"Shaping up: Shape Analysis driven by Biomedical Applications: Past and Future

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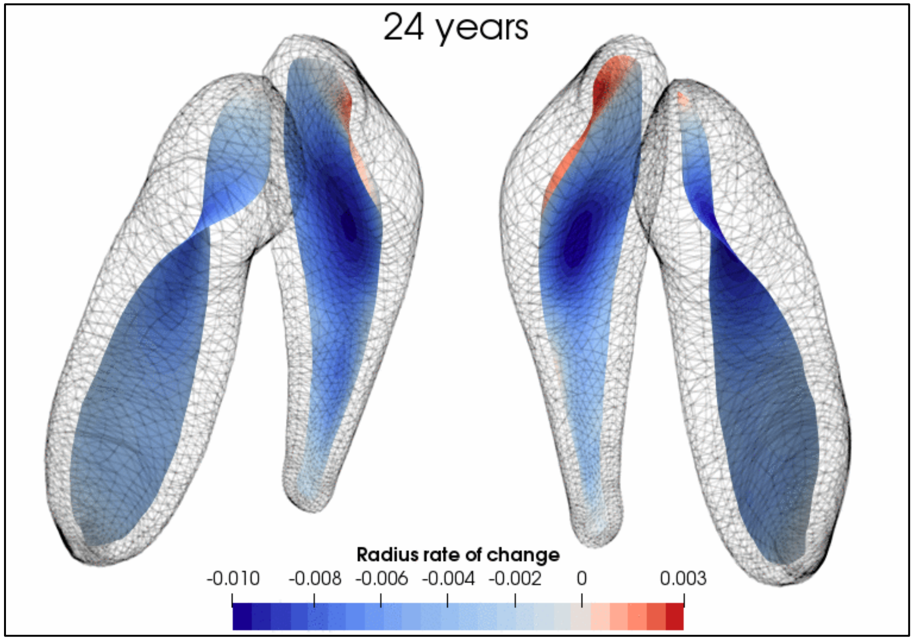


Please see links to slides and videos of long lectures on next slide.

This talk is a short & updated version of two long lectures given at the MISS 2014 Summer School

Medical Imaging Summer School 2014

28 July - 1Aug 2014 Favignana, Sicily

Medical Imaging meets Computer Vision

Programme and Slides:
https://iplab.dmi.unict.it/miss14/programme.html

Guido Gerig (slides)
Shaping up! Introduction into Shape Analysis

Xavier Pennec (slides)
Geometric Structures for Statistics on Shapes and Deformations in Computational Anatomy
Guido Gerig (slides)
Quantification of Object Dynamics by Spatiotemporal Shape Analysis

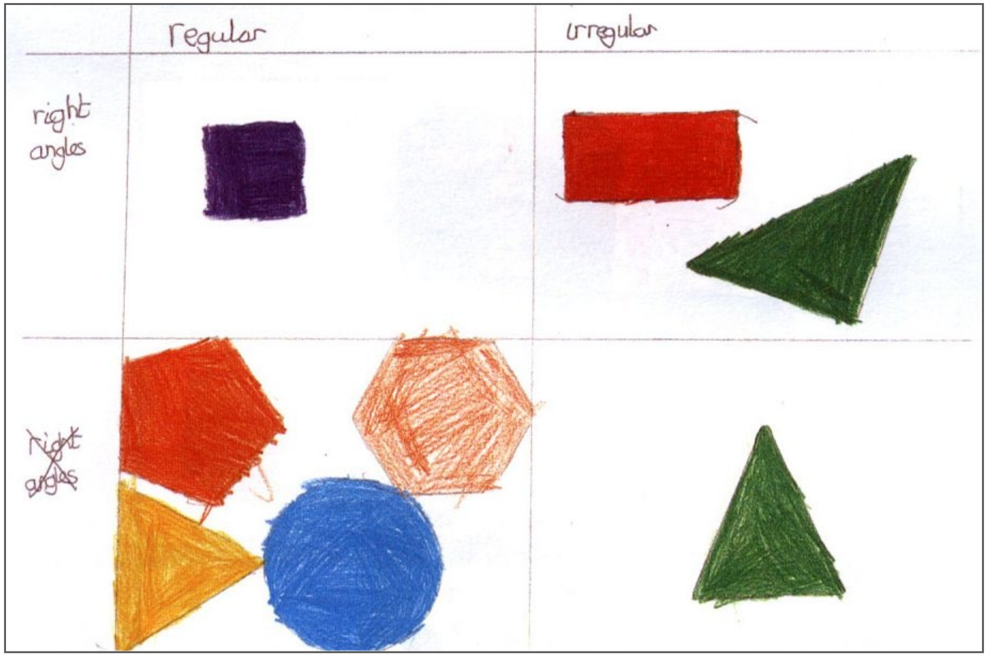
Video Lectures:
https://iplab.dmi.unict.it/miss14/speakers&Syllabus.htm
Link to VIDEO LECTURES

Contents

- Abridged History of Shape Analysis
  - Kendall Shape Space, SSM, ASM, AAM
  - Geometry Representations: Boundary, Skeleton, Harmonics, Graph Spectra, Distance Transform, ..
  - Shape Statistics via Deformations
- Current and Future
  - Problems with Size Normalization
  - Longitudinal Shape Analysis
  - Shapes come with covariates (sex, age, diagnosis, test scores, …)

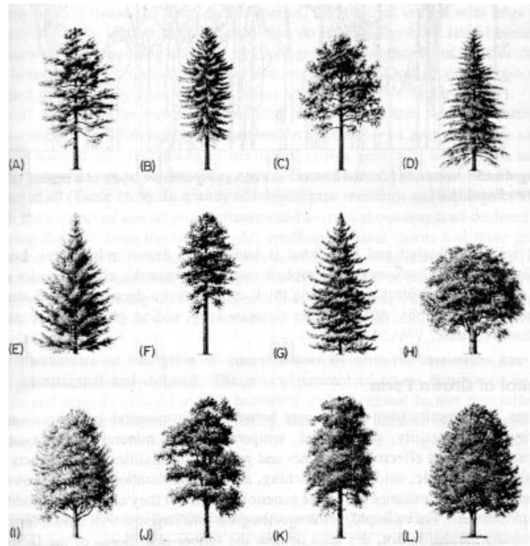
Shape

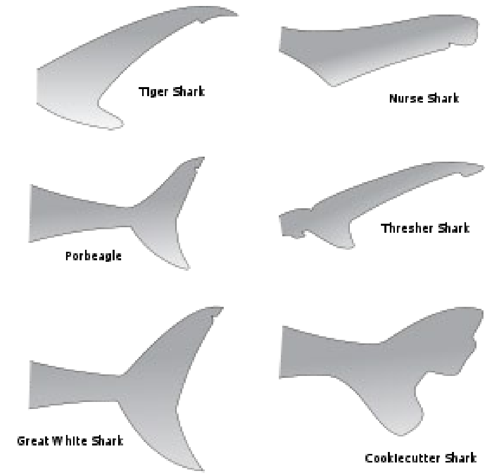
The word "shape" is commonly used in everyday language, usually referring to the geometry of an object.



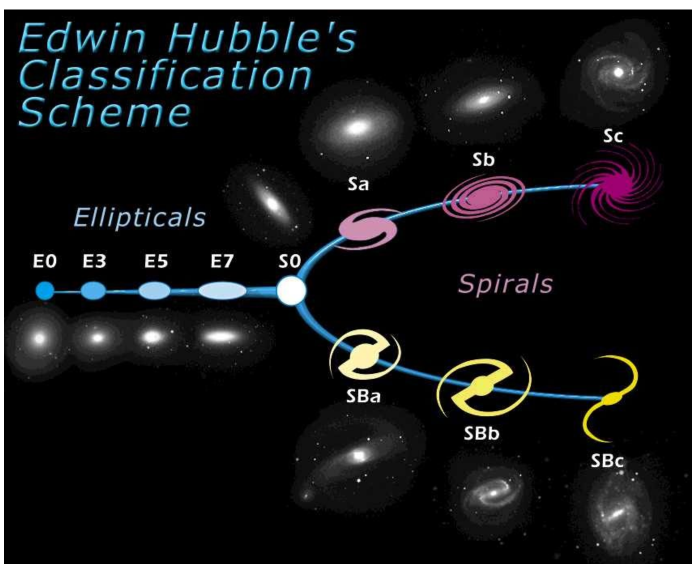
School performance test

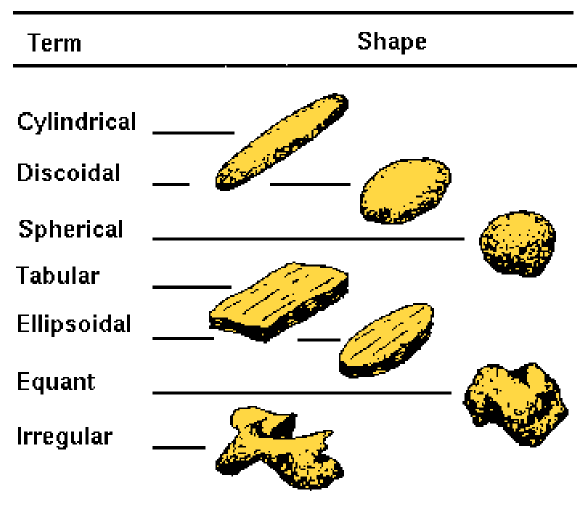
Application Domains



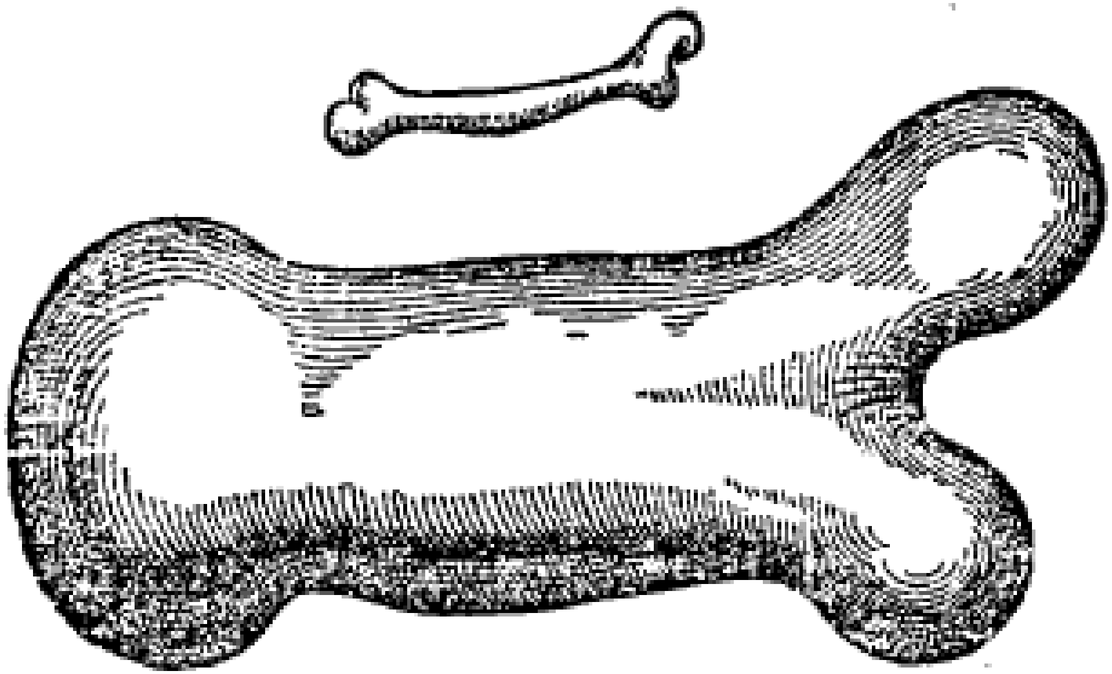


Shark Tails
The Diversity of Form and Function





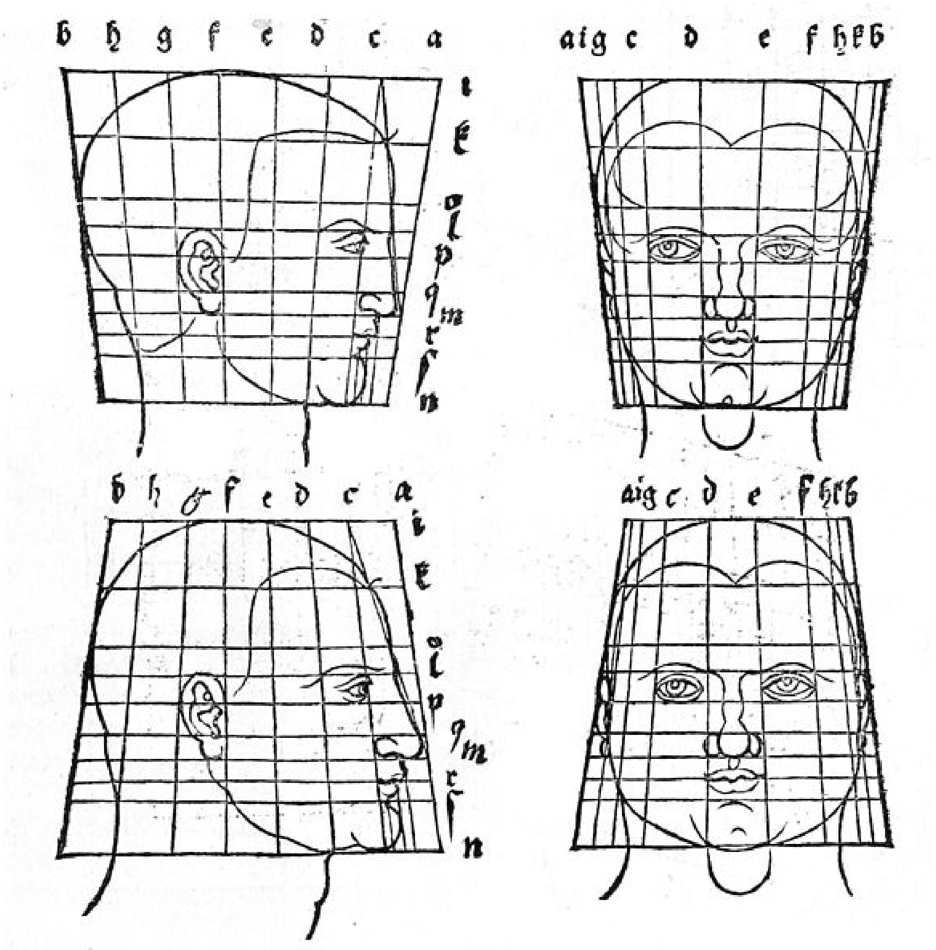
Concept of shape is not new



From Galileo (1638) illustrating the differences in shapes of the bones of small and large animals.

Even earlier…

Albrecht Dürer (1471-1528): German painter, printmaker, engraver and mathematician.



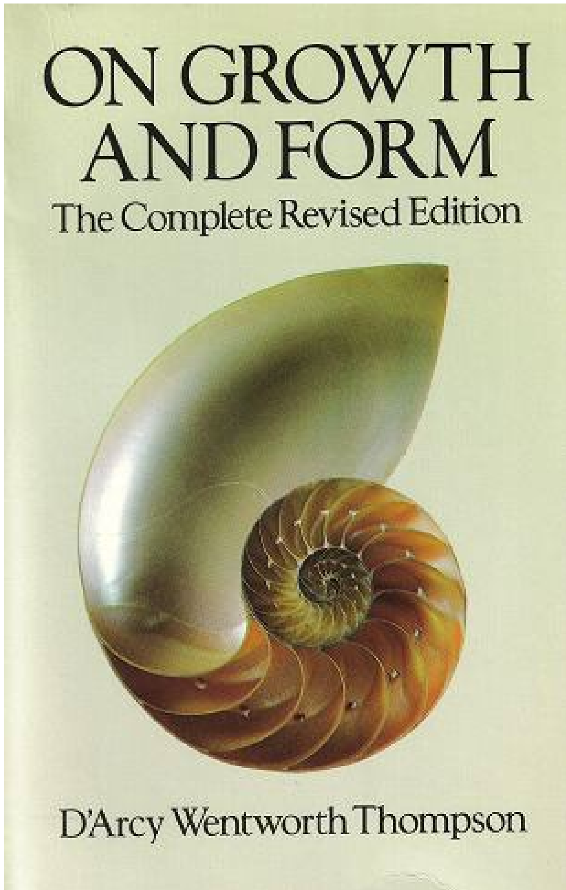
Face transformations by Albrecht Dürer

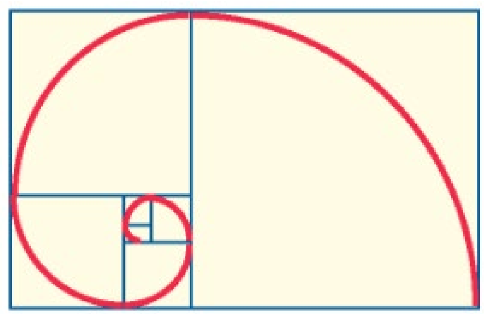
Studies of human proportions.

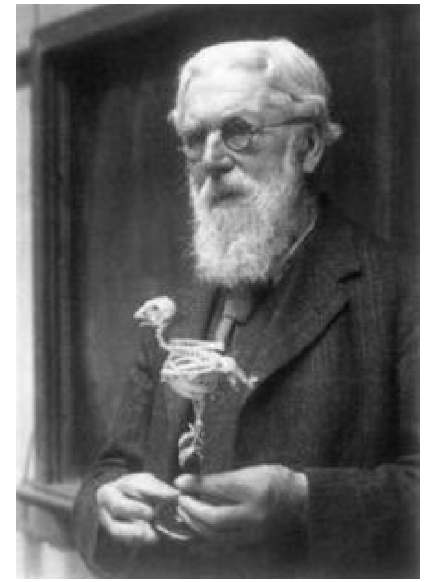
http://commons.wikimedia.org/wiki/Albrecht_Durer

http://commons.wikimedia.org/wiki/File:Durer_face_transforms.jpg

Highly Recommended Reading



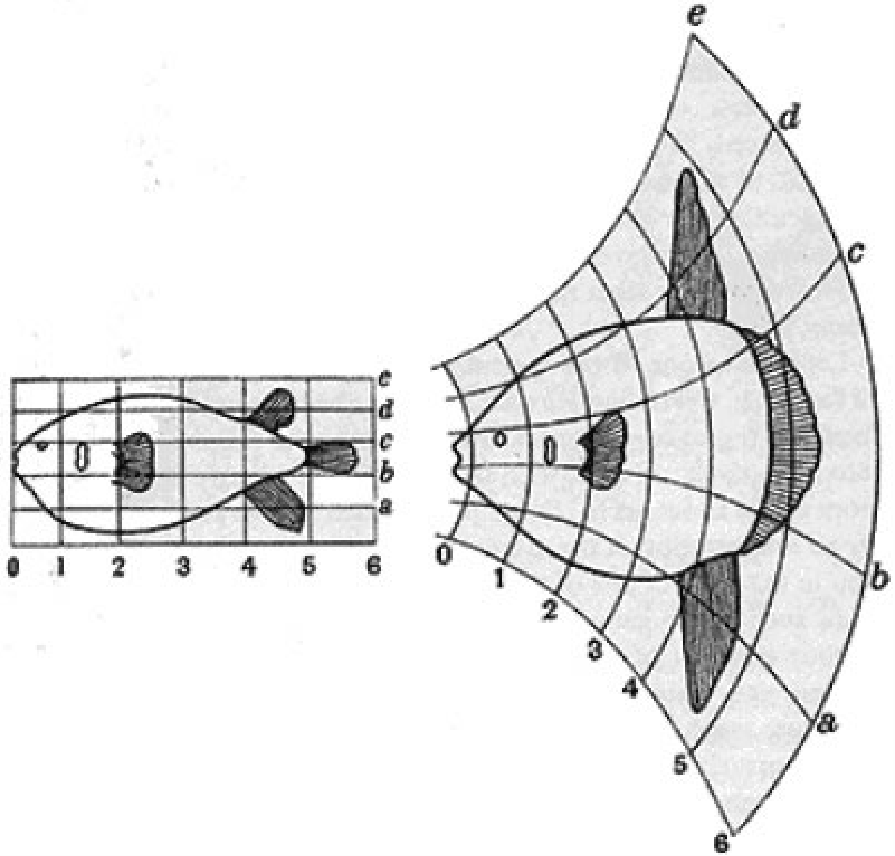


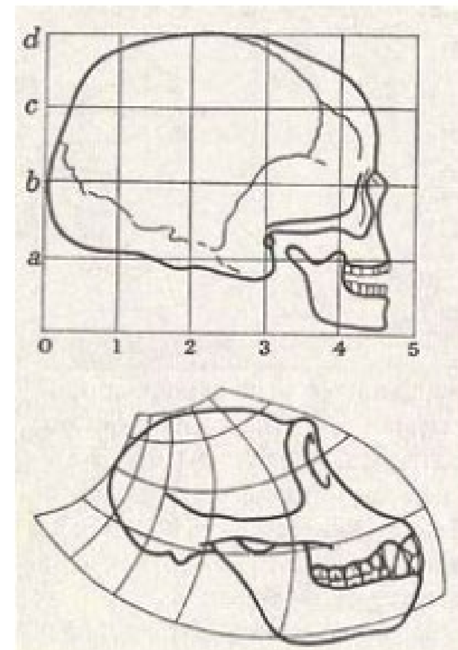


http://archive.org/download/ongrowthform00thom/ongrowthform00thom.pdf
http://ia700301.us.archive.org/10/items/ongrowthform00thom/ongrowthform00thom.pdf

D'Arcy Wentworth Thompson, On Growth and Form (1917, mathematics and biology)

Transformation Models

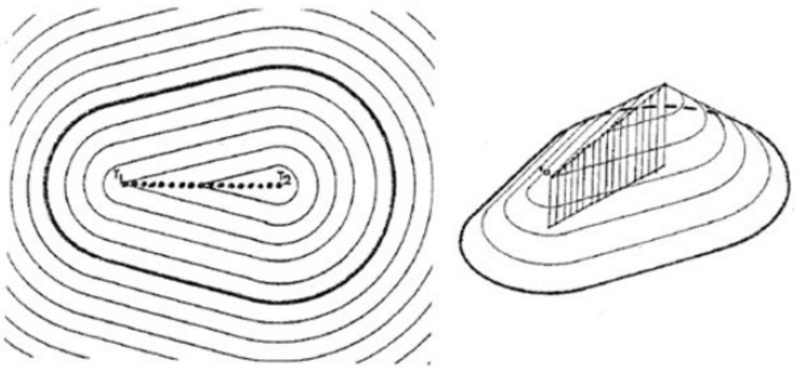


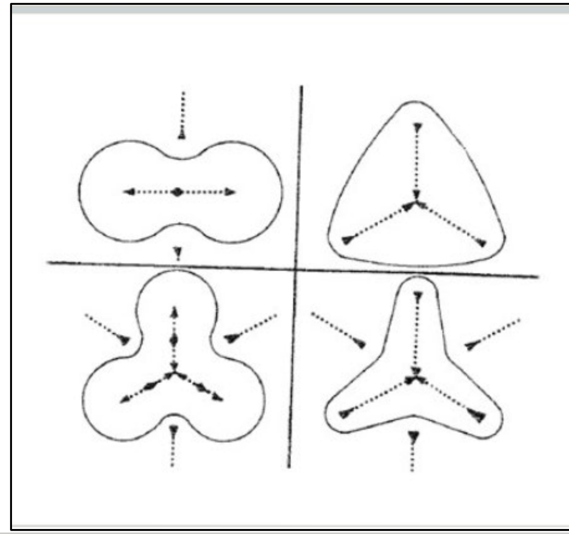


From D'Arcy Thompson, *On Growth and Form*, 1917.

Later: Bookstein's work on Thin-Plate-Splines

"A transformation for extracting new descriptors of shape", Harry Blum (1967).





An early optomechanical device for obtaining grassfire propagation using photographic defocussing.

