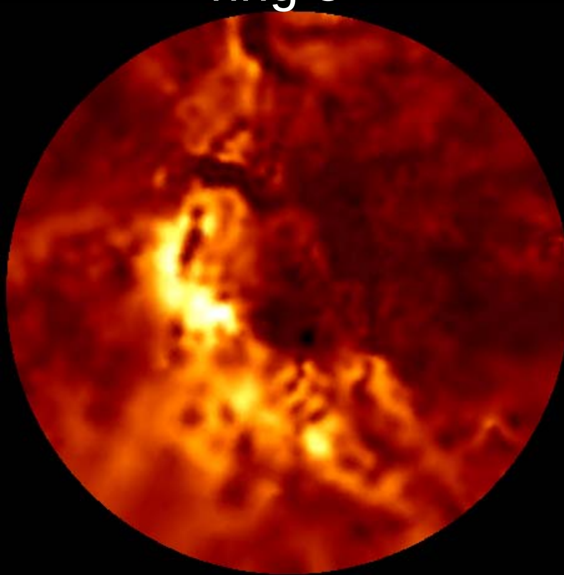
ring 3



ring 4

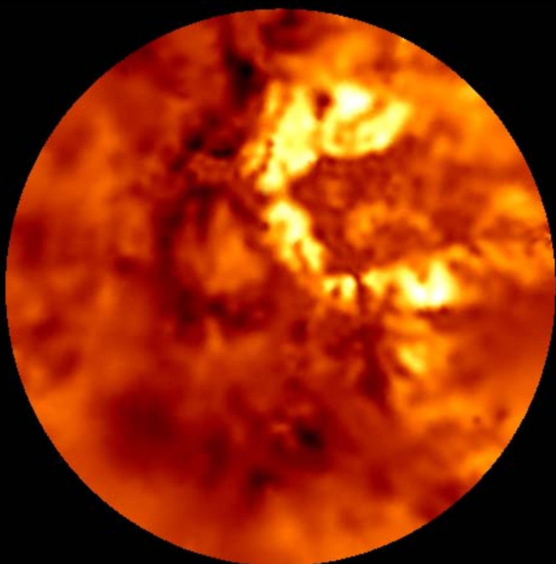


ring 5

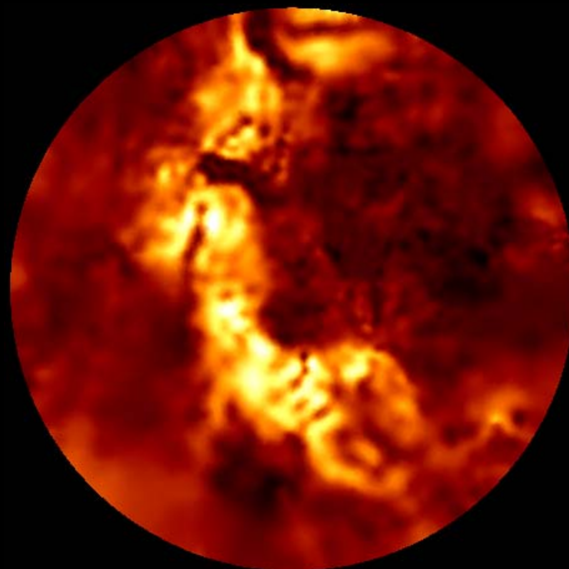


Patient Example

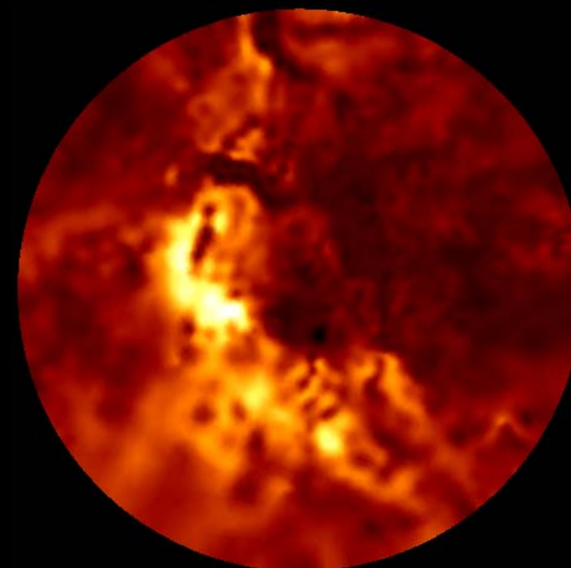
ring 1

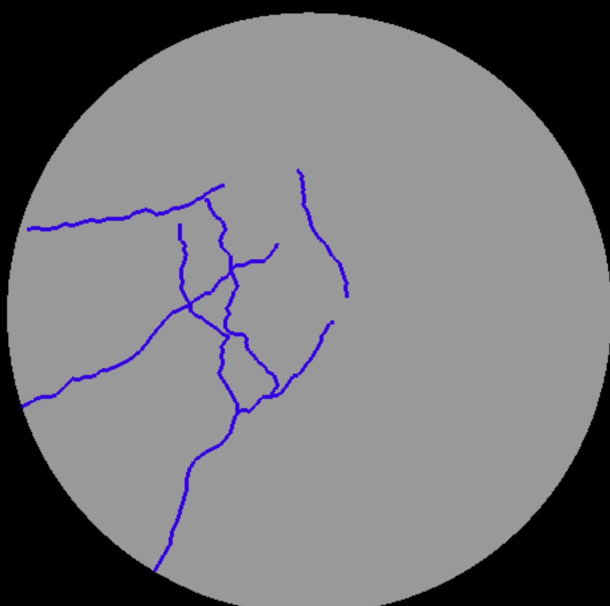


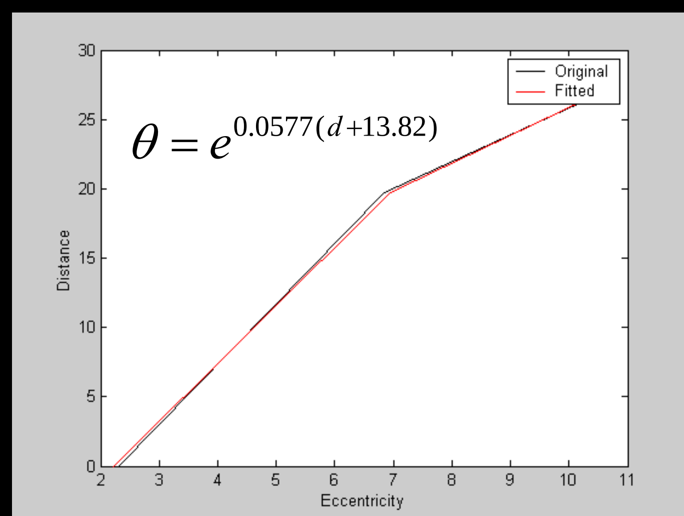
ring 4



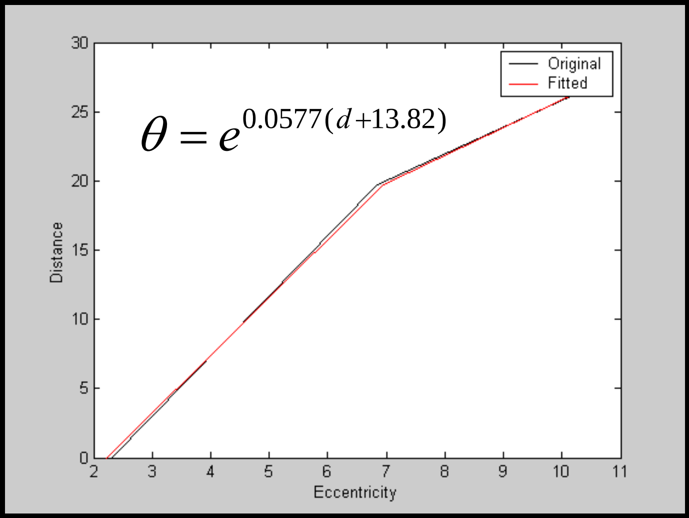
ring 5

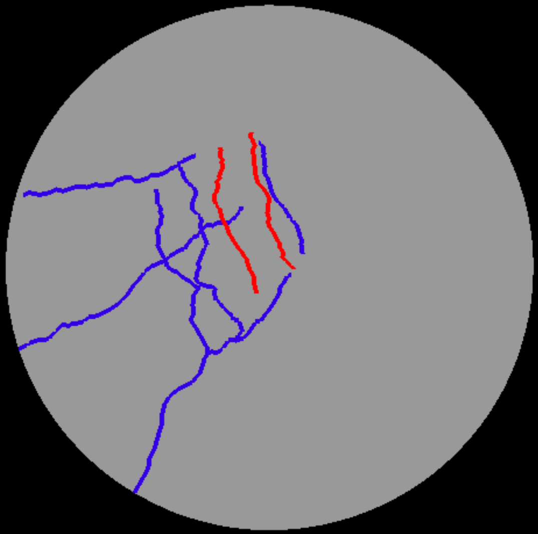