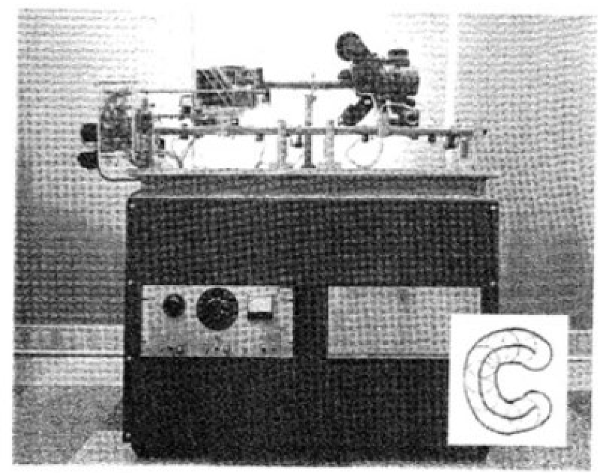
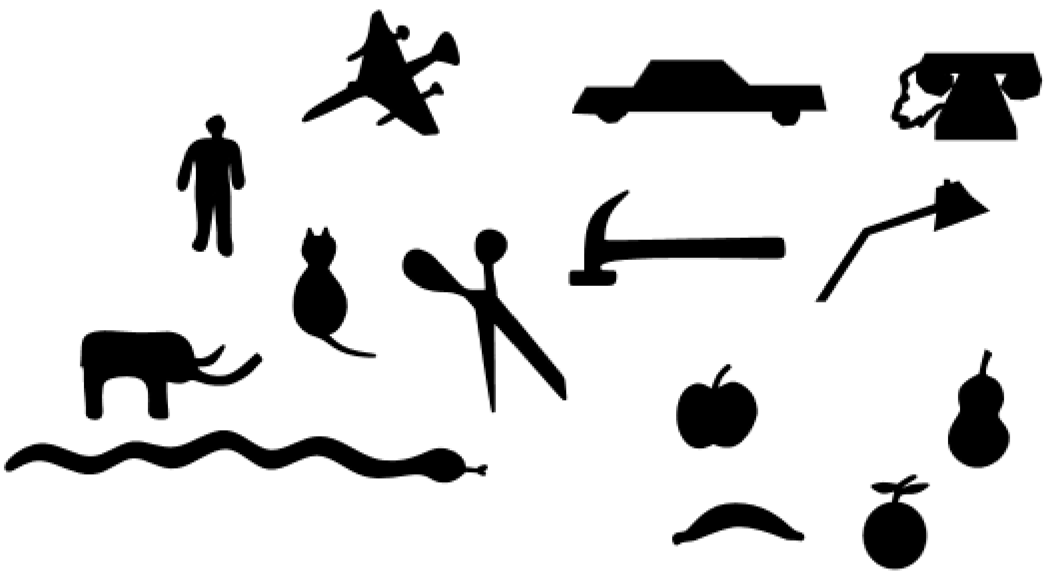


Fig. 19. An early opticomechanical device for obtaining grassfire propagation using photographic defocussing.

Harry Blum (January 30, 1924[1] – April 19, 1987) was a researcher at the National Institutes of Health,[2] known for his work in 1967 introducing the medial axis and grassfire transform of a shape,[3] and more generally for his work on shape analysis, topological skeletonization,[4] biological form, and visual perception.

Shape and Human Vision

"Our Visual world contains a vast arrangement of objects, yet we are amazingly robust in recognizing them. This includes objects projected from novel viewpoints, or partially occluded objects. We are even able to describe totally unfamiliar objects, or to recognize unexpected ones out of context."



What aspect of the geometry should be computed to allow robust recognition?

Formal Definition? Theory of Shape?

Kimia, Tannenbaum, Zucker, IJCV 1995

What is Shape?

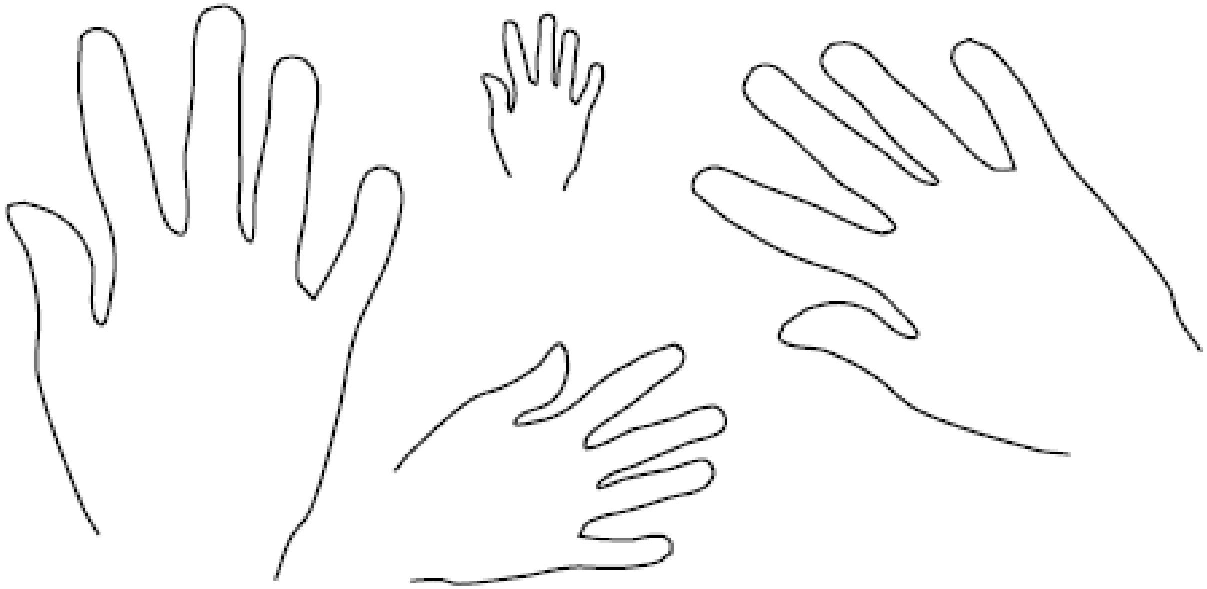
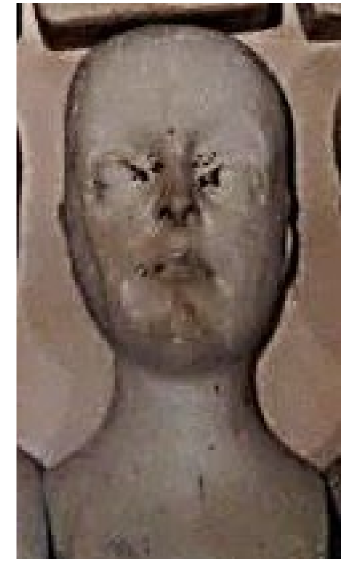


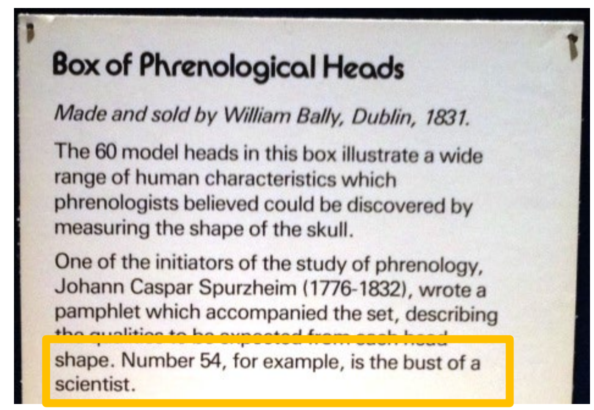
Figure 1: Four copies of the same shape, but under different Euclidean transformations.

Shape is the geometry of an object modulo position, orientation, and size.

Kendall '77, Dryden, Mardia
From: Stegmann and Gomez, [Kendall, 1977]

Shape Statistics: Variability





science museum
Brought to Life
Exploring the History of Medicine

link

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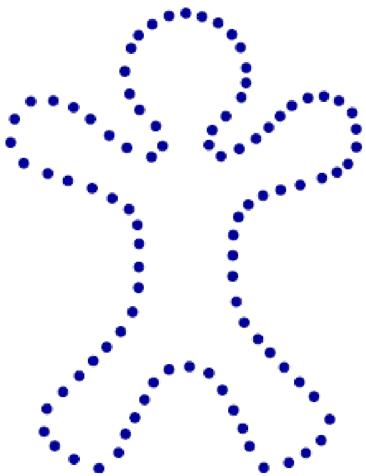
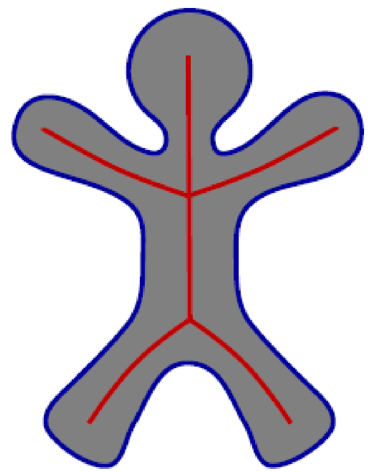
Shape Representations

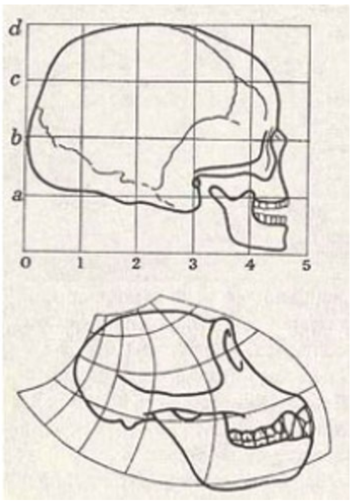


Dense Boundary Points

Continuous Boundary (Fourier, splines)

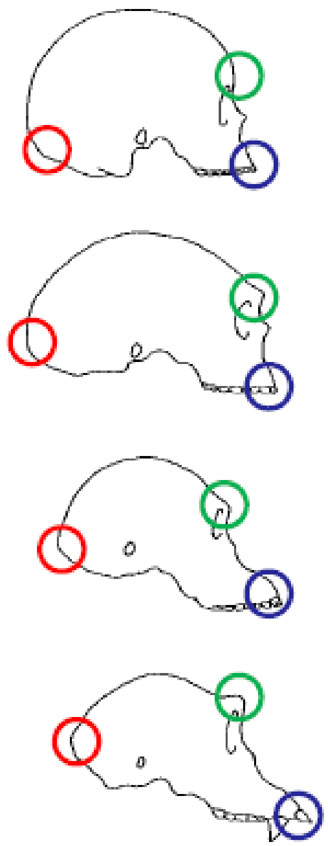


Medial Axis (solid interior)



Deformation Field

Landmark Correspondence



From C. Small, *The Statistical Theory*

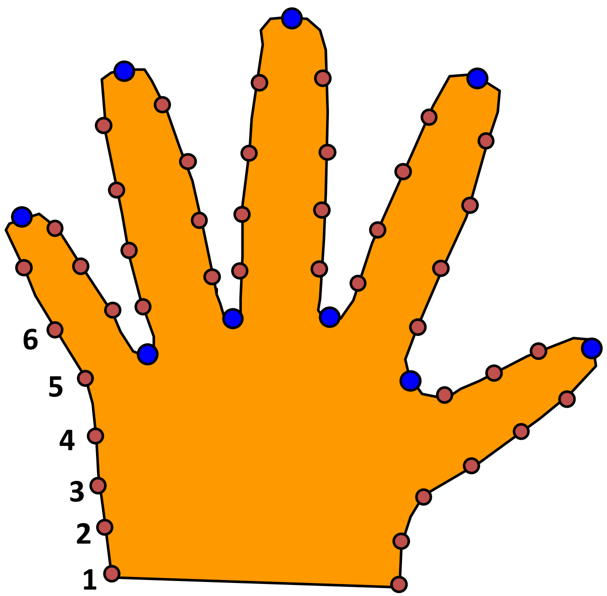
Homology:

Corresponding (homologous) features on skull images.

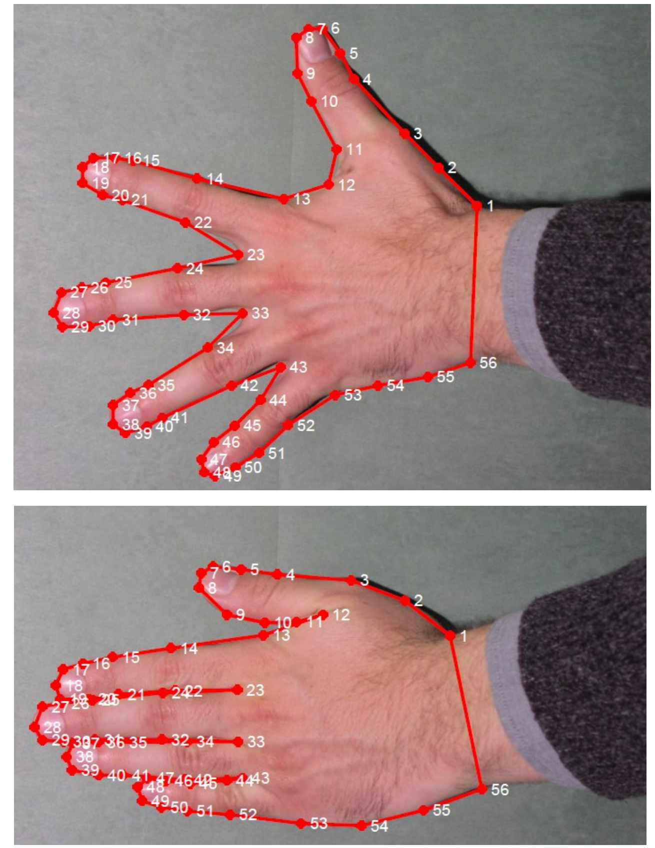
Modelling Shape

- Define each example using points
- Each (aligned) example is a vector

$$\mathbf{x}_i = \{x_{i1}, y_{i1}, x_{i2}, y_{i2} \ldots x_{in}, y_{in}\}$$



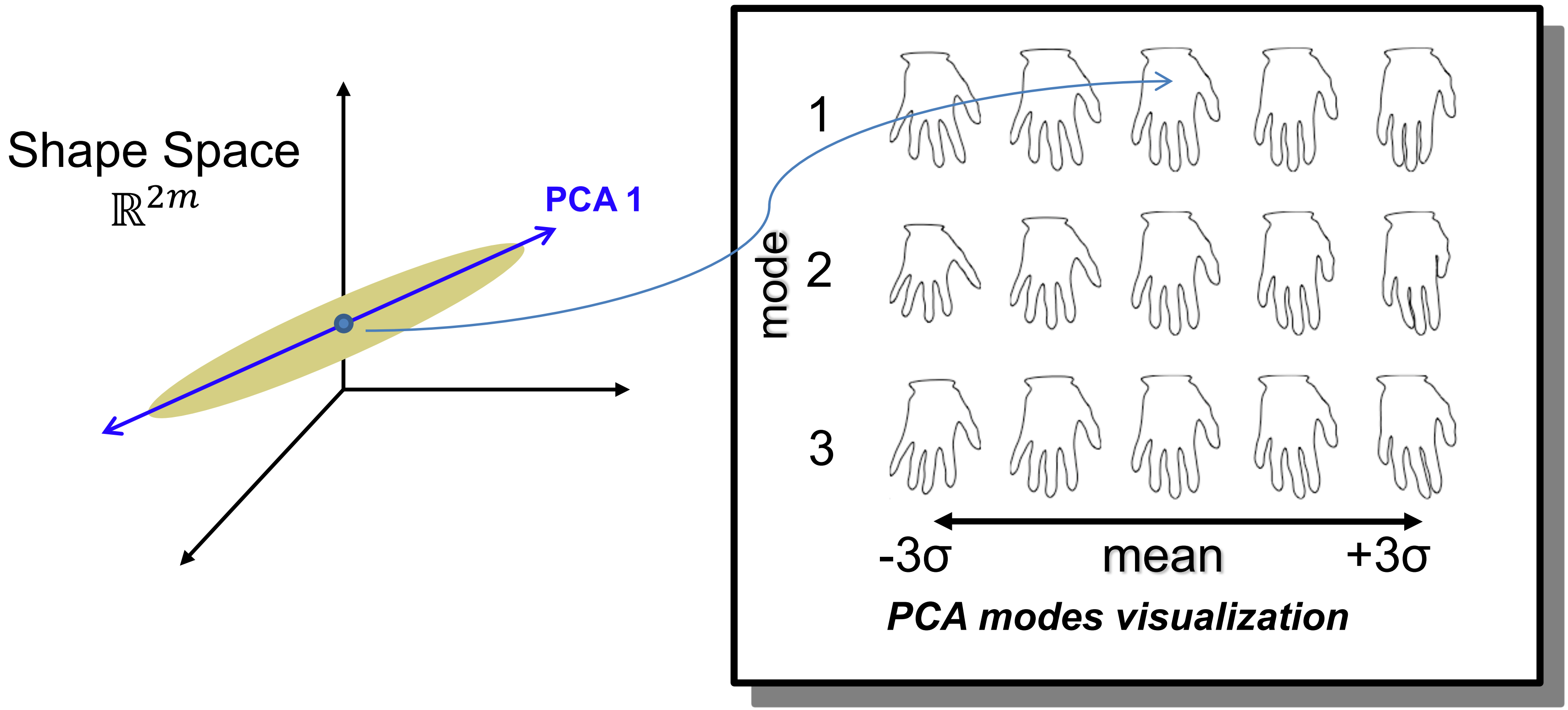
Cootes, Taylor 1993



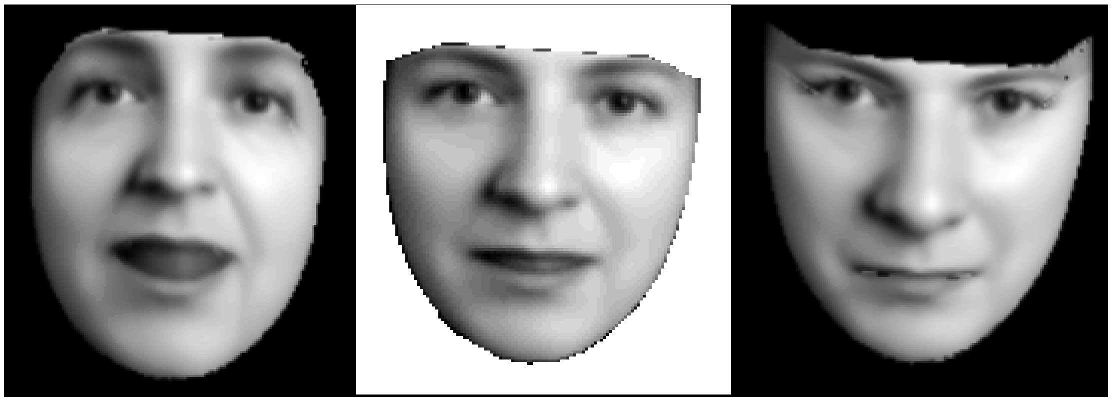
Stegmann and Gomez, 2002

Statistics in Shape Space

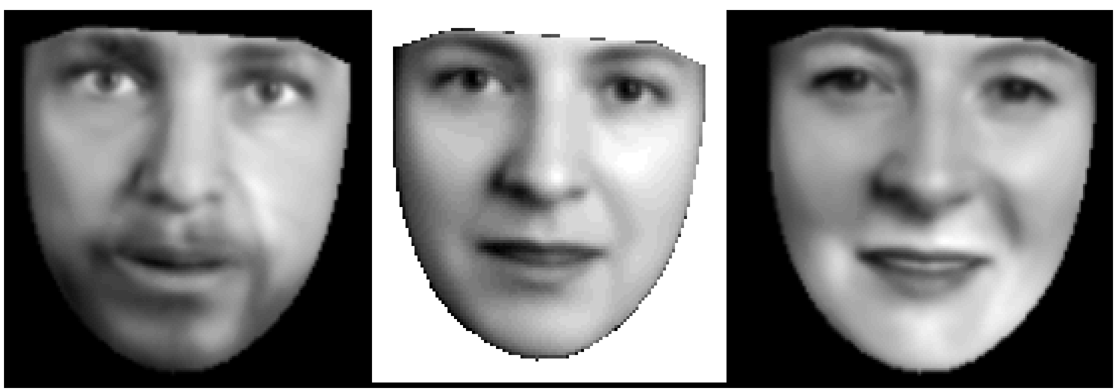
- Manual/automatic correspondences
- Gaussian models
- PCA for dimensionality reduction in shape space



Shape and Texture Modes: Active Shape and Appearance Model ASM



Shape variation (texture fixed)



Texture variation (shape fixed)

Courtesy of Chris Taylor, 1995

Eigenfaces: Sirovich & Kirby 87, Turk & Pentland 91

“Good” and “Bad” Correspondence

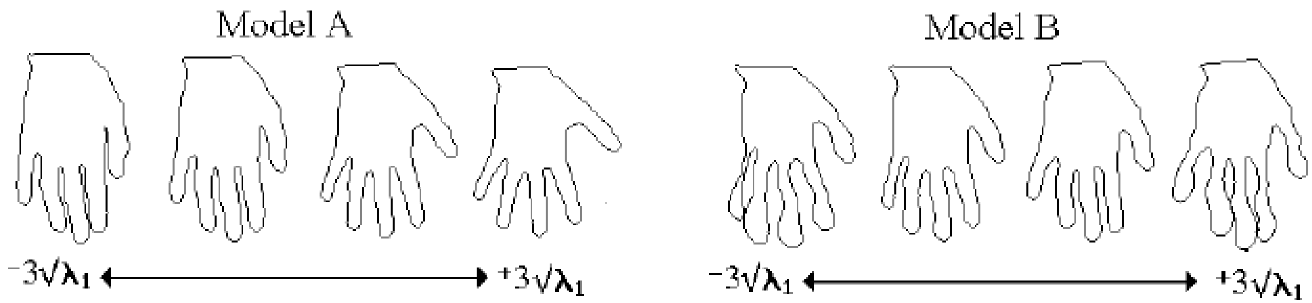
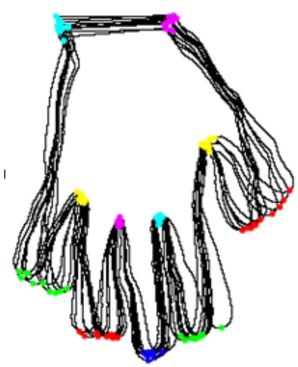


Figure 3.4. The first mode of variation of models A and B. The first parameter (b_1) is varied by $\pm 3\sqrt{\lambda_m}$.



A: Manual placement of corresponding landmarks

B: Arc-length parametrization

“Good” placement:

- R. Davis: Simplest Model has minimum stochastic complexity → Information Theory, Minimum Description Length (MDL)
- May lead to better, more compact statistical shape models.

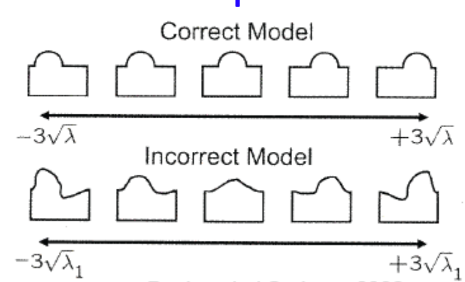
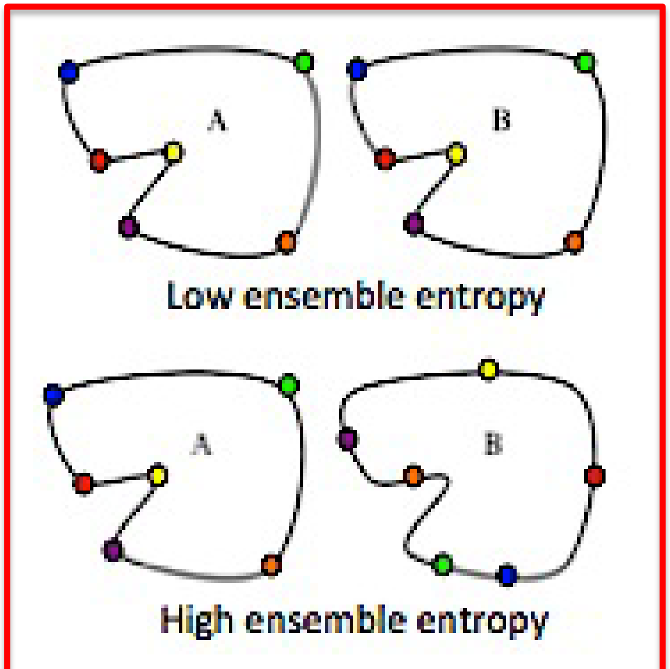


Image: Davies et al Springer 2008

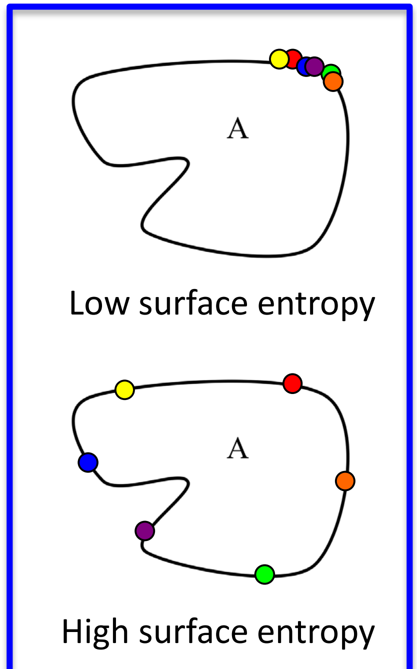
From: PhD thesis Rhodri Davies

Entropy-based Particle Systems

- Contours/Surfaces as discrete point sets, no parameterization
- Dynamic particles, positions optimize the information of the system: ensemble entropy, surface entropy

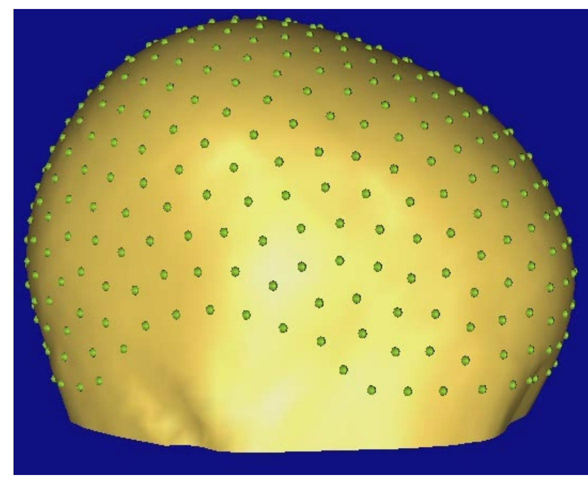


low is better



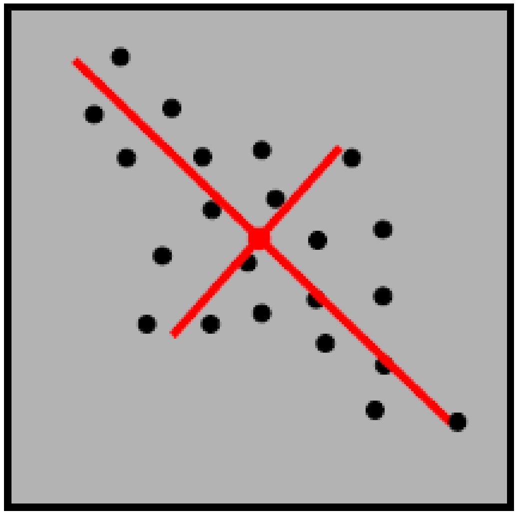
high is better

$$Q = H(Z) - \sum_k H(P^k)$$

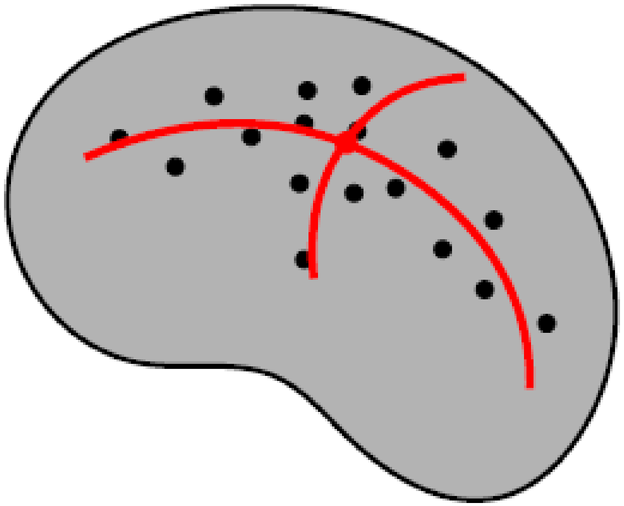


Datar, Cates, Oguz, Fletcher, Gouttard, Gerig, Whitaker, Particle-based Shape Regression, MICCAI 2009

Generalizing PCA: Principal Geodesic Analysis



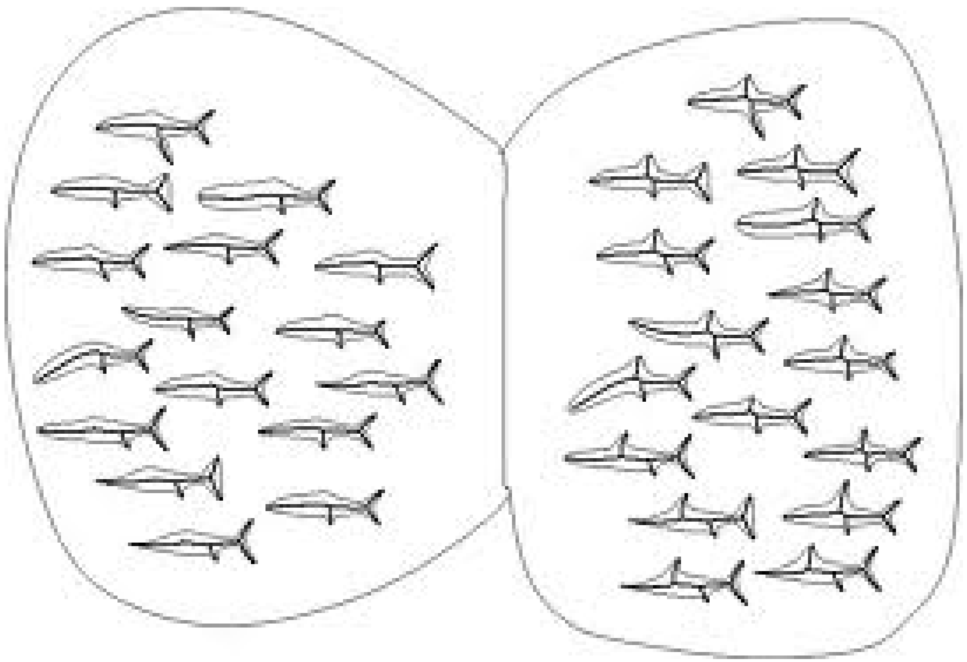
Linear Statistics
Principal Components Analysis
(PCA)



Curved Statistics
Principal Geodesics Analysis
(PGA)

Fletcher et al., IEEE TMI 2004

Shock Graph: Shape Transformation



Invariance of shock graph to flexibly deformable objects.

Matching dog to cat via shock graph editing

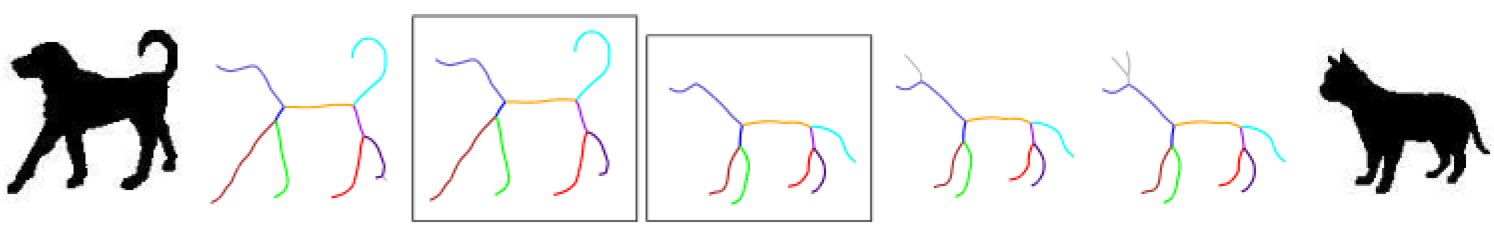
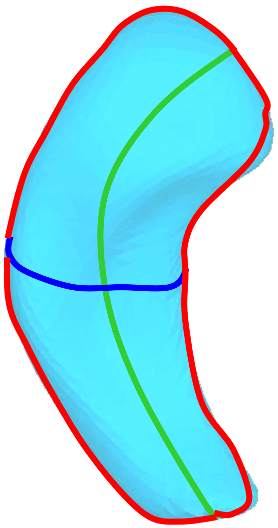


Figure 5: This figure from [43] intermediate shock graphs resulting from applying the edits in the optimal edit sequence for matching a cat and dog. The boxed shock graphs have the same topology. The distance between the shapes is the sum of all edit costs.

Sebastian and Kimia, Signal Processing, 2005

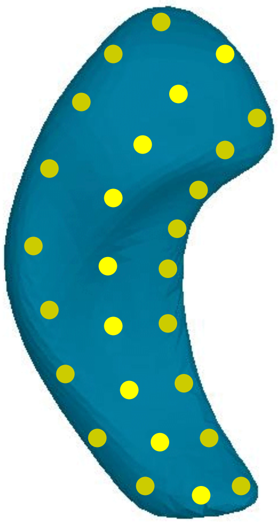
3D Shape Representations



SPHARM

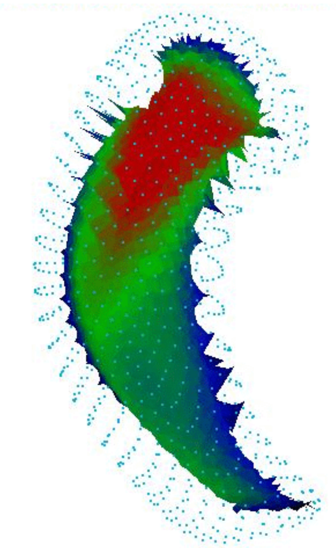
Boundary, fine scale, parametric

$$\boldsymbol{r}(\theta,\phi)=\sum_{k=0}^{\infty}\sum_{m=-k}^{k}\underline{\boldsymbol{c}}_k^m \boldsymbol{Y}_k^m(\theta,\phi)$$



PDM

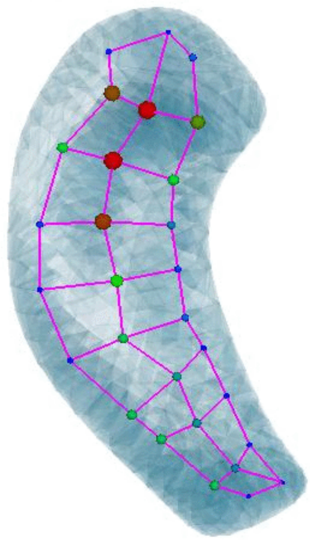
Boundary, fine scale, sampled



Skeleton

Medial, fine scale, sampled

<u>Skeleton from boundary points</u>



S-rep

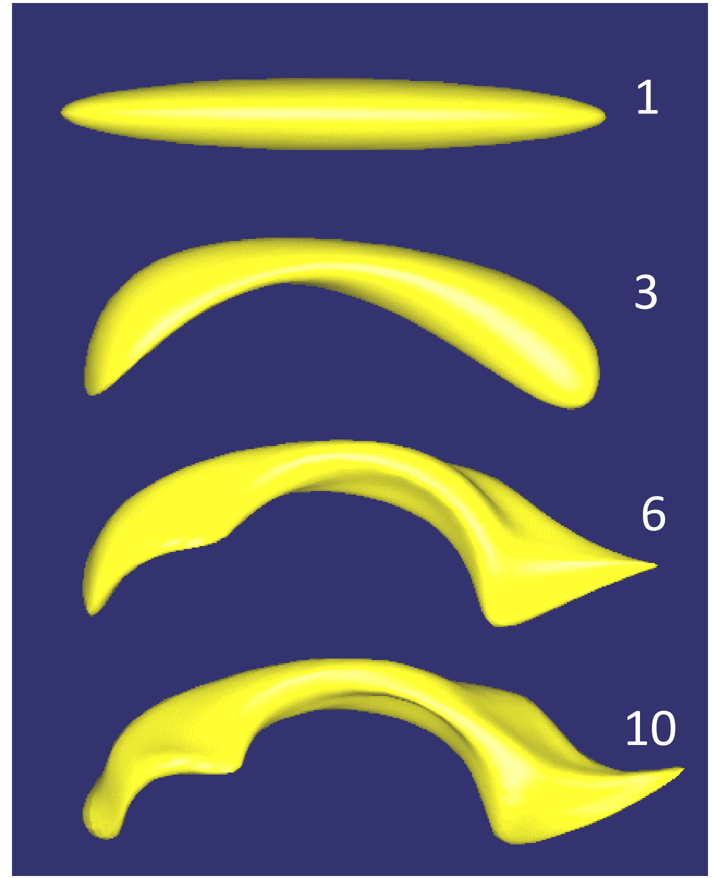
Medial, coarse scale, sampled

<u>Implied Surface</u>

$$m=\left(\underline{x},r,F,\theta\right)$$

Spherical Harmonics (SPHARM)

1. Extract voxel surface
2. Area preserving parameterization
3. First order ellipsoid alignment
4. Fit SPHARM to coordinates
5. Sample parameterization and reconstruct object

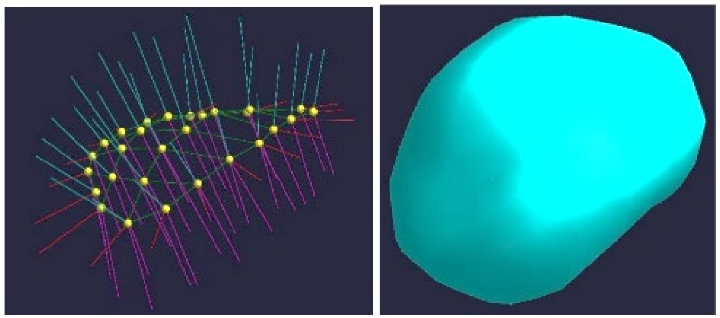


$$\begin{pmatrix} x \\ y \\ z \end{pmatrix} \rightarrow \boldsymbol{r}(\theta,\phi) = \begin{pmatrix} x(\theta,\phi) \\ y(\theta,\phi) \\ z(\theta,\phi) \end{pmatrix}$$

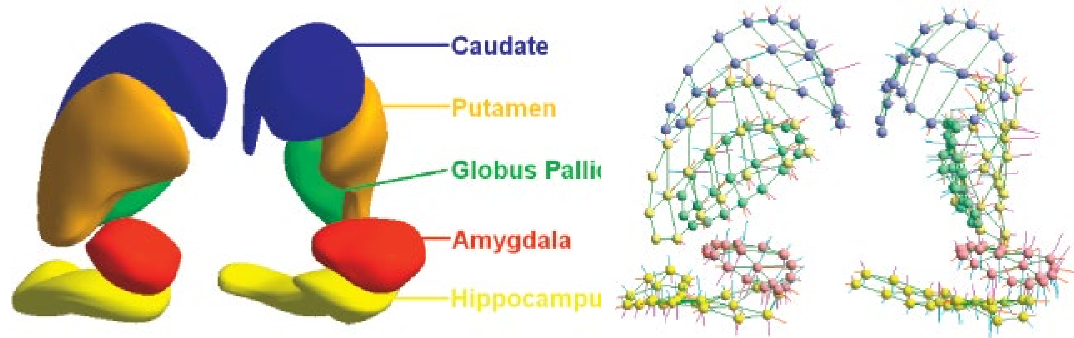
$$\boldsymbol{r}(\theta,\phi) = \sum_{k=0}^{K} \sum_{m=-k}^{k} \boldsymbol{c}_k^m \boldsymbol{Y}_k^m(\theta,\phi) \rightarrow \boldsymbol{c}_k^m = \begin{pmatrix} c_{xk}^m \\ c_{yk}^m \\ c_{zk}^m \end{pmatrix}$$

Szekely, Kelemen, Brechbuehler, Gerig, MedIA 1996, Styner et al.

Medial Axis / Skeletal Representation: Intrinsic Shape Model

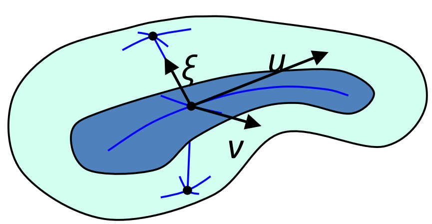


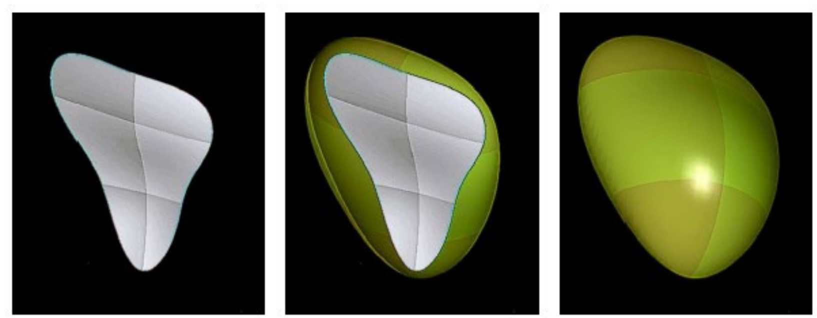
S-rep: Prostate s-rep and implied boundary: Pizer et al. (discrete)



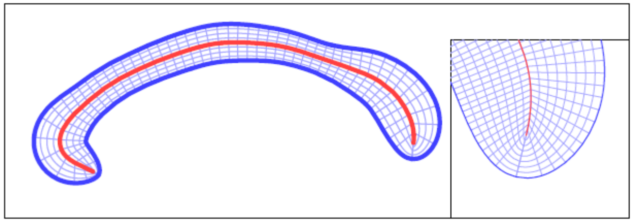
Gorczowski , Pizer, Styner, Gerig et al., T-PAMI 2010, Stats on deformations vs. thickness

CM-rep: Yushkevich (continuous, parametric) Yushkevich et al., TMI 2006

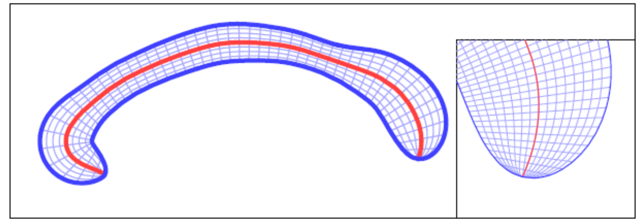




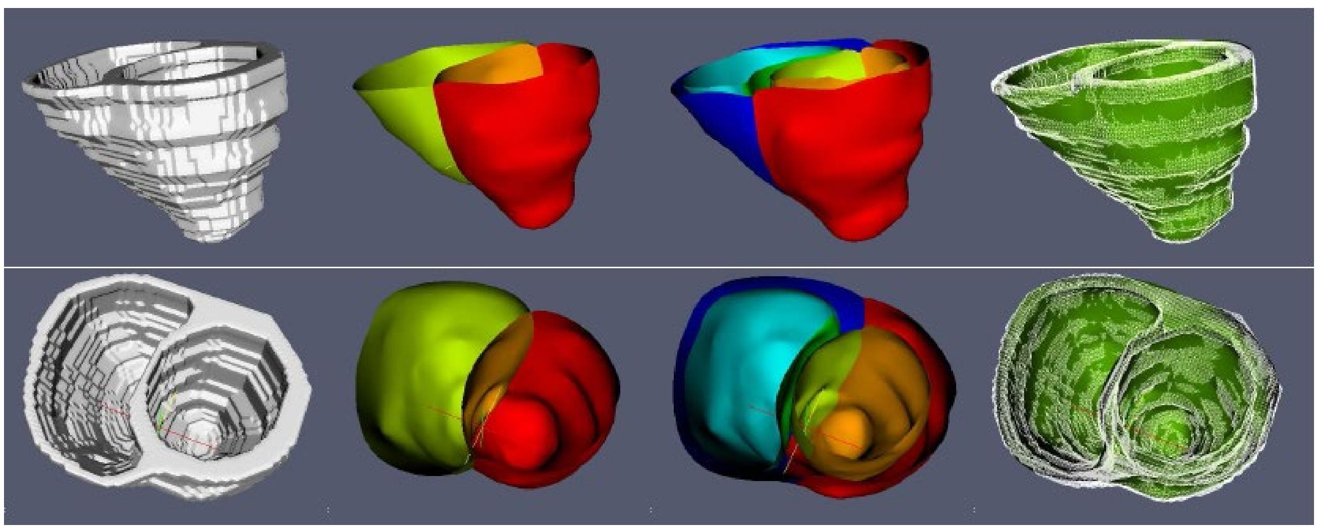
CM-rep



(a) Blum Skeleton Based parametrization



(b) SLS Based parametrization



Sun, Yushkevich et al. 2007, IEEE TMI

Level-Set Formulation: Shapes as signed distance functions

- Embed shape contour as 0-level set
- Calculate Euclidean distance transform.
- Contour represented as image with embedded set of signed distance functions.

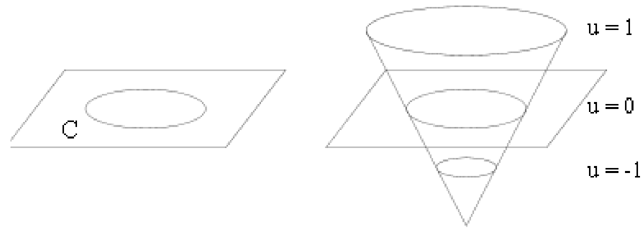
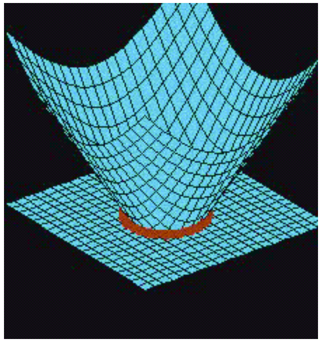
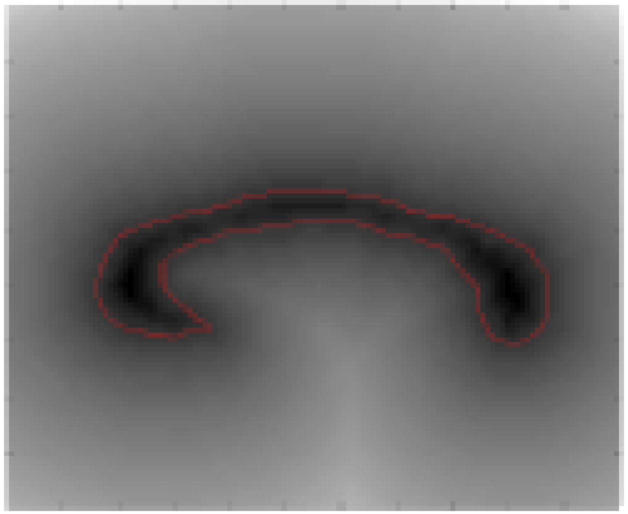


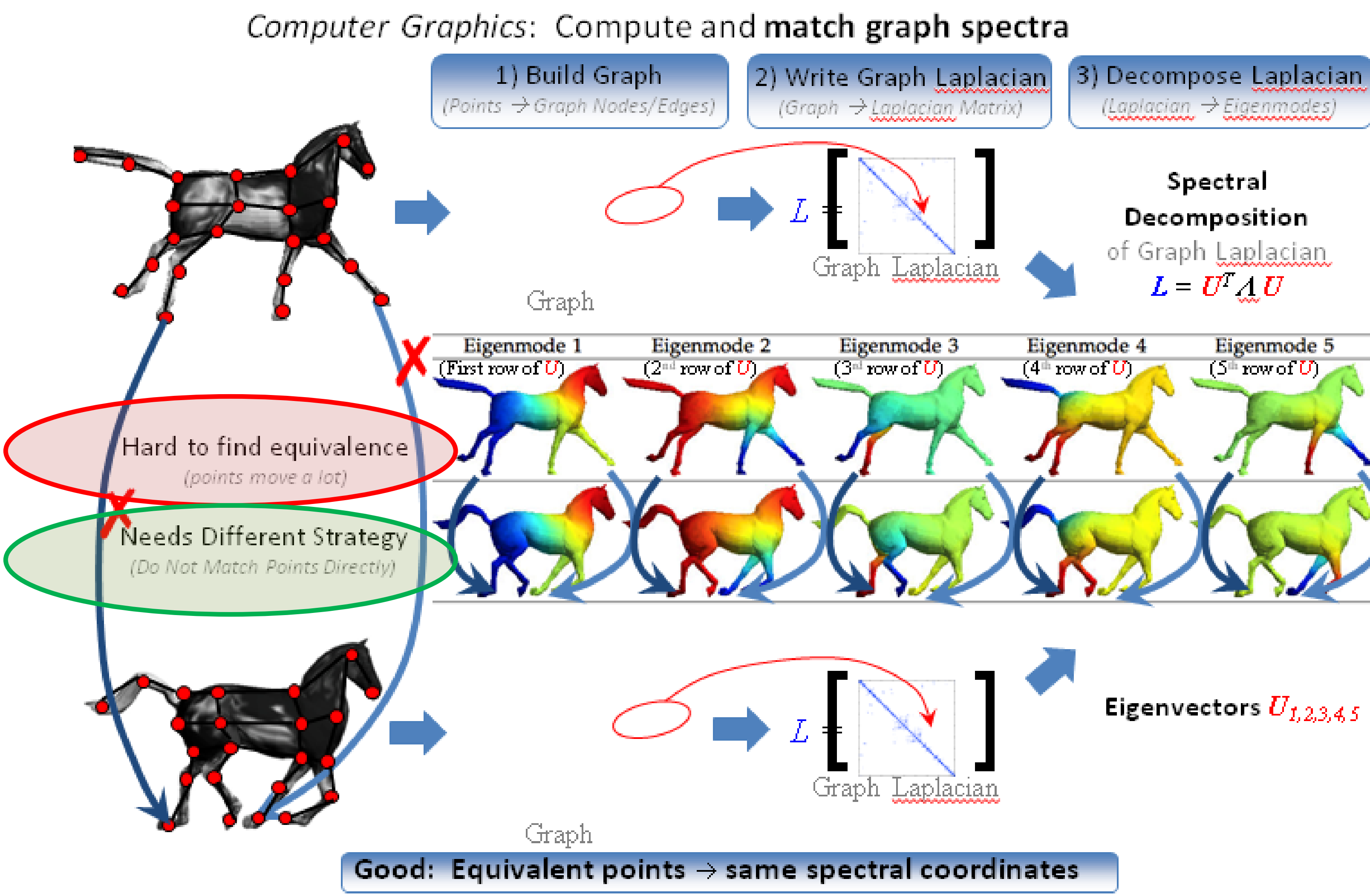
Figure 1. Level sets of an embedding function u for a closed curve C in $\Re^2$.