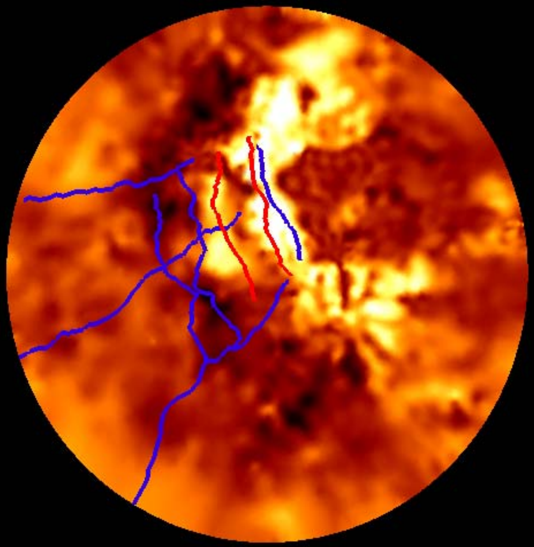


Patient Example

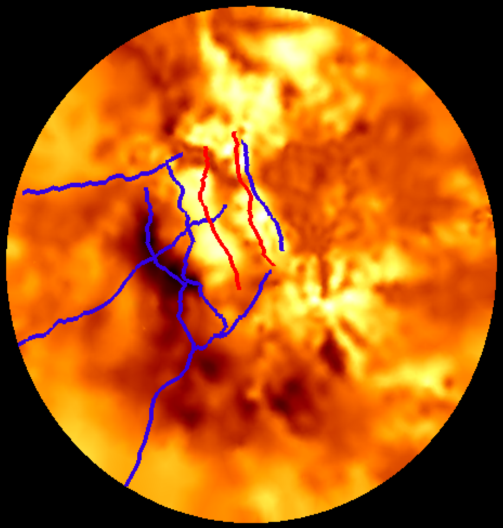




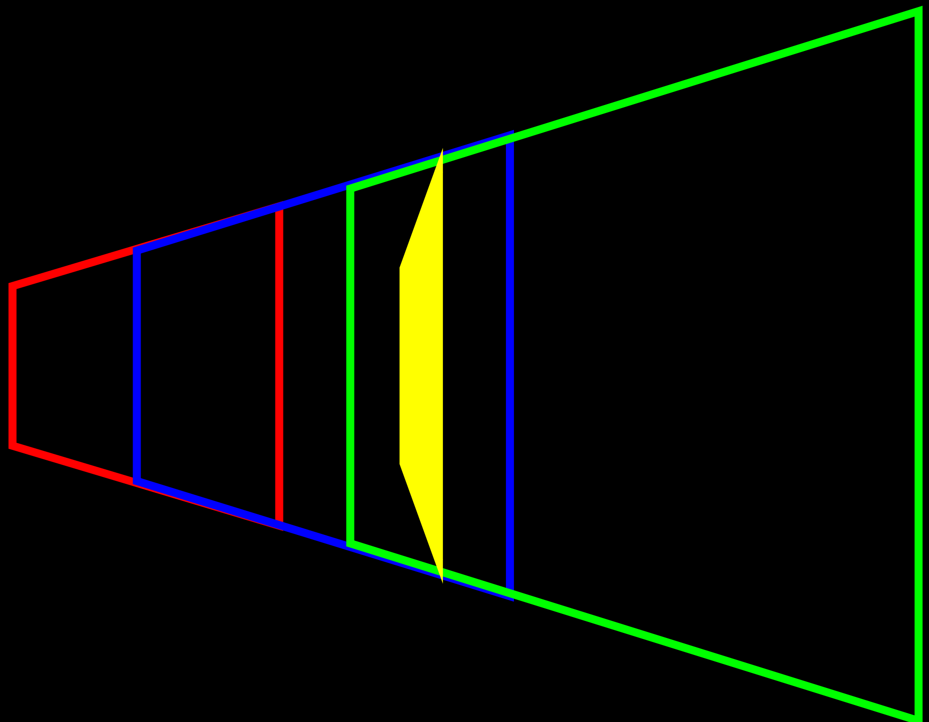
ring 2
d2 = 4.62 mm



ring 3
d3=13.89mm



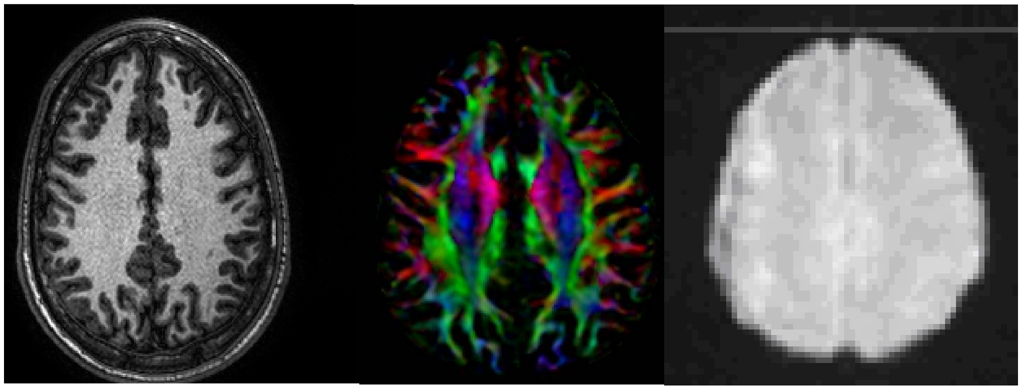
Patient Example



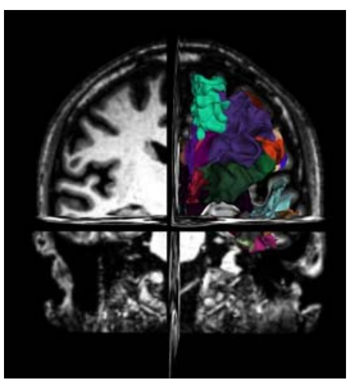
Computational Functional Anatomy (CFA) is the mathematical study of anatomical configurations and signals associated with anatomy and functions in anatomical coordinates.

1 MultiModal Images

MRI DTI fMRI



2 Segmentation

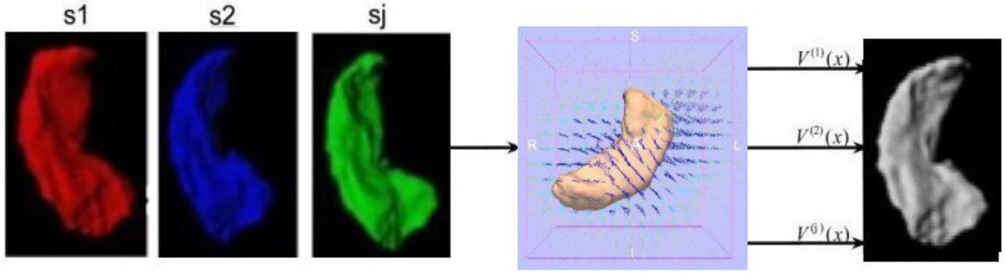


3 LDDMM Shape Analysis

LDDMM Variational Problem

$$\int_0^1 \|v_t\|^2 dt \quad \varphi . I_{temp} = I_{target}$$

s1 s2 sj



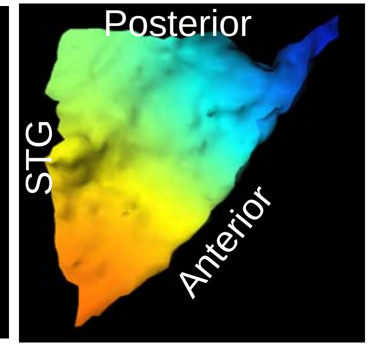
shape population

template

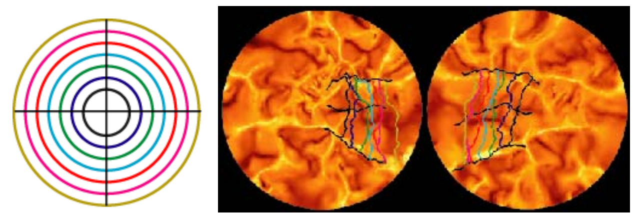
5 Statistical Analysis

shape in AD

thickness in SCZ

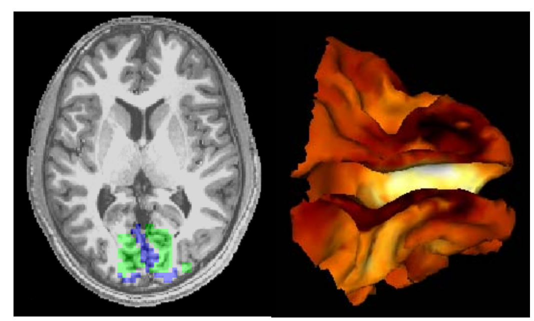


retinotopic mapping



4 Functions in Anatomy

volume surface



Acknowledgments:

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J. Tilak Ratnanather	Michael P. Harms	Way Cherng Chen
Patrick Barta		Ying Sun
Steven Yantis		
et. al. ….		

Thank you!

http://www.bioeng.nus.edu.sg/cfa/

bieqa@nus.edu.sg