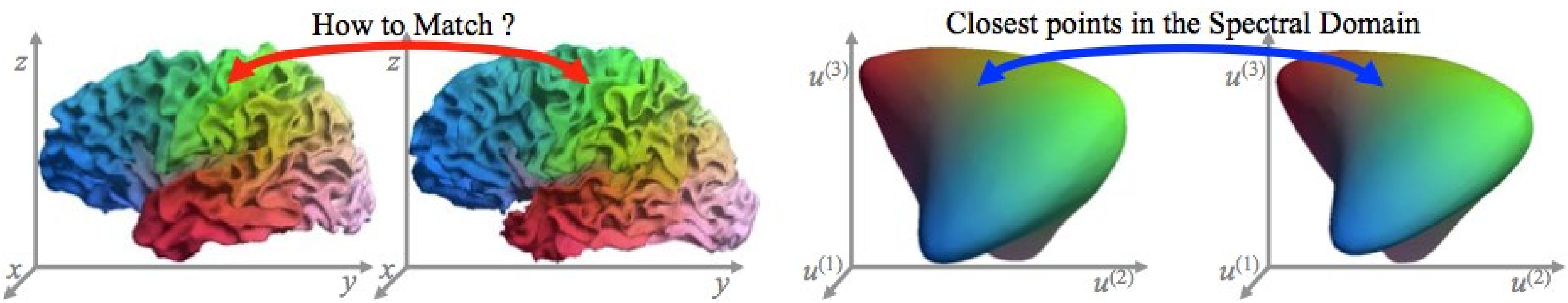
Leventon, Grimson, Faugeras, CVPR 2000

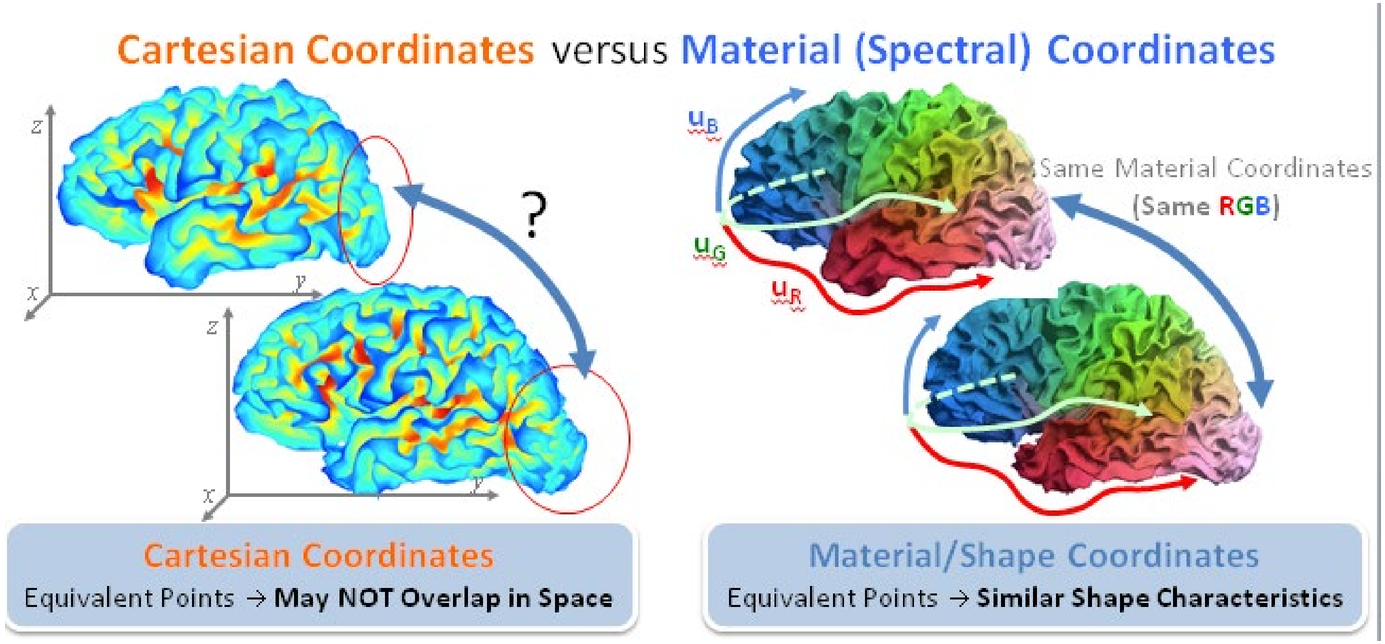
Graph Spectra/Laplacian



Hervé Lombaert, Jon Sporring, Kaleem Siddiqi, Mc Gill, IPMI 2013

Graph Spectra/Laplacian





Hervé Lombaert, Jon Sporring, Kaleem Siddiqi, Mc Gill, IPMI 2013

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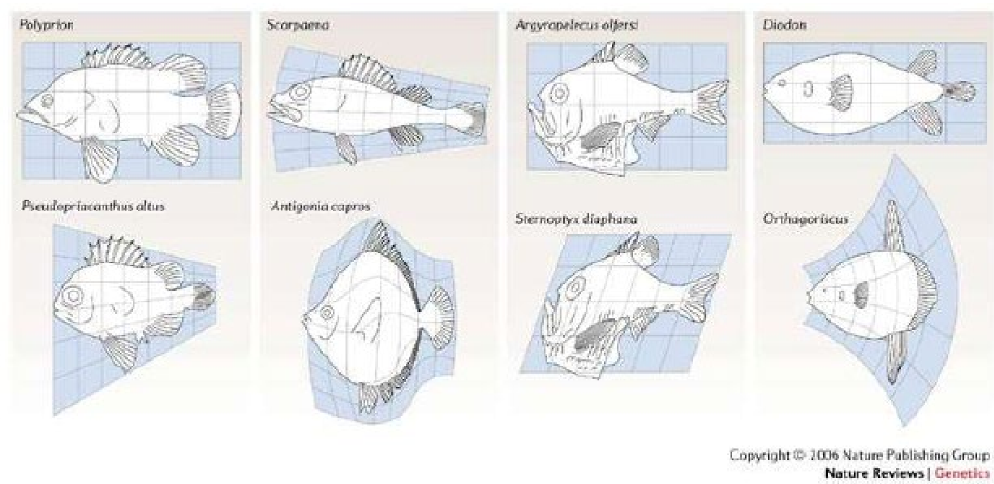
Biological variation through mathematical transforms

D'Arcy Thompson laid out his vision in his treatise “On Growth and Form“. In 1917 he wrote:

In a very large part of morphology, our essential task lies in the comparison of related forms rather than in the precise definition of each; and the deformation of a complicated figure may be a phenomenon easy of comprehension, though the figure itself may be left unanalyzed and undefined."



Shape Spaces: Kendall vs. Deformations

Kendall Shape Space:

- We are interested in the way the points of a shape move (or displace), but there is <u>no general concept of a deformation</u> -- analysis is based on the parameterization of the shape.
- Shape Space forms a complex projective space $\mathbb{CP}^{k-2}$.

Shape Spaces: Kendall vs. Deformations

Kendall Shape Space:

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- Shape Space forms a complex projective space $\mathbb{CP}^{k-2}$.

D'Arcy Thompson inspired deformation based analysis:

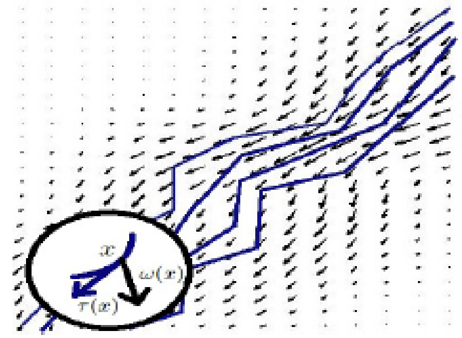
- Interested in the way the ambient space deforms.
- Statistical analysis is centered on the deformations of space, not movement & displacement of points on shapes.
- What is the Shape Space? Information via deformations.

“Correspondence-free” Registration: **Currents**

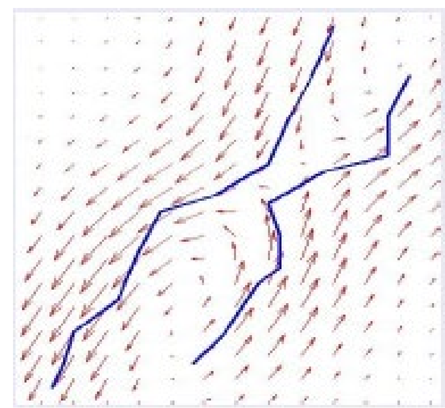
Topology and shape differences and noise can make point-to-point correspondence hard:

- **Currents**: Objects that integrate vector fields
- **Shape**: Oriented points = Set of normals (tangents)
- **Distance** between curves:

$$d(L_1, L_2)^2 = \int_{L_1} \omega_1(x)^t \tau_1(x) dx + \int_{L_2} \omega_2(x)^t \tau_2(x) dx - \int_{L_1} \omega_2(x)^t \tau_1(x) dx - \int_{L_2} \omega_1(x)^t \tau_2(x) dx$$



$$L(\omega) = \sum_{i=1\ldots4} \int_{L_i} \omega(x)^t \tau(x) d\lambda(x)$$



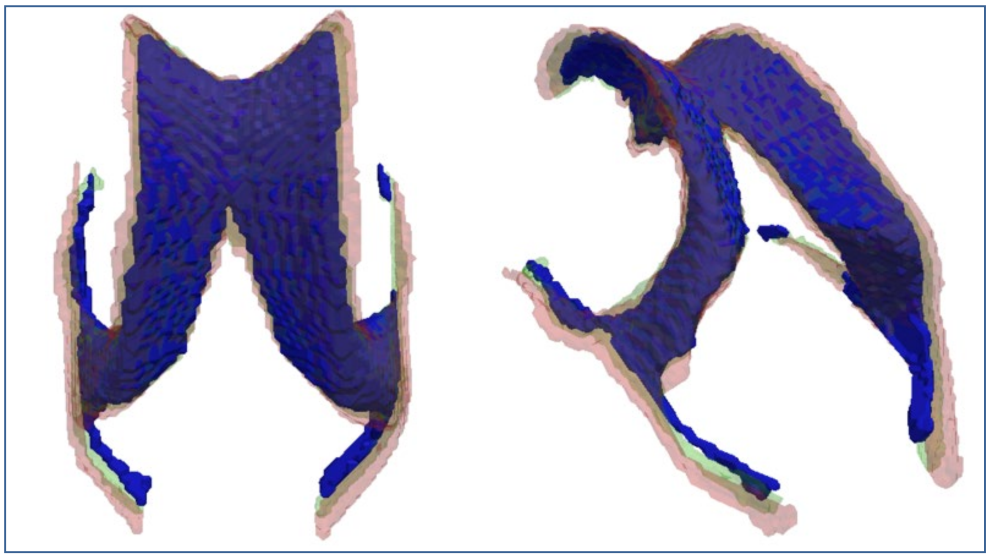
[Glaunes2004] Glaunes, J., Trouve, A., Younes, L. Diffeomorphic matching of distributions: a new approach, … CVPR 2004.

[Durrleman2008] S. Durrleman, X. Pennec, A. Trouvé, P. Thompson, N. Ayache, Inferring Brain Variability from Diffeomorphic Deformations of Currents: an integrative approach, Medical Image Analysis 2008

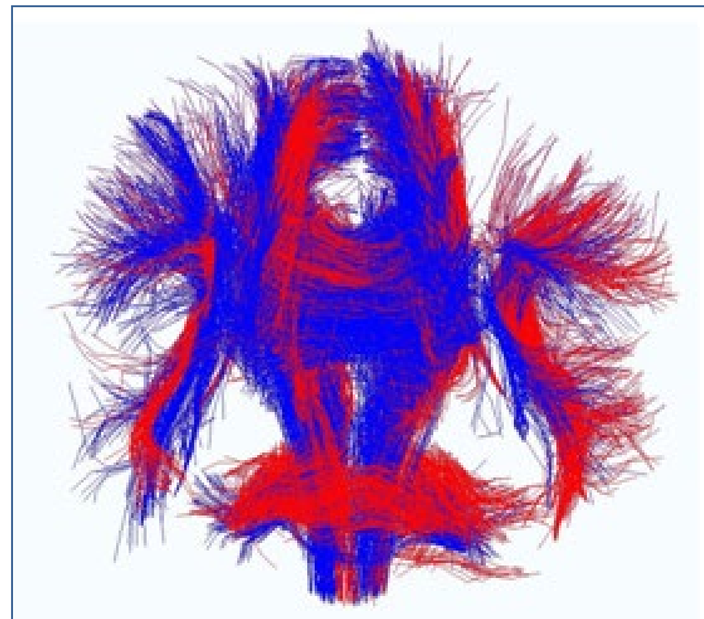
Correspondence-free Shape Analysis

Problems so far:

- Correspondence depends on shape parameterization
- Shapes with variable topology: correspondence undefined
- Now with **currents**:



Brain ventricles for infants 6mo to 2yrs



DTI Fiber Tracts from two subjects

movie

Durrleman, Pennec, Trouve, Ayache et al., IJCV 2013

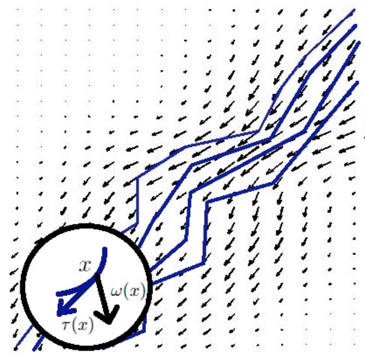
Correspondence-free similarity measures

- Depends on the kind of objects:
  - Images: sum of squared differences $\int |I(x) - I'(x)|^2 \, dx$
  - Landmarks: sum of squared differences $\sum_k |x_k - x'_k|^2$
  - Surface mesh and curves:
    - Currents [Glaunès'05]

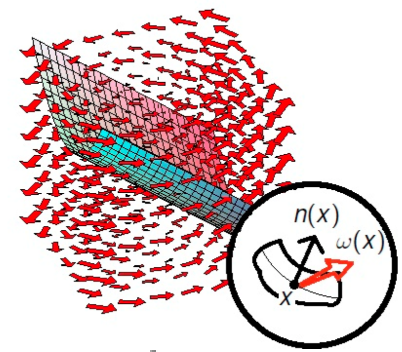
$$||F - F'|| = \sup_{||\omega||<1} |F(\omega) - F'(\omega)|$$

$$\langle F, F' \rangle = \sum_p \sum_q \exp\left(- \frac{|x_p - x'_q|^2}{\sigma_W^2} \right) \tau_p^T \tau'_q$$

τ: tangents of curves/normals of surfaces



$$F(\omega) = \sum_i \int_{C_i} \omega(x)^T \tau_i(x) d\lambda_i(x)$$

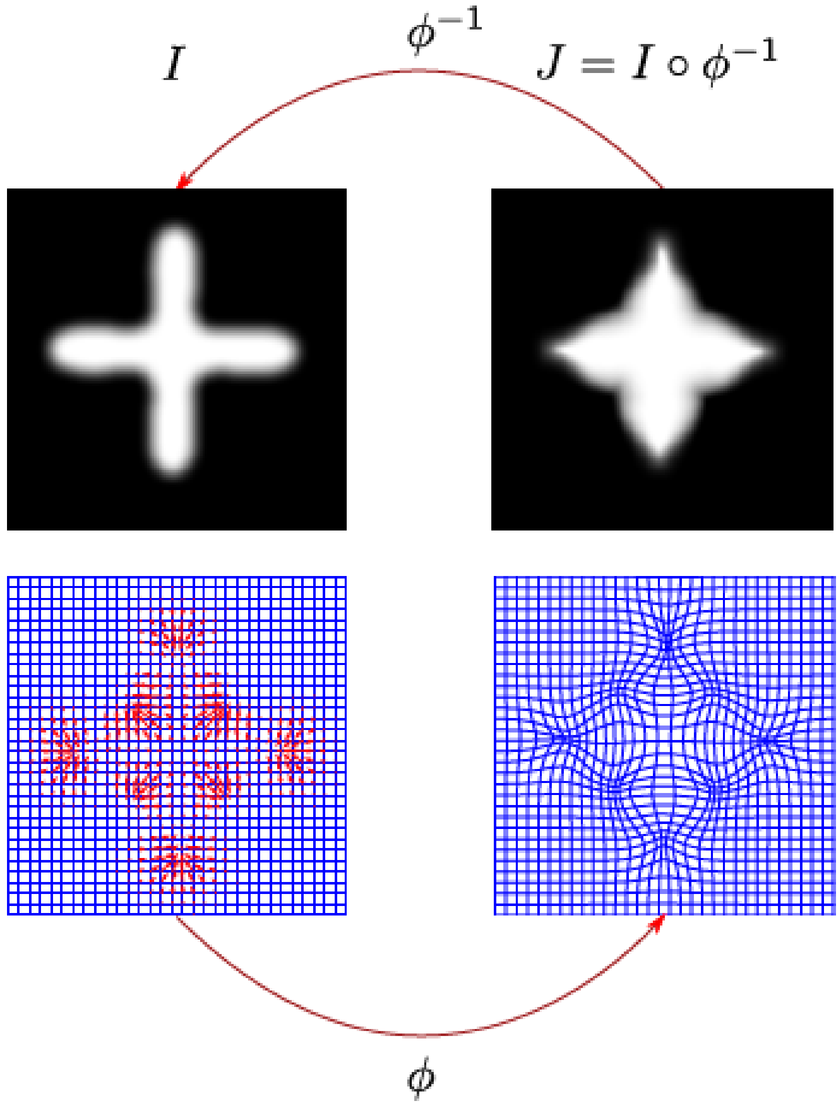


$$S(\omega) = \int_S \omega(x)^T n(x) d\sigma(x)$$

- No point correspondence needed
- Efficient numerical schemes (FFT)
- Robust to changes in topology
- Robust to differences in
  - mesh sampling
  - mesh imperfections…

→ ***Usable routinely on large data sets***

Ambient Space Deformation

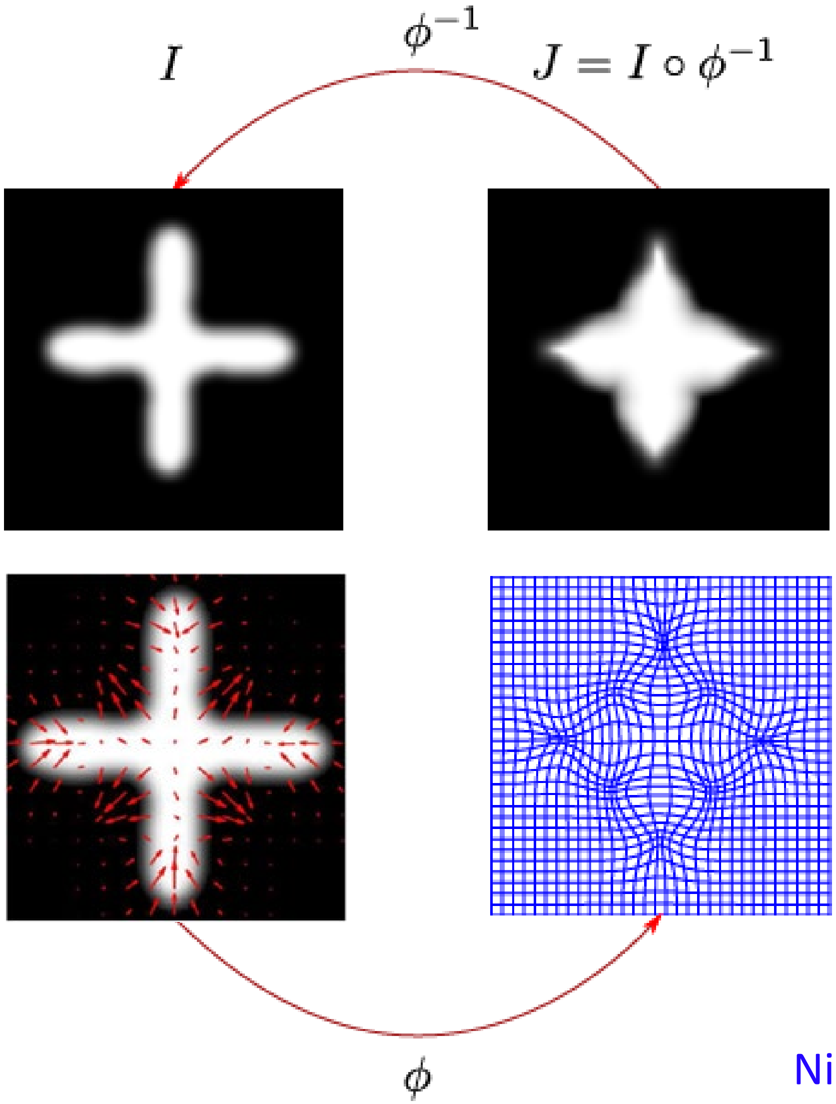


Initial velocity* as a smooth vector field and the corresponding diffeomorphic flow that transforms the shape “plus" to “flower".

*velocity: momenta after convolution with kernel

Nikhil Singh, PhD thesis Utah 2013

Ambient Space Deformation

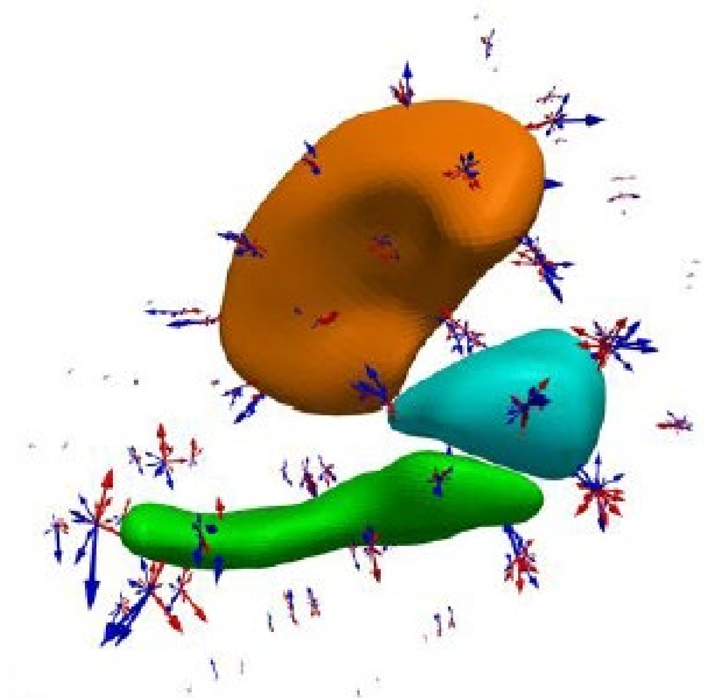


Momenta and the corresponding diffeomorphic flow that transforms the shape “plus" to “flower".

Statistics on momenta.

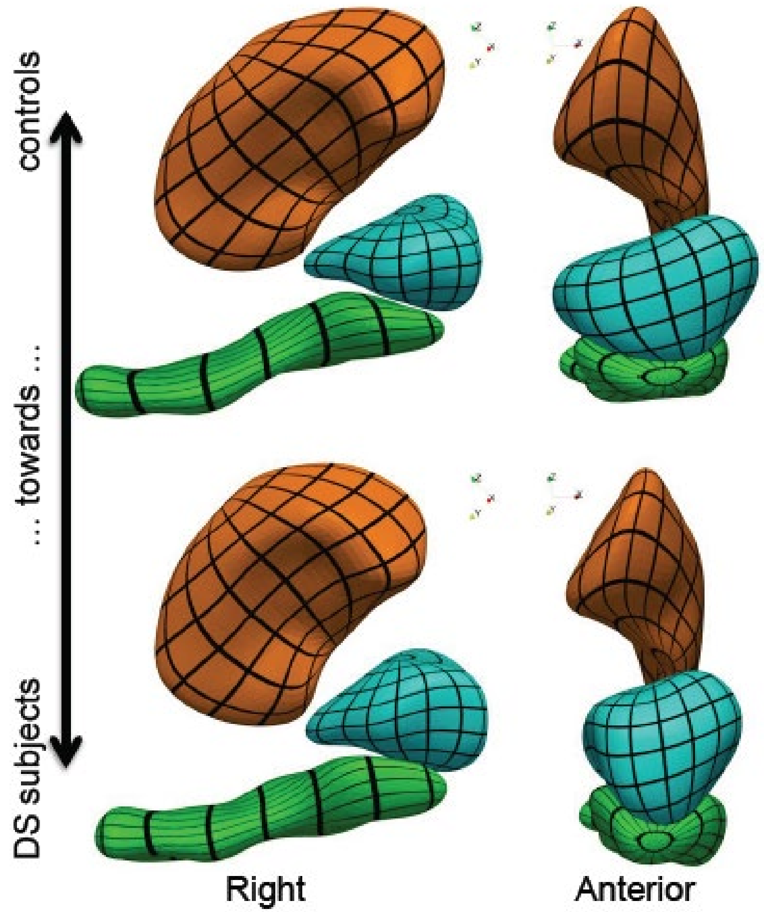
Nikhil Singh, PhD thesis Utah 2013, Tom Fletcher
James Fishbaugh, GSI conference, Springer 20014

Statistics on Deformations



Geodesics from atlas to each subject share the same tangent space.

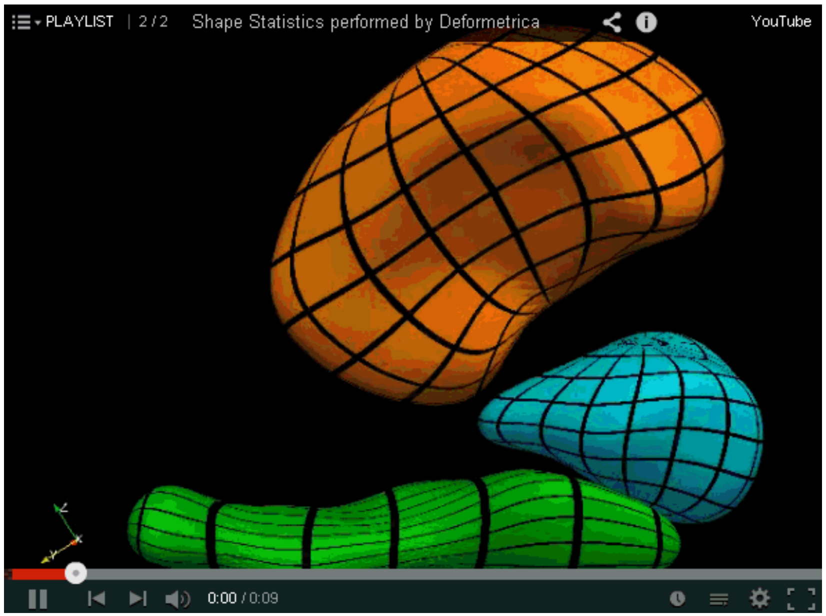
Momentum vectors of DS subjects (red) and controls (blue) in atlas coordinate space.



Most discriminative deformation axis between Down's and Controls.

Durrleman et al, Neuroimage 2014

Statistics on Deformations



Most discriminative deformation axis between Down's Syndrome and Controls.

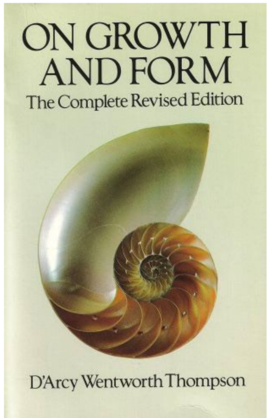
Durrleman et al, Neuroimage 2014

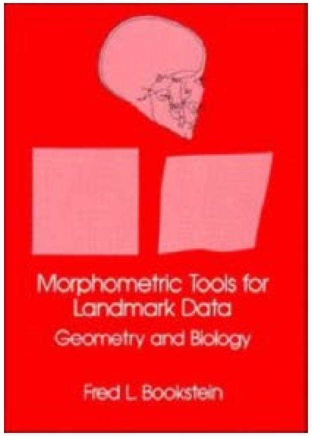
Main advantages:

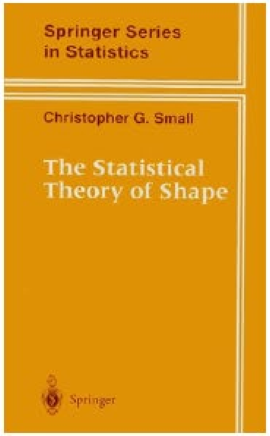
- Shape space **independent** on shape representation.
- Natural way to handle **multiple shapes**, **topology variations**, combinations of points, lines, contours, image intensity etc.
- **Statistics on low #features rather than high-dimensional oversampled shape representation.**

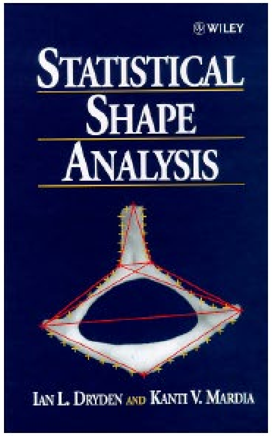
Where to Learn More

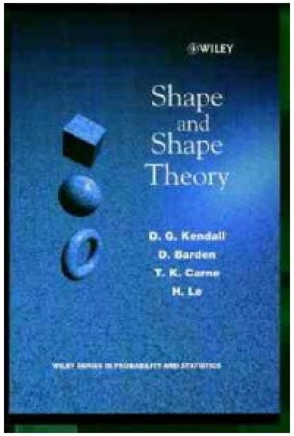
- **Pioneers: d'Arcy Thompson, Fred Bookstein, and David Kendall.**
- Bookstein (1991, Cambridge).
- Kendall, Barden and Carne, Shape and Shape Theory, Wiley, 1999.
- Dryden and Mardia, Statistical Shape Analysis, Wiley, 1998.
- Small, The Statistical Theory of Shape, Springer-Verlag, 1996.
- Grenander, HISTORY AS POINTS AND LINES, 1998-2003
- Lele and Richstmeier (2001, Chapman and Hall).
- Krim and Yezzi, Statistics and Analysis of Shapes, Birkhauser, 2006.

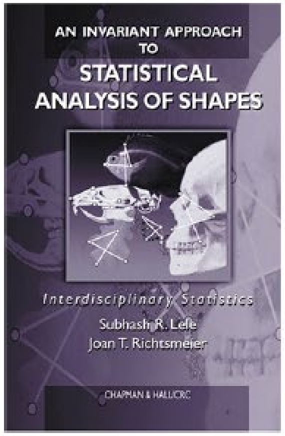












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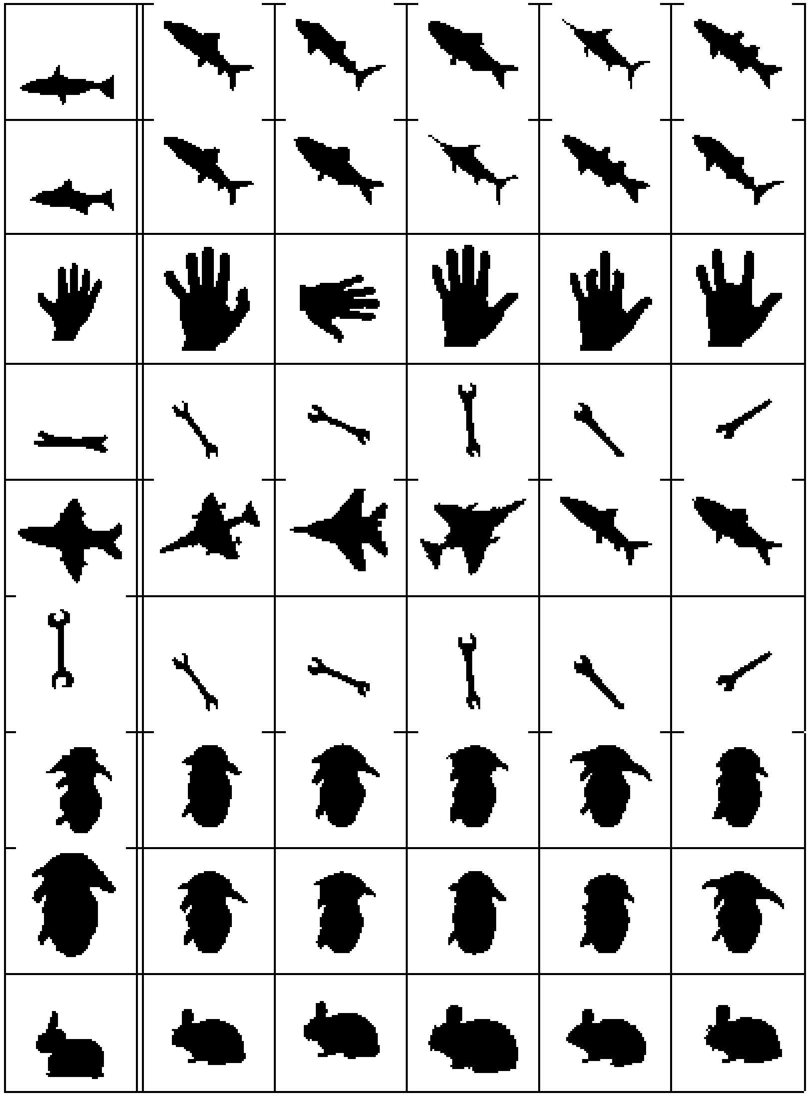
Shape Definition

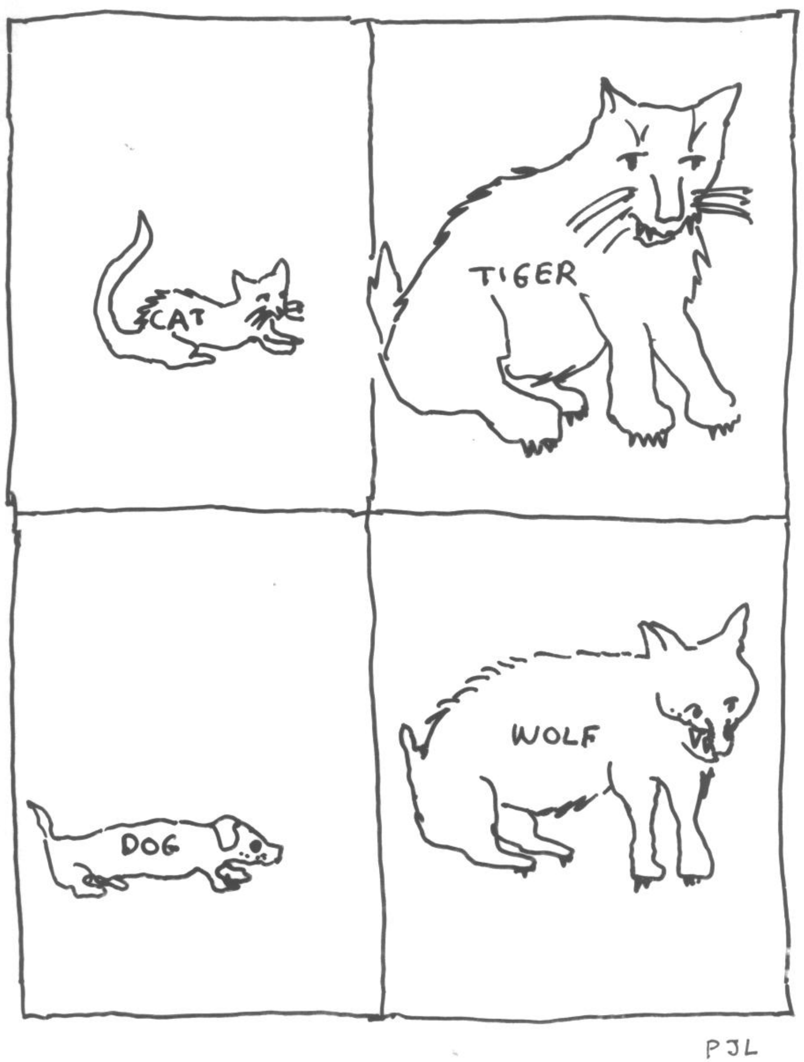


Dryden/Mardia, (Kendall 1977):

Shape is all the geometrical information that remains when location, scale and rotational effects are filtered out from an object.

Image: Sebastian and Kimia 2005

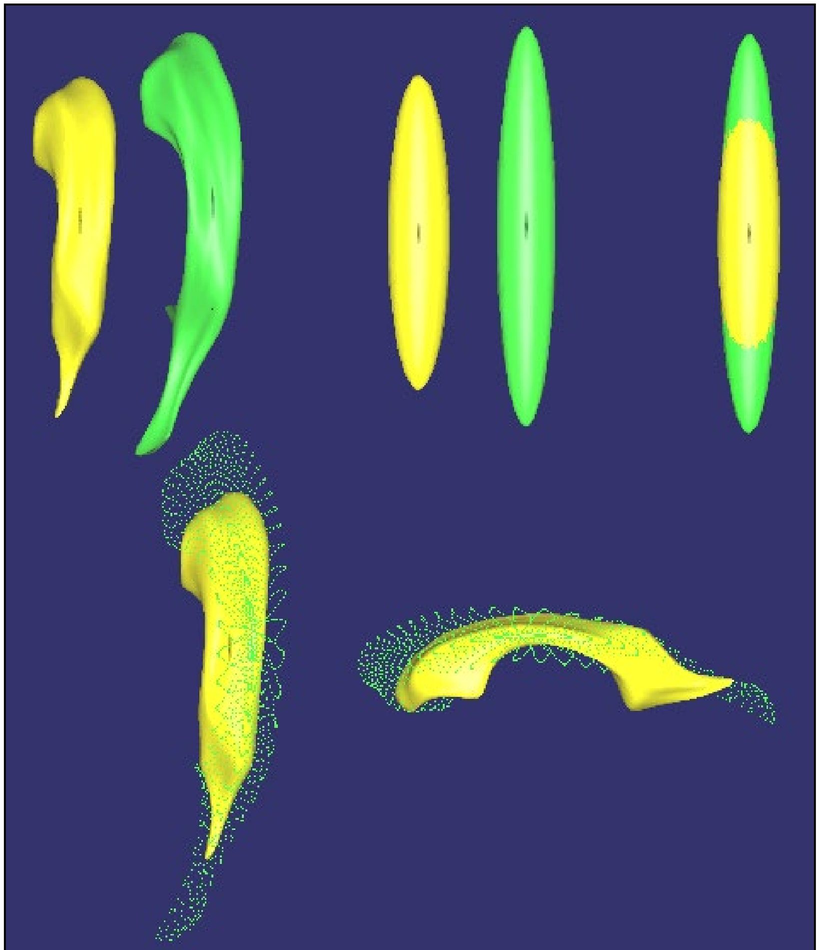
The Problem of Size and Shape

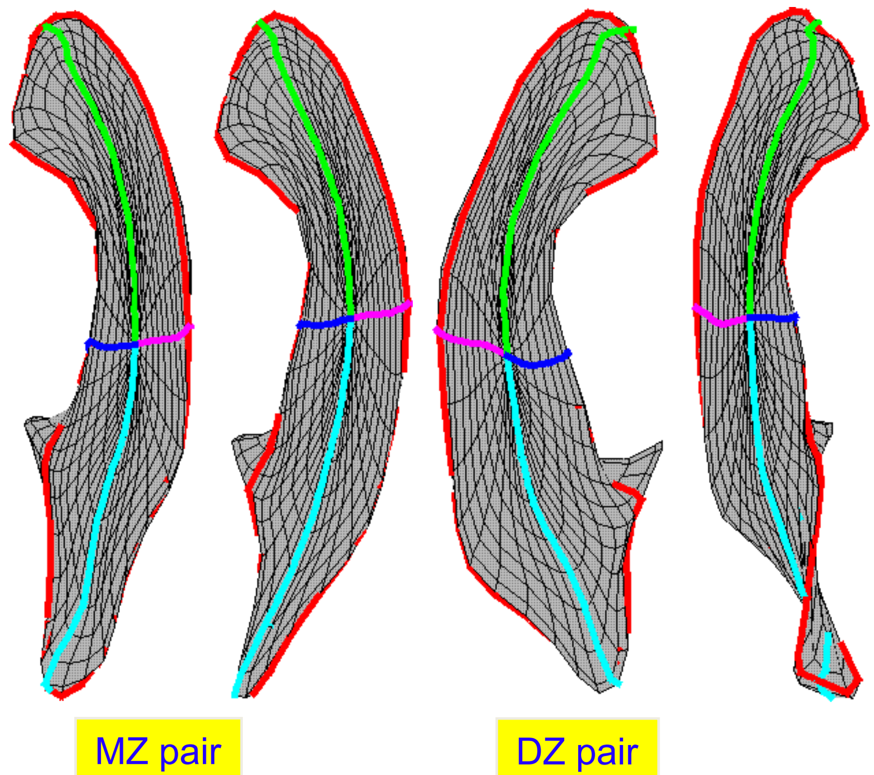


Dryden/Mardia (Kendall 1977): *(Sometimes we are also interested in retaining scale information as well as shape)*

Size-and-Shape is all the geometrical information that remains when location and rotational effects are filtered out from an object.

Object Alignment & Surface Homology with Biological Shapes

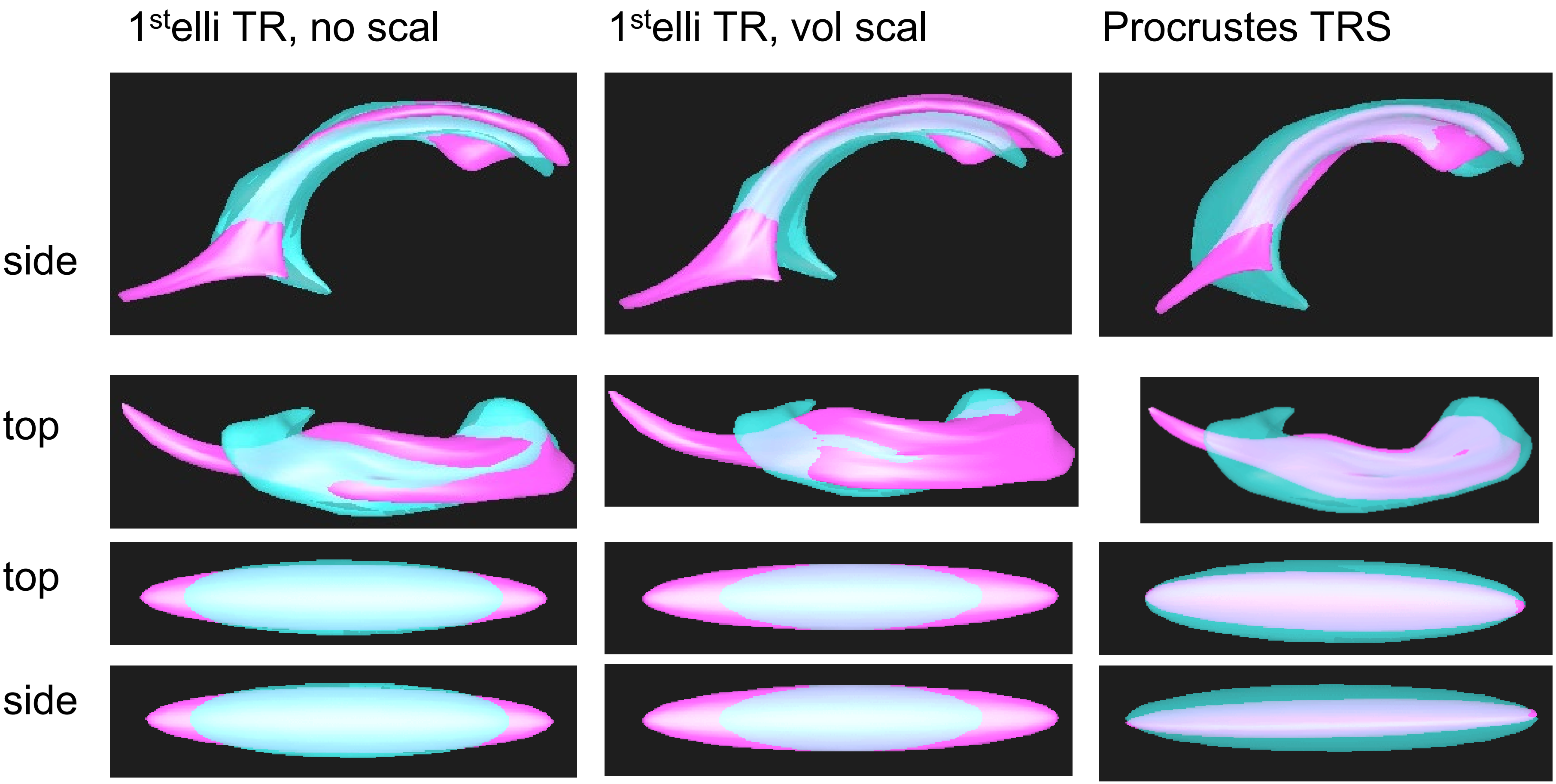




Surface Correspondence

Styner and Gerig, PNAS 2005

Object Alignment & Surface Homology with Biological Shapes



Global scaling is mathematically appealing, but may not optimally represent biological shape difference or change.

Discussion: Normalization by Translation/Rotation/Scaling

- Biological/anatomical shapes are deformable.
- Different definitions of TRS will result in very different findings of shape differences:
  - shorter/longer
  - thinner/thicker
  - locality: differences at tail, or middle, or head: Message for clinicians?
- Intrinsic versus extrinsic shape representations
- Choices to be tuned to problem at hand

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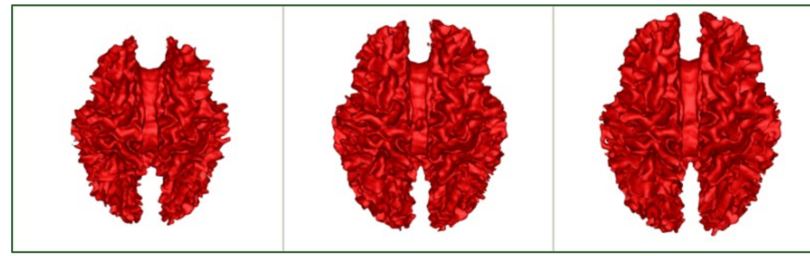
Longitudinal Shape Analysis

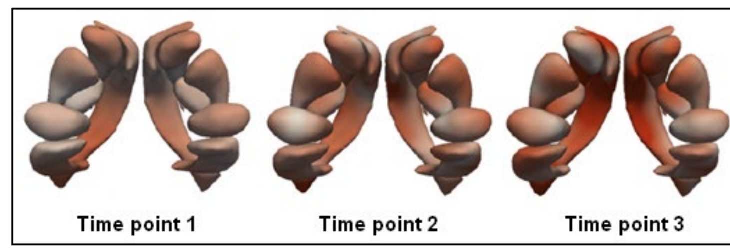
Clinicians most often study phenomena related to dynamic processes:

- Development, degeneration, monitoring recovery & efficacy of treatment
- Baseline to follow-up
- Disease progression
- Prediction of onset of clinical symptoms
- Personalized health care: Individual trajectories compared to expected “norm”
- Often: Longitudinal more powerful than cross-sectional analysis

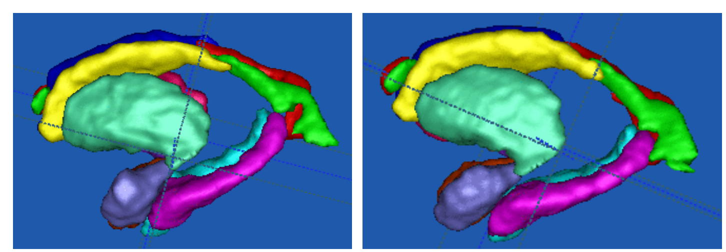
Pediatrics: (A)typical Brain Growth



Aging / Neurodegeneration



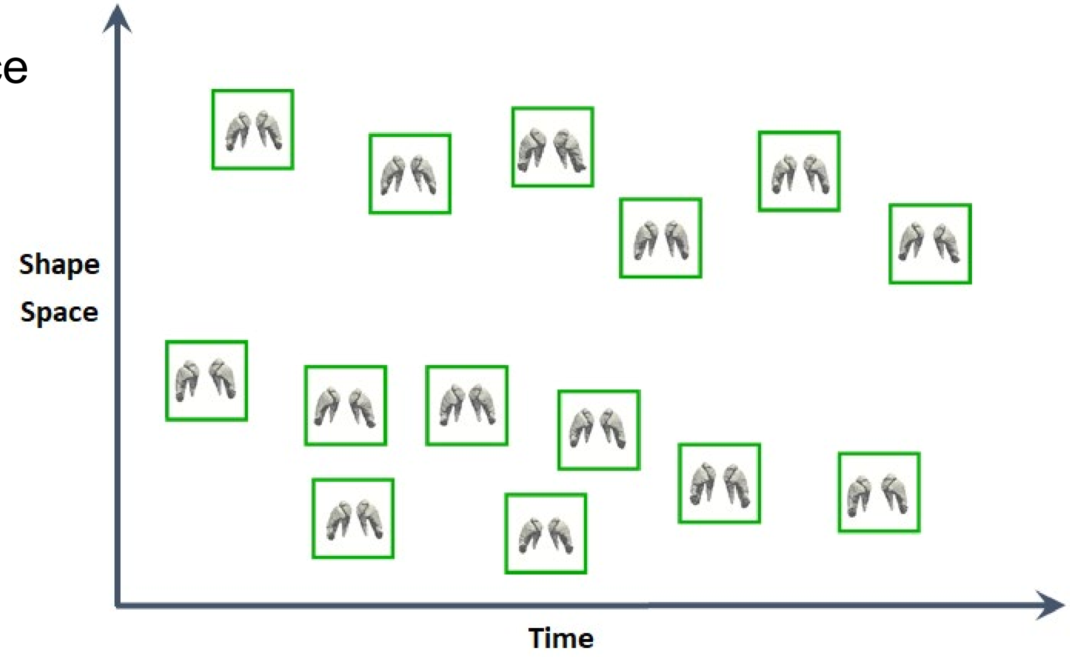
Ventricles & Nuclei (age 2 to 4)



Why Shape Regression?

Observed Anatomical Shapes: Aging caudate/putamen

Sparsely observed shape sequence as function of age 20 to 75

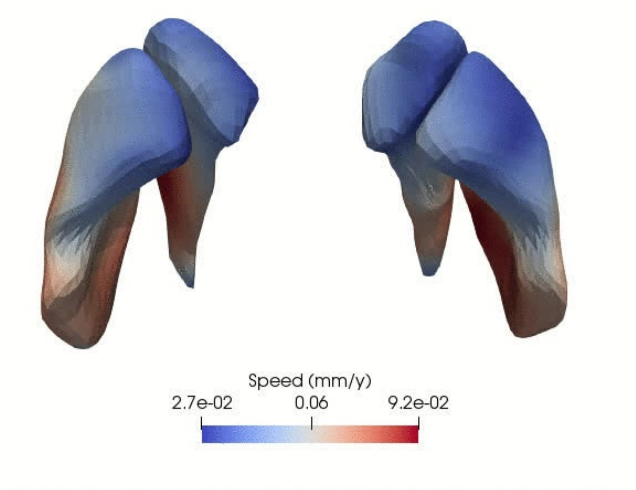


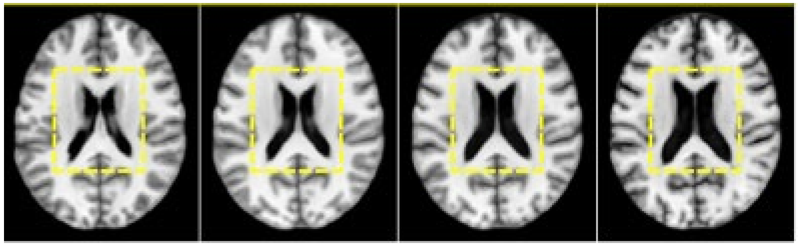
Sungmin Hong, MICCAI 2019

Why Shape Regression?

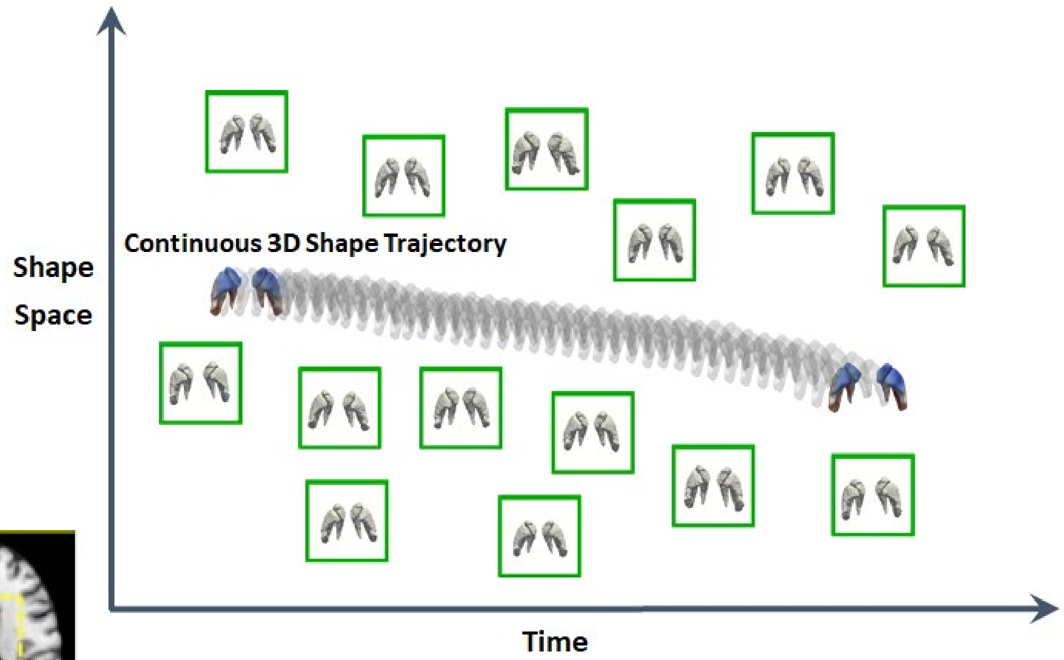
Modeling Spatio-Temporal Shape Change

Continuous shape sequence age 20 to 75



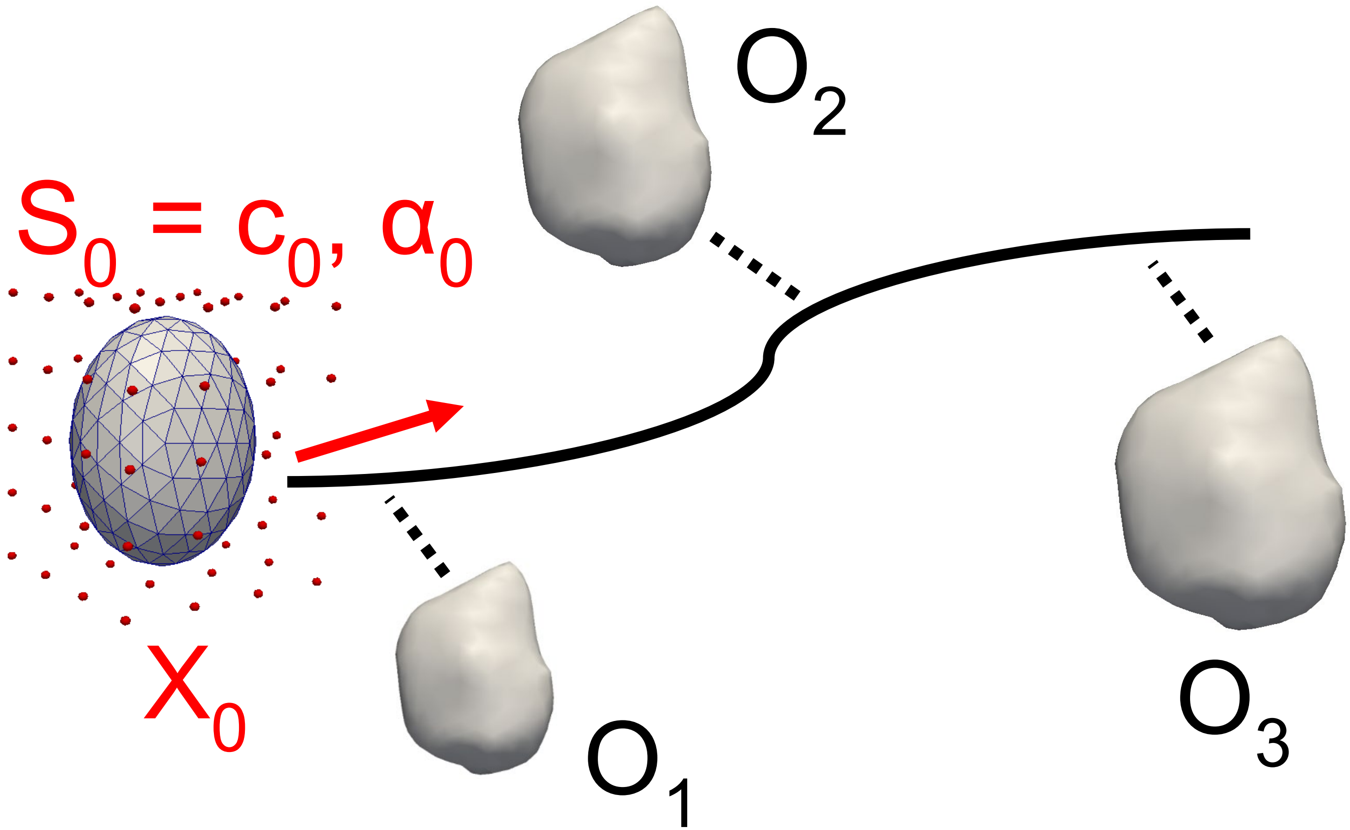


Ventricular enlargement due to brain atrophy



Sungmin Hong, MICCAI 2019

Geodesic Shape Regression



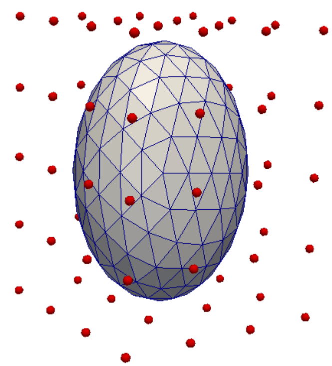
Geodesic shooting to evolve control points

Trajectory of control points defines **flow** of diffeomorphisms

James Fishbaugh,MedIA 2019

Control Point Formulation

Geodesic shooting to evolve control points



$$\begin{cases} \dot{c}_i(t) = \displaystyle\sum_{p=1}^{N_c} K(c_i(t), c_p(t))\alpha_p(t) \\ \dot{\alpha}_i(t) = -\displaystyle\sum_{p=1}^{N_c} \alpha_i(t)^t \alpha_p(t) \nabla_1 K(c_i(t), c_p(t)) \end{cases}$$

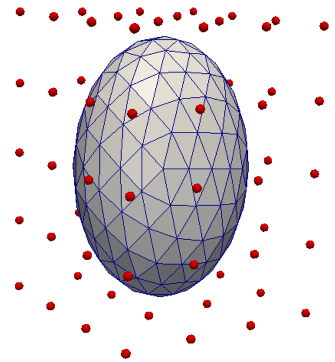
Trajectory of control points defines **flow** of diffeomorphisms

$$\dot{\phi}_t(x) = v(x,t) = \sum_{p=1}^{N_c} K(x, c_p(t))\alpha_p(t)$$

James Fishbaugh,MedIA 2019

Regression Criterion

$S_0 = c_0, \alpha_0$



$$E(\mathbf{X}_0, \mathbf{S}_0) = \sum_{i=1}^{N_{obs}} \frac{1}{2\lambda^2} D(\mathbf{X}(t_i), \mathbf{O}_{t_i}) + L(\mathbf{S}_0)$$

D is squared distance on currents

$$D(\mathbf{X}(t_i), \mathbf{O}_{t_i}) = ||(\phi_{t_i}(\mathbf{X}_0) - \mathbf{O}_{t_i})||_{W^*}^2$$

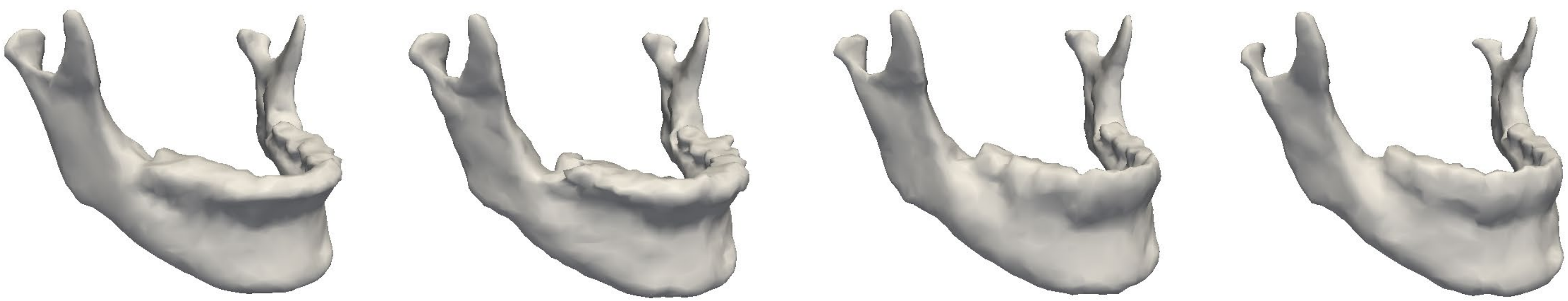
Regularity defined by kinetic energy of control points

$$L(\mathbf{S}_0) = \sum_{p,q} \alpha_{0,p}^t K(c_{0,p}, c_{0,q}) \alpha_{0,q}$$

James Fishbaugh,MedIA 2019

Longitudinal Shape Modeling

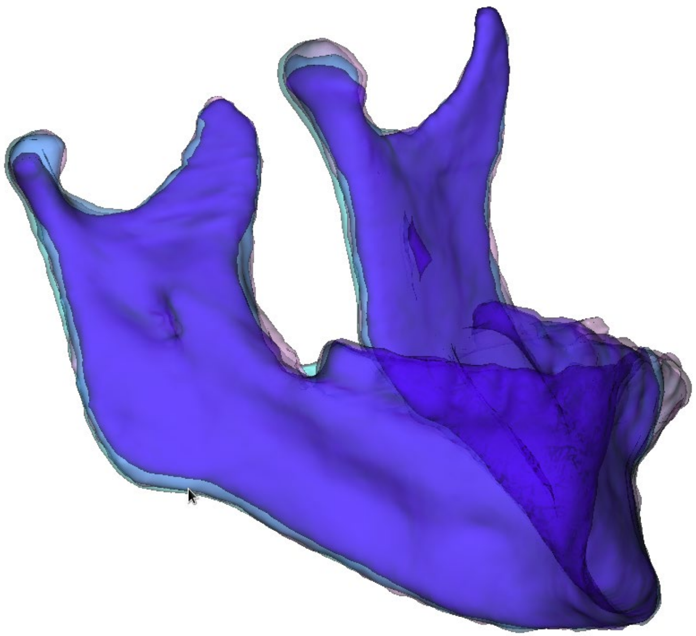
Example mandibular surgery case (Prof. L. Cevidanes), 16-22 years post-surgery.

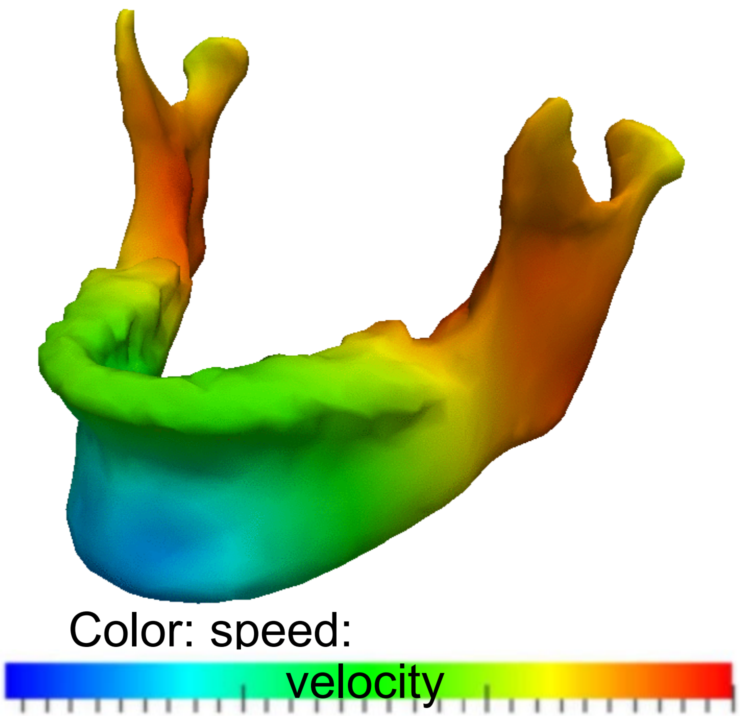


Follow-up scans in 2 years intervals.

Longitudinal Shape Modeling

Example mandibular surgery case (Prof. L. Cevidanes), 16-22 years post-surgery.

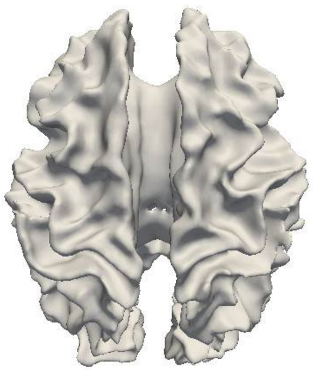




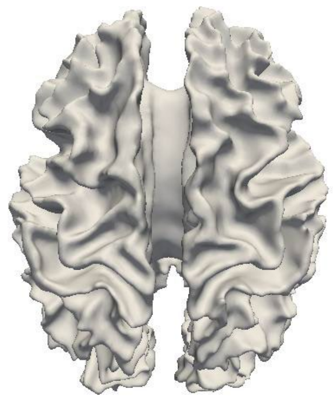
Qualitative analysis from overlay: Do we understand remodeling?

Spatio-temporal shape regression: Local and global.

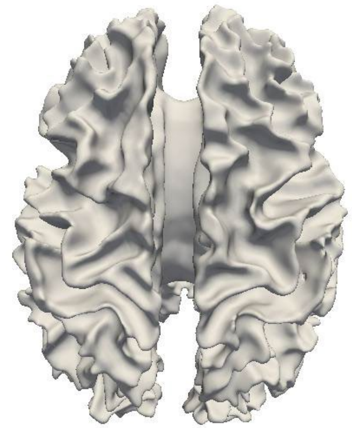
Early Brain Development: 4D Shape Trajectories



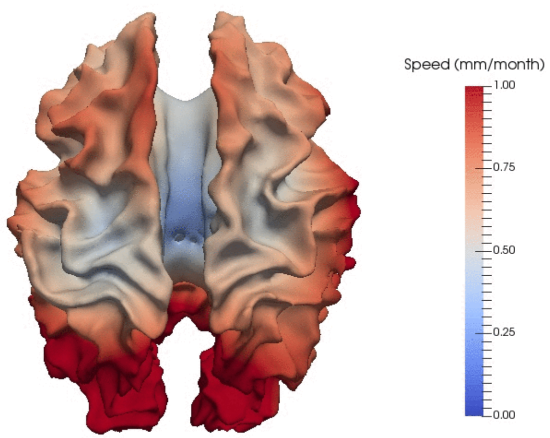
6 month



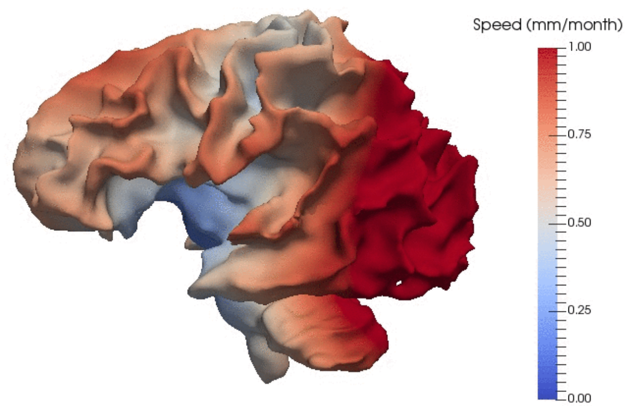
12 month



24 month



6.00 months

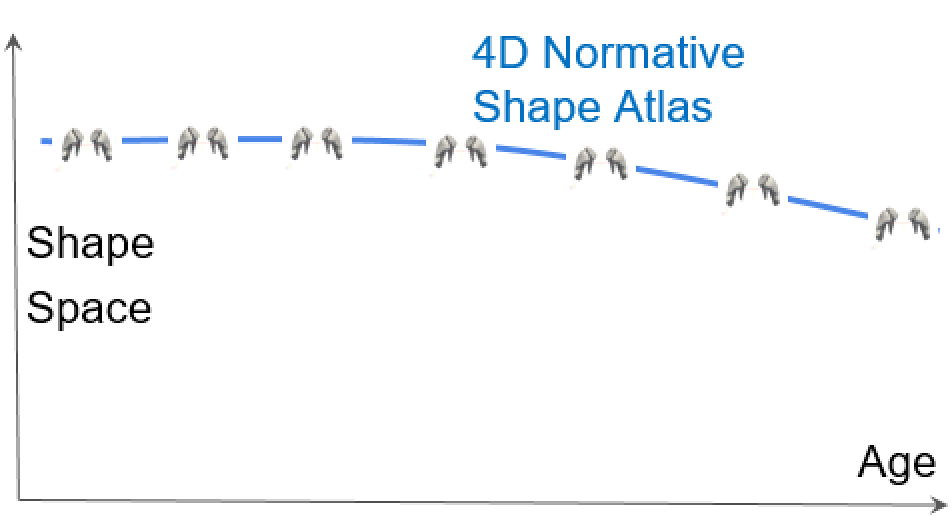


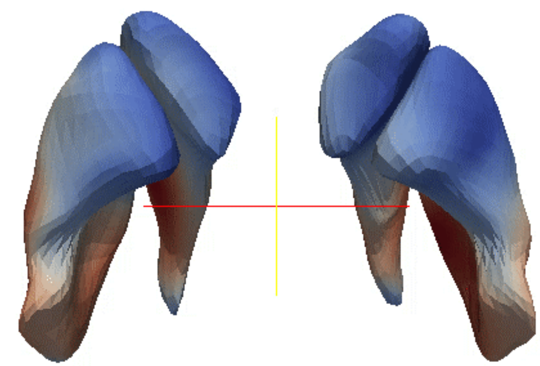
6.00 months

Geodesic Image Regression: Fishbaugh, Durrleman et al., 2015 / 2017 / 2019

Towards subject-specific analysis

Question: Longitudinal Change in Normal versus Abnormal (Genetic Risk Huntingtons)?





4D Normative Shape Atlas:
23 to 88 years, 243 subjects
Cross-sectional Regression

S. Hong et al, SPIE 2017, MICCAI 2019

Towards subject-specific analysis

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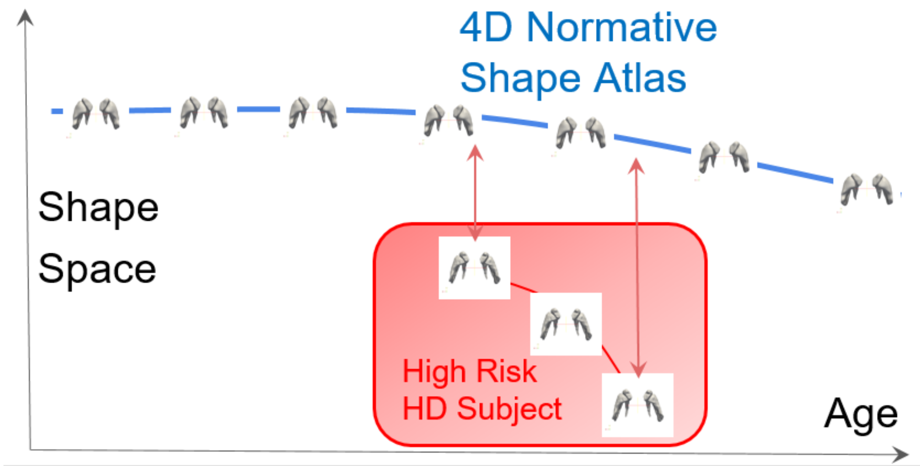
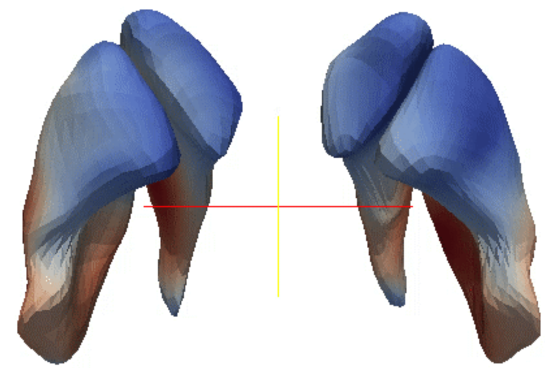




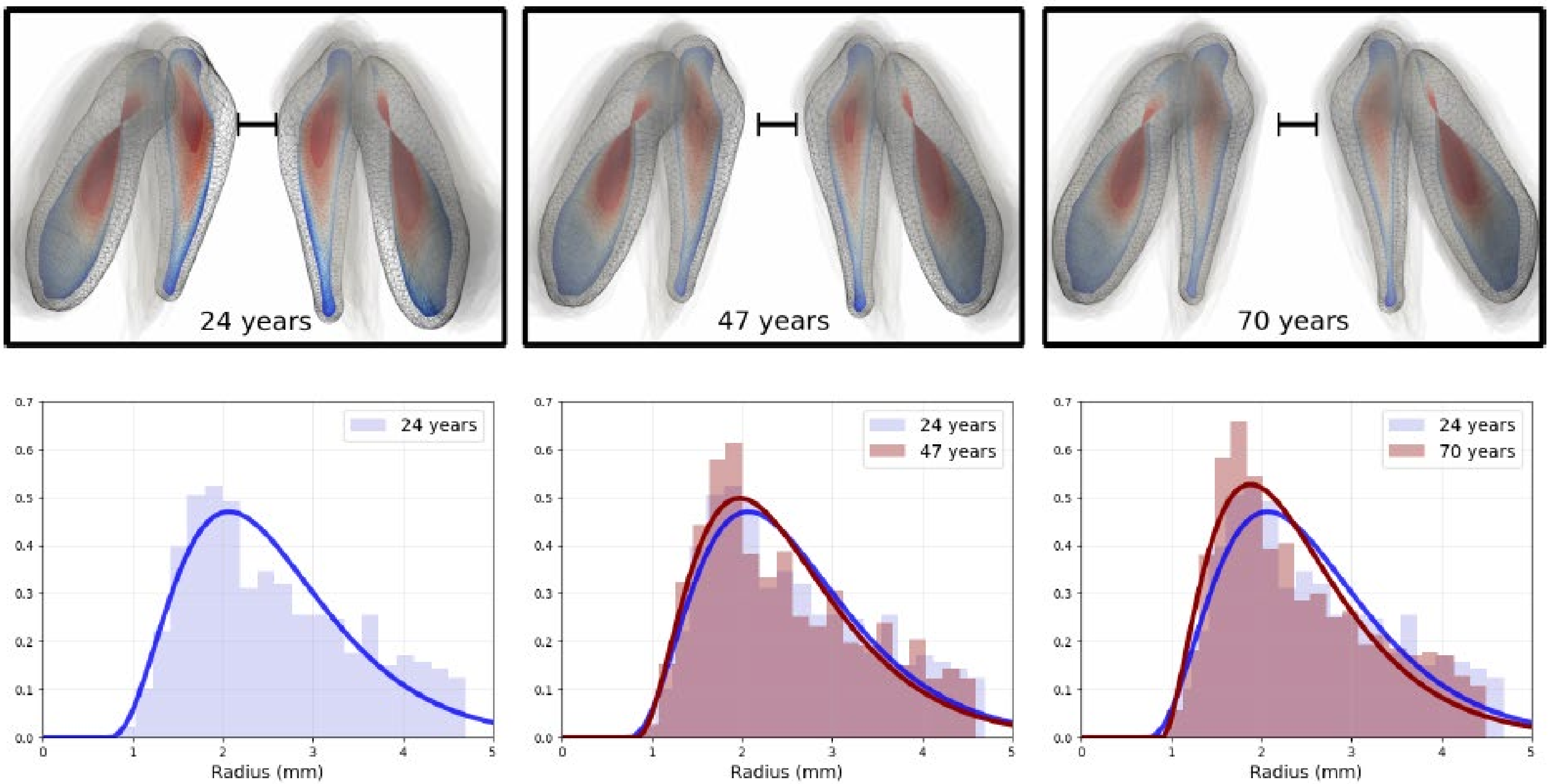
4D Normative Shape Atlas: 23 to 88 years, 243 subjects

- Map 4D Model of Individuals into 4D Normative Atlas
- Analysis of Shape Distance to Norm: Decoupling of age effects versus pathological progression
- Compare change trajectories

S. Hong et al, SPIE 2017, MICCAI 2019

See also: Disentangling normal aging from Alzheimer's disease in structural magnetic resonance images, Lorenzi, Pennec, Frisoni, Ayache, ADNI, Neuriobiology of Aging, 2015

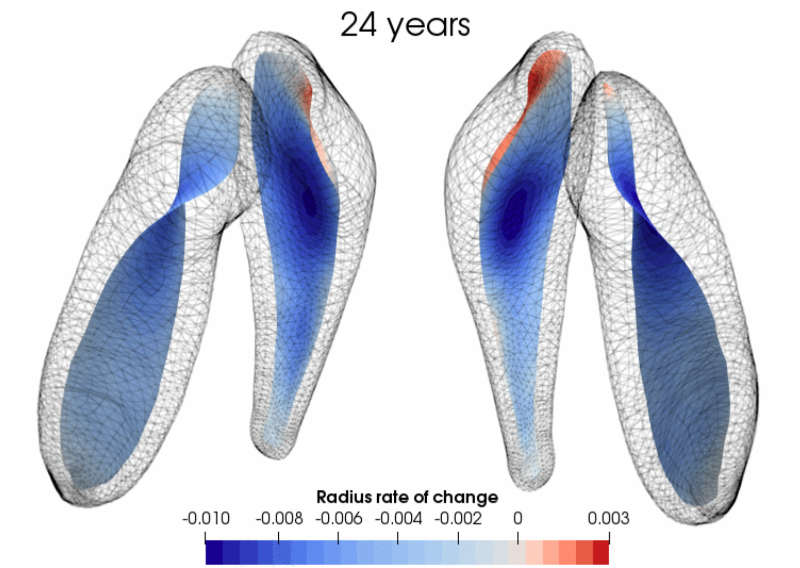
Age-related changes: Longitudinal CMreps

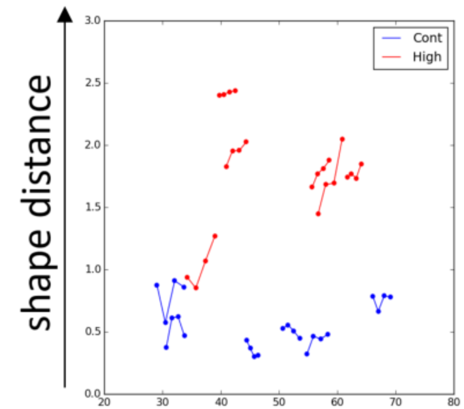


Skeletal radius histogram: Thinning from 24 to 70 years

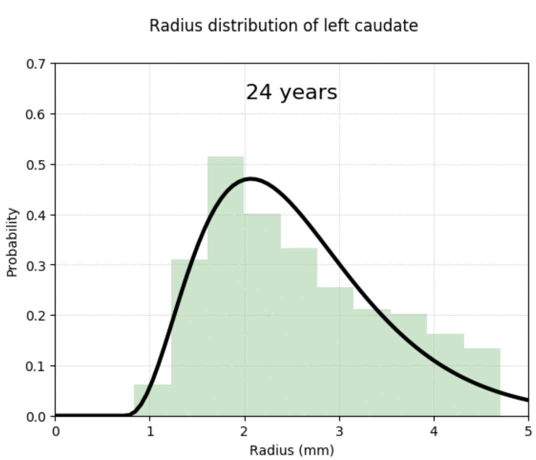
S. Hong, J. Fishbaugh et al, SPIE 2017, MICCAI 2019

Preliminary Results Huntington's



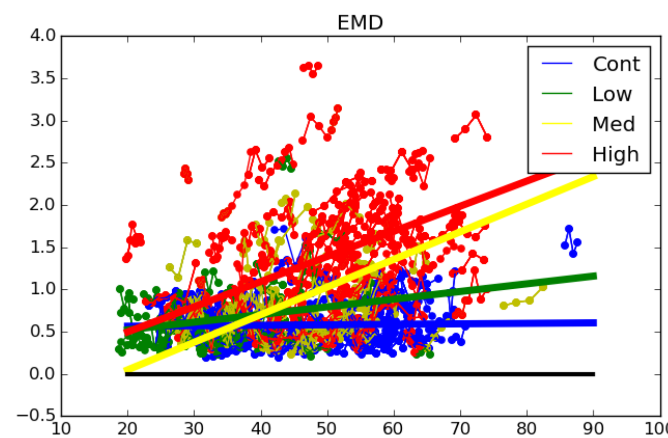


- Controls
- High Risk



Shape Thinning/ Degeneration:

Shift to lower values (left)



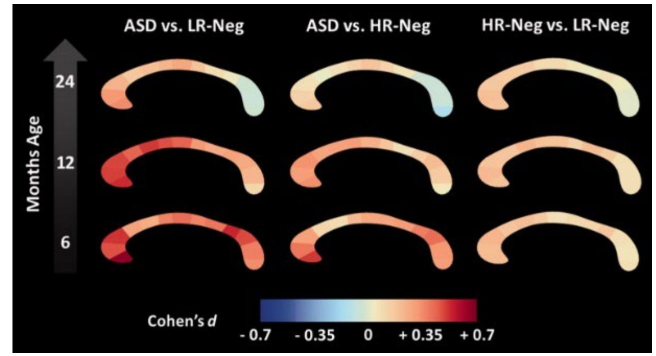
S. Hong, J. Fishbaugh et al, SPIE 2017, MICCAI 2019

Contents

- Abridged History of Shape Analysis
  - Kendall Shape Space, SSM, ASM, AAM
  - Geometry Representations: Boundary, Skeleton, Harmonics, Graph Spectra, Distance Transform, ..
  - Shape Statistics via Deformations
- Current and Future
  - Problems with Size Normalization
  - Longitudinal Shape Analysis
  - Shapes come with covariates (sex, age, diagnosis, test scores, …)

Biological Shape Analysis

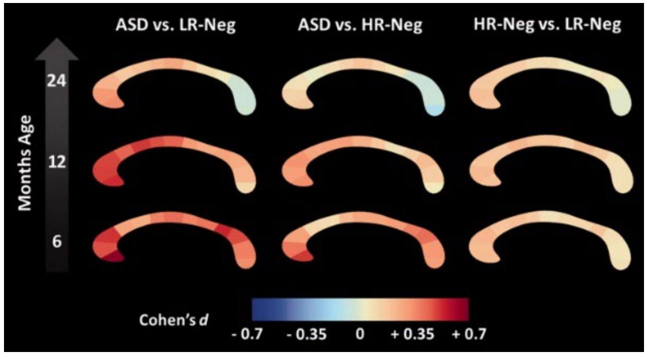
- Shape analysis is rarely just a two group classification problem.
- Biological shapes comes with covariates: Age, sex, group, disability score, etc.
- Traditional concept:
  - Extract shape parameters
  - Hand “numbers” over to biostatisticians



Statistical shape modeling followed by generalized linear modeling with covariates and group testing (e.g. Wolff, Gerig, et al., Brain 2015).

Biological Shape Analysis

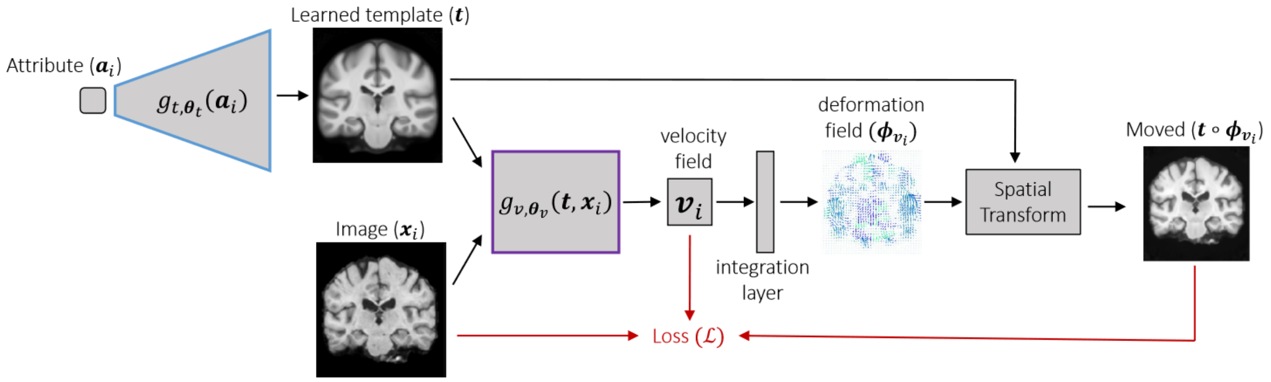
- Shape analysis is rarely just a two group classification problem.
- Biological shapes comes with covariates: Age, sex, group, disability score, etc.
- Traditional concept:
  - Extract shape parameters
  - Hand "numbers" over to biostatisticians
- New: Integrate covariates into shape modeling & analysis step.
- Goal: Improved understanding of shape/covariate relationships.



Statistical shape modeling followed by generalized linear modeling with covariates and group testing (e.g. Wolff, Gerig, et al., Brain 2015).

Voxelmorph

- Dalca et al., Learning Conditional Deformable Templates with Convolutional Networks, NeurIPS 2019



- The network takes as input an image **and an optional attribute vector.** The upper network gt,θt (·) outputs a template, which is then registered with the input image by the second network gv,θv (·). The loss function, derived from the negative log likelihood of the generative model, leverages the template warped into t ◦ ϕvi .
- framework also enables learning a conditional template function given instance attributes, such as the age and sex of the subject in an MRI. Once learned, this function enables rapid synthesis of on-demand conditional templates. For example, it could construct a 3D brain MRI template for 35 year old women

https://arxiv.org/abs/1908.02738

Conditional Atlas Building: VoxelMorph: DL-Based Approach

- Use **all study image data** with multiple covariates.
- Conditional template estimation as function of continuous and/or categorical attributes (age, sex, diagnosis, etc.)

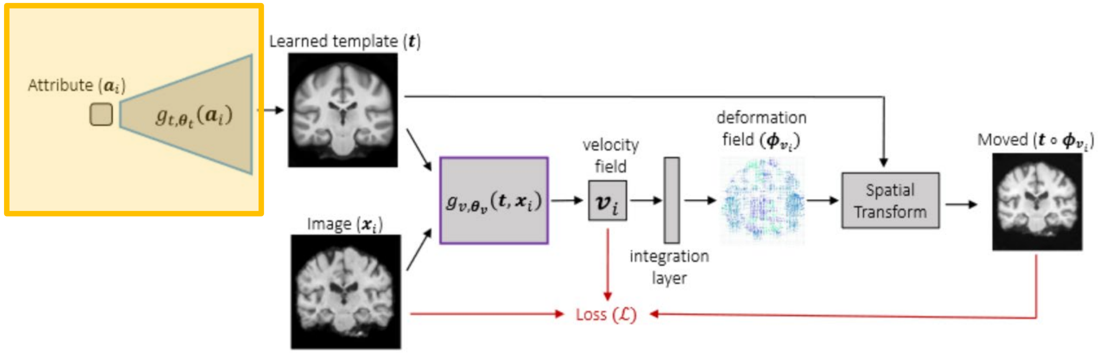


Figure 2: **Overview.** The network takes as input an image and an optional attribute vector. The upper network $g_{t,\theta_t}(\cdot)$ outputs a template, which is then registered with the input image by the second network $g_{v,\theta_v}(\cdot)$. The loss function, derived from the negative log likelihood of the generative model, leverages the template warped into $t \circ \phi_{v_i}$.

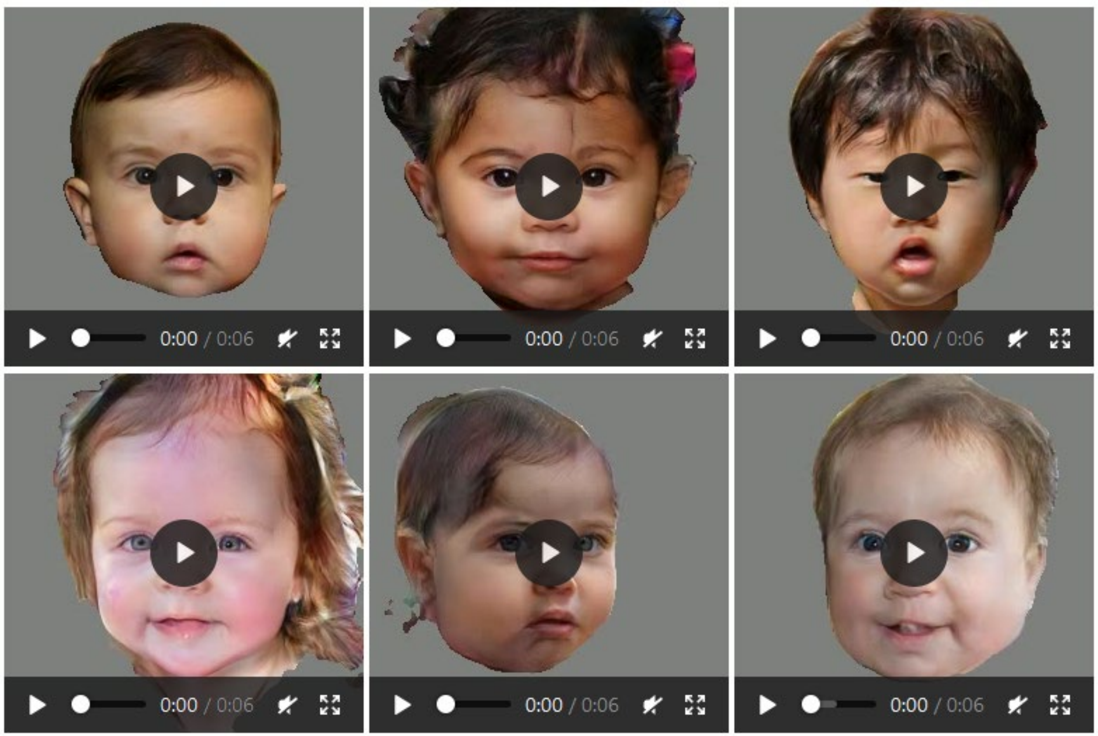
Adrian Dalca, et al.. Learning conditional deformable templates with convolutional networks. In Advances in neural information processing systems, pages 806–818, 2019. VoxelMorph

Dey, Ren, Dalca, Gerig. “Generative Adversarial Registration for Improved ConditionalDeformable Templates", ICCV, 2021.

Shapes/Images with Covariates

Lifespan Age Transformation Synthesis

Roy Or-El[1] Soumyadip Sengupta[1] Ohad Fried[2] Eli Shechtman[3] Ira Kemelmacher-Shlizerman[1]
[1]University of Washington [2]Stanford University [3]Adobe Research



FFHQ Dataset

Lifespan Age Transformation Synthesis
Roy Or-El, et al., ECCV 2020

Dataset consists of 70,000 high-quality PNG images.

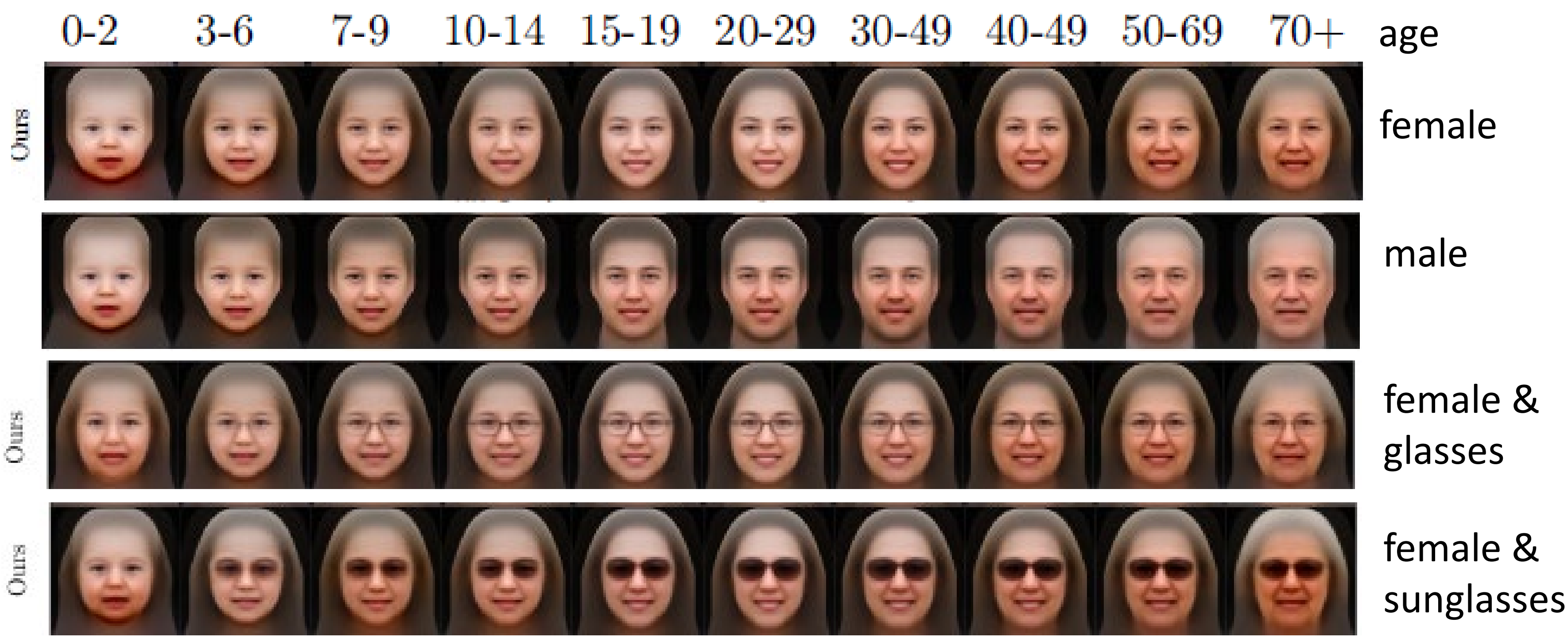
Life-span: Ages 0—70
Conditions: male/female, Age, (sun)glasses

http://grail.cs.washington.edu/projects/lifespan_age_transformation_synthesis/
https://arxiv.org/pdf/2003.09764.pdf

Conditional Atlas Building: FFHQ

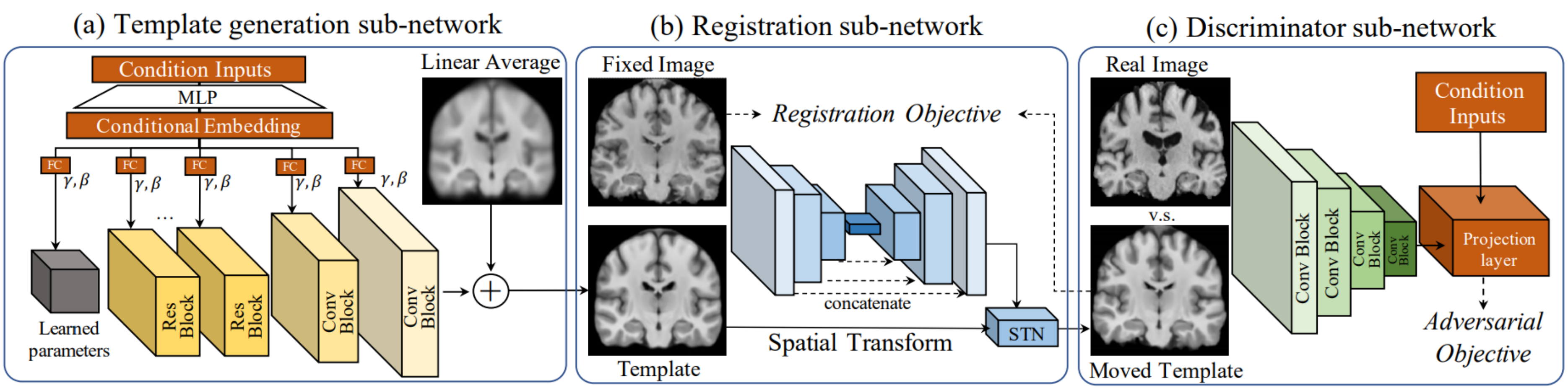
FFHQ Aging Dataset:

Fig. 3: FFHQ-Aging dataset. We label 70k images from FFHQ dataset [18] for gender and age via crowd-sourcing. In addition, for each image we extracted face semantic maps as well as head pose angles, glasses type and eye occlusion score.



Dey, Ren, Dalca, Gerig. “Generative Adversarial Registration for Improved Conditional Deformable Templates", ICCV, 2021.

Framework Overview
(Dey, Dalca at al., ICCV 2021)



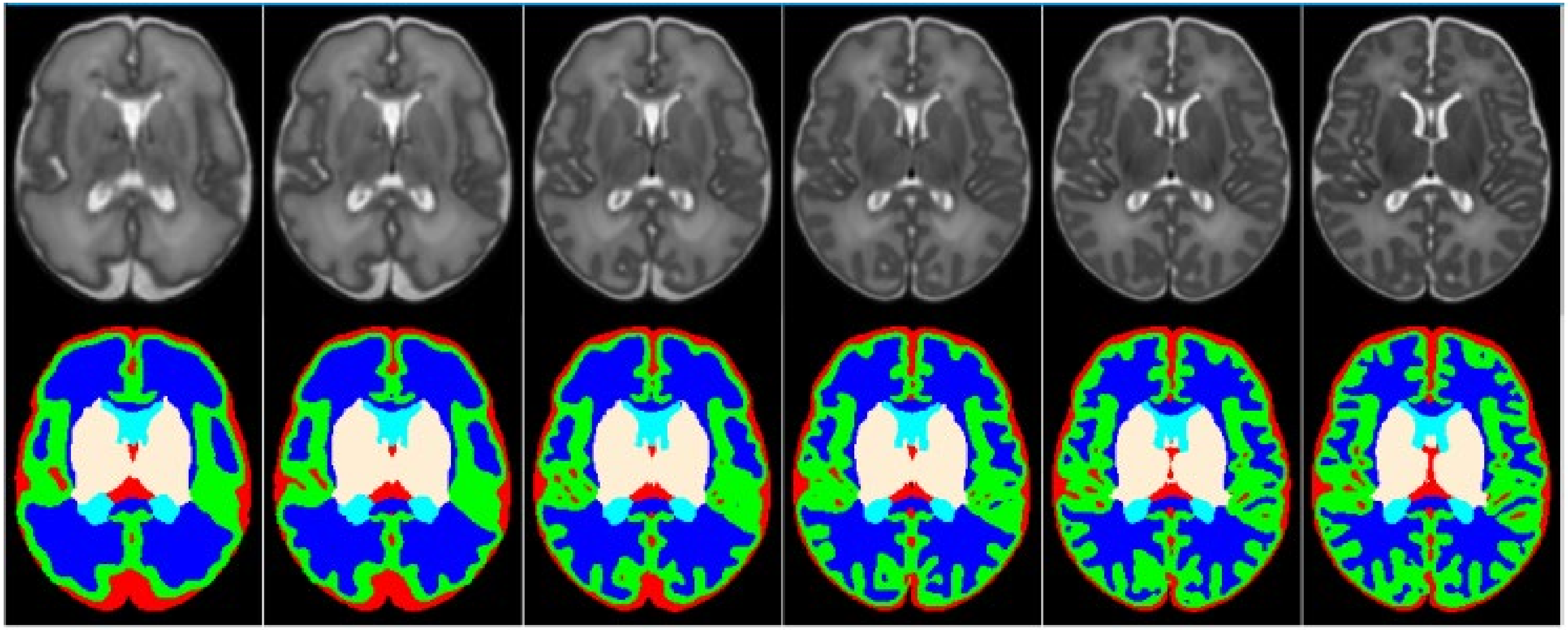
- Feature-level conditioning
- High parameter-efficiency for several conditioning attributes

- Diffeomorphic Displacements via Stationary Velocity Fields
- Smooth & *central* deformations

- GAN conditioning for continuous *and* categorical attributes
- Extensive training stability pipeline

Dey, Ren, Dalca, Gerig. "Generative Adversarial Registration for Improved ConditionalDeformable Templates", ICCV, 2021.

Conditional Atlas Building



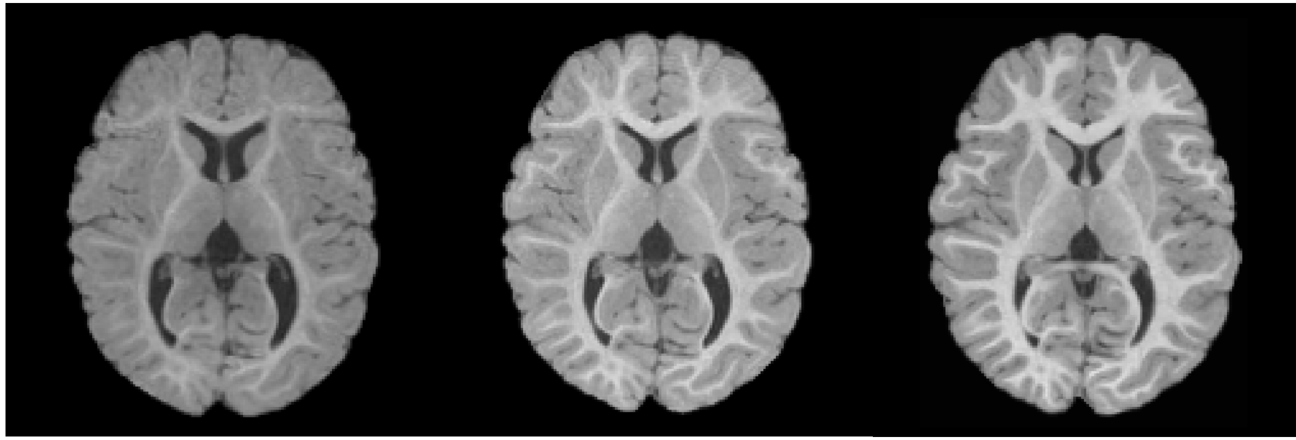
558 T2w postnatal MR images from dHCP release 2, 20 to 44 weeks:
http://www.developingconnectome.org/project/

- Emer J Hughes, et al. A dedicated neonatal brain imaging system. Magnetic resonance in medicine, 78(2):794–804, 2017.
- Antonios Makropoulos et al. The developing human connectome project: A minimal processing pipeline for neonatal cortical surface reconstruction. Neuroimage, 173:88–112, 2018.

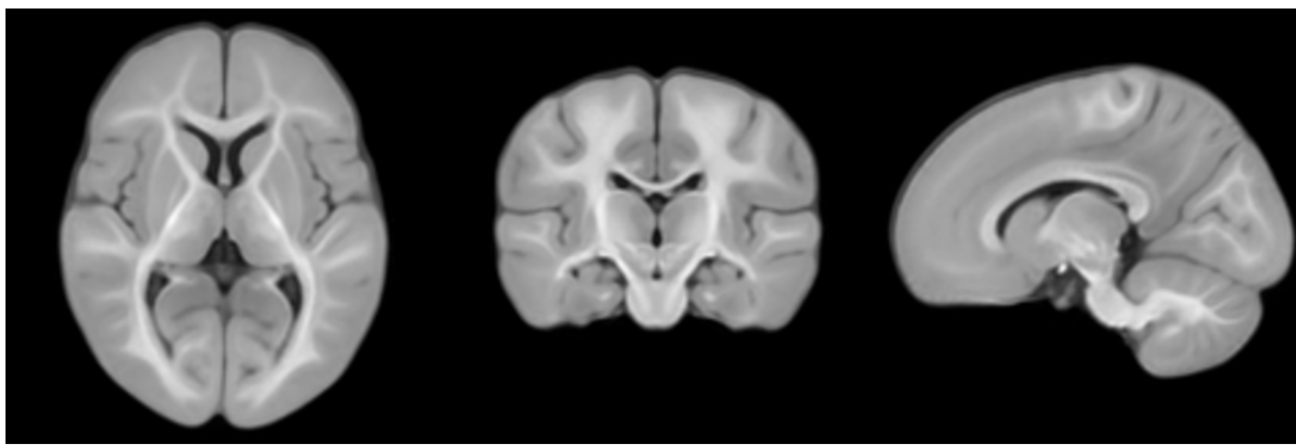
Dey, Ren, Dalca, Gerig. "Generative Adversarial Registration for Improved ConditionalDeformable Templates", ICCV, 2021.

ACE-IBIS: Continuous Growth Templates

All 6/12/24 month T1w/T2w images used (>1200 image data).

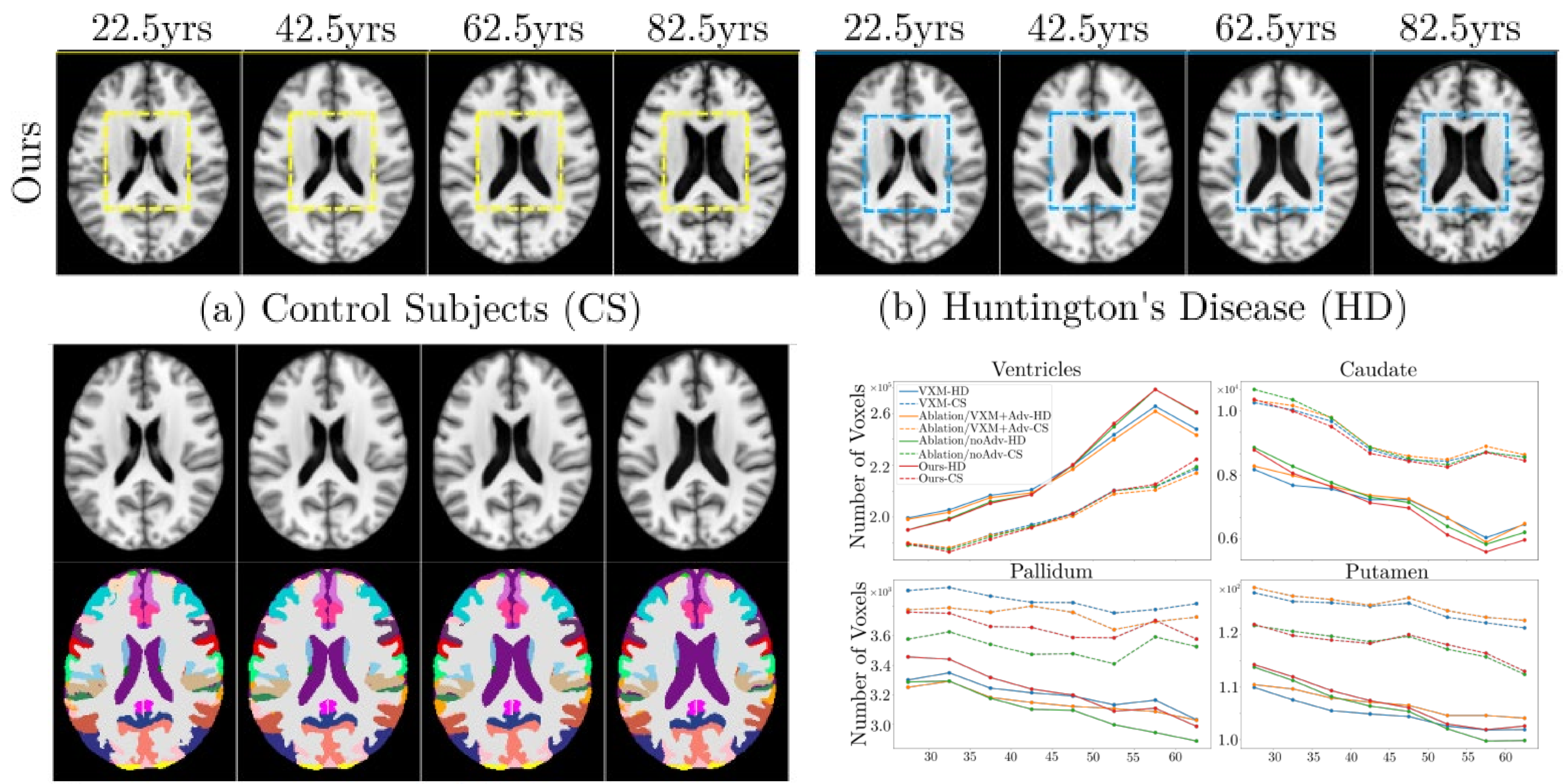


Conditionally, the synthesized templates faithfully capture the process of neuro-development.



Neel Dey, Mengwei Ren, Adrian V. Dalca, Guido Gerig; "Generative Adversarial Registration for Improved Conditional Deformable Templates", Proc. ICCV'21

Conditional Atlas Building
HD study: Controls vs. Diagnosed

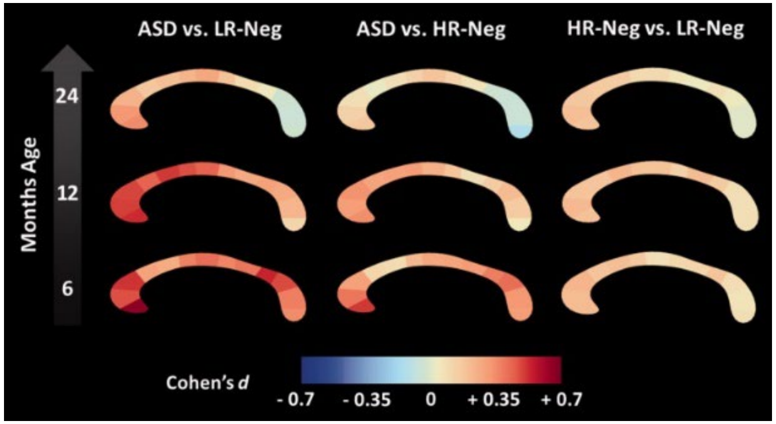


Work in Progress: Analysis of longitudinal image changes as functions of covariates (here age and group).

Dey, Ren, Dalca, Gerig. "Generative Adversarial Registration for Improved Conditional Deformable Templates", under review at ICCV, 2021.

Folding Statistical Modeling into Shape Analysis

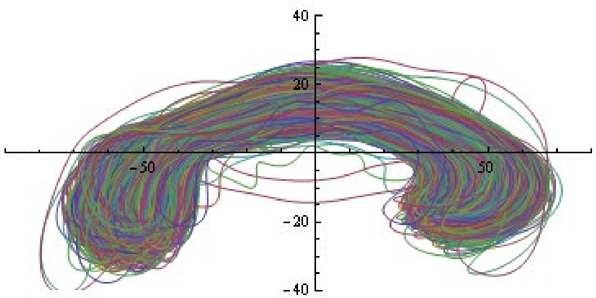
- **Approaches so far:**
  - YOU do the shape modeling
  - Statistical shape modeling followed by generalized linear modeling with covariates and group testing (e.g. Wolff, Gerig, et al., Brain 2015).
- **New:**
  - Novel hierarchical multi-geodesic model that can account for the effect of subject-specific covariates to the development (slope) of a shape change.
  - **Hierarchical Multi-Geodesic Model for Longitudinal Analysis of Temporal Trajectories of Anatomical Shape and Covariates**
- **Goal**:
  - Improved understanding of shape/covariate relationship.



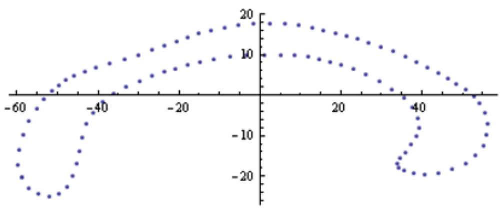
Statistical shape modeling followed by generalized linear modeling with covariates and group testing (e.g. Wolff, Gerig, et al., Brain 2015).

Joint Shape & Covariate Analysis

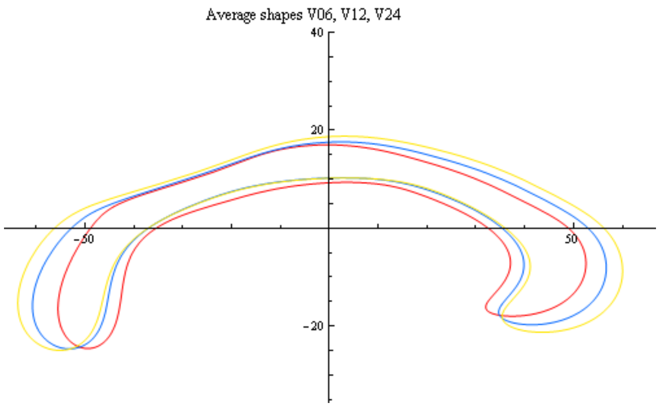
Shape space is non-Euclidean: Geodesic model on Riemannian manifold.



1040 corpus callosum shapes, ACE-IBIS, sampled by boundary points.



Longitudinal Shape Change per Subject



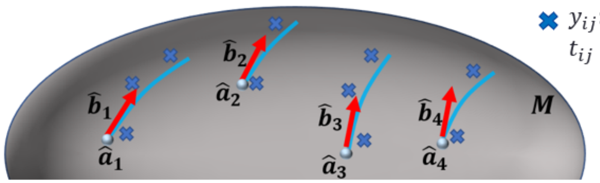
Sungmin Hong et al., MICCAI 2019

Hierarchical Model ("mixed effects model"), but with covariates and time

Estimate a subject-wise trend as a univariate geodesic model [1].

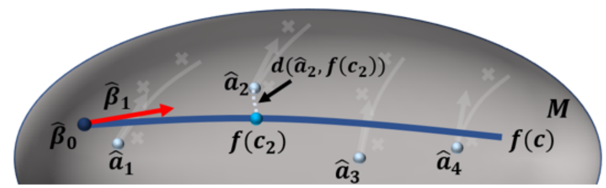
$$(\hat{a}_i, \hat{b}_i) = \underset{a_i, b_i}{\operatorname{argmin}} \sum_{j=1}^{N^i_{obs}} d^2(y_{ij}, Exp(a_i, b_i t_{ij})), \qquad Y_i = Exp(\hat{a}_i, \hat{b}_i t)$$

Y_i : Subject-wise model
y_{ij}: Observations
t_{ij} : Observation Times



The intercept model $f(\eta)$ formulated as a multivariate geodesic model [2].
Models the effects of covariates to the baselines of subject-specific trends.

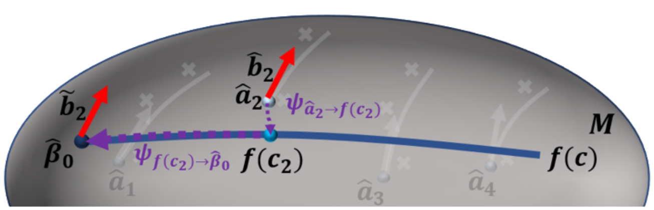
$$f(\boldsymbol{\eta}) = Exp(\beta_0, \beta_1\eta_1 + \ldots + \beta_{N_\eta}\eta_{N_\eta})$$



Population Level $Y = Exp(Exp(f(\boldsymbol{\eta}), g(\boldsymbol{\theta})t), \epsilon)$

- Estimate a multi-geodesic model with a set of subject-specific geodesic models

Slope Model $g_0(\boldsymbol{\theta}) = \gamma_0 + \gamma_1\theta_1 + \ldots + \gamma_{N_\theta}\theta_{N_\theta}$ $\hat{g}(\boldsymbol{\theta}) = \psi_{\hat{\beta}_0 \to \hat{f}(\boldsymbol{\eta})}(\hat{g}_0(\boldsymbol{\theta}))$



Stop-Over Parallel Transport

40/61

Sungmin Hong et al., MICCAI 2019

Study on ACE-IBIS Data (72 shapes, 24 ASD* subjects)

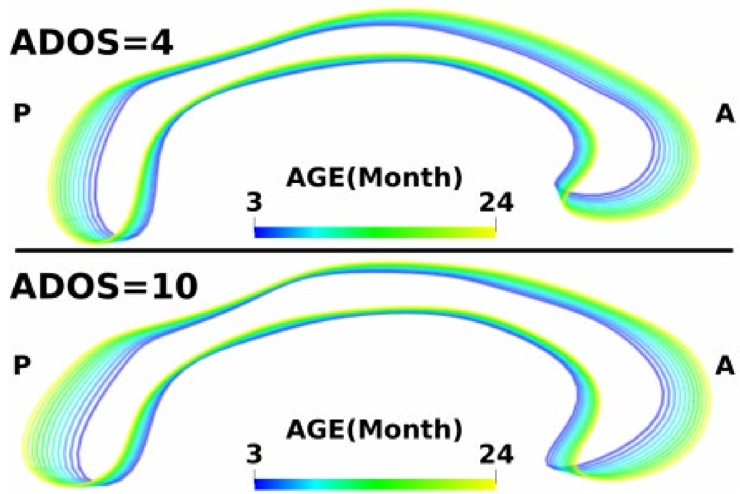
Towards <u>Interpretability</u> of Shape Analysis

Corpus Callosum

Autism Diagnostic Observation Schedule (ADOS) Score

- Clinical test score on the behavioral and cognitive abilities
- 4 : Low ~ 10 : High

Shape Space : Scale x Kendall Shape - $\mathbf{M} = \mathbf{R} \times \mathbf{CP}^{\mathbf{k}-2}$



Finding: Increased expansion of the anterior CC (genu and rostral body) over time for subjects with higher ADOS scores confirms expansion of CC in ASD.

*Autism Spectrum Disorder

Sungmin Hong et al., MICCAI 2019

Study on ACE-IBIS Data (72 shapes, 24 ASD* subjects)

Towards Interpretability of Shape Analysis

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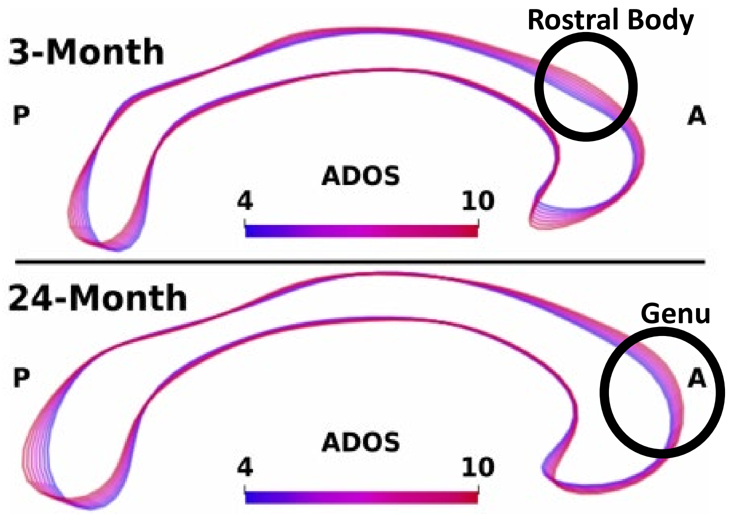

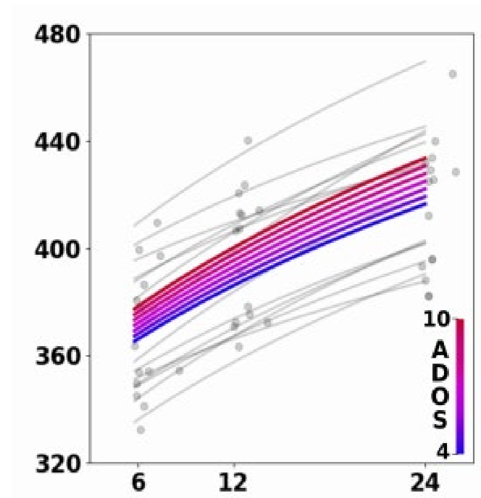

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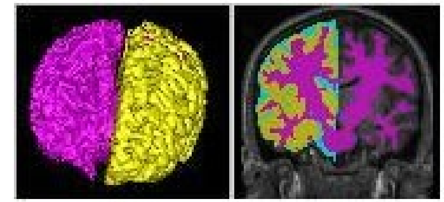
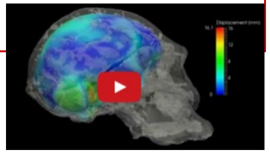
* **S. Hong**, **J. Fishbaugh**, J. Wolff, M. Styner, **G. Gerig**, "HMG Model for Longitudinal Analysis of Temporal Trajectories of Anatomical Shape and Covariates," MICCAI 2019

Software Engineering & Sharing

- Open-source/open-platform
- Industrial collaborations

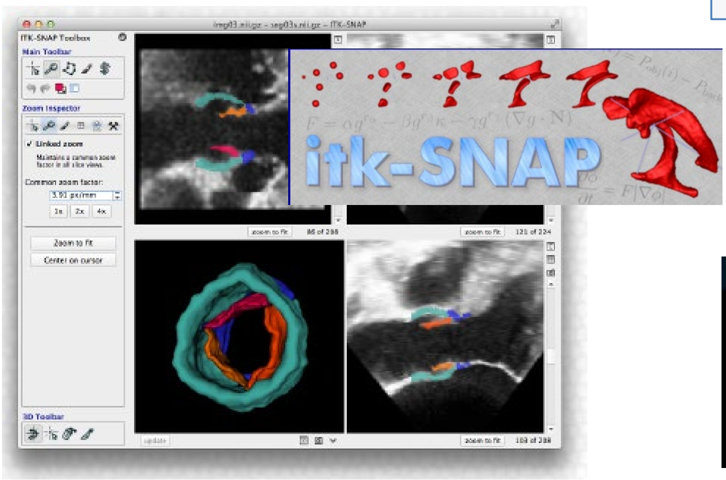


Deformetrica



3DSlicer

neel-dey / Atlas-GAN



Slicer SALT
Shape AnaLysis Toolbox

Acknowledgements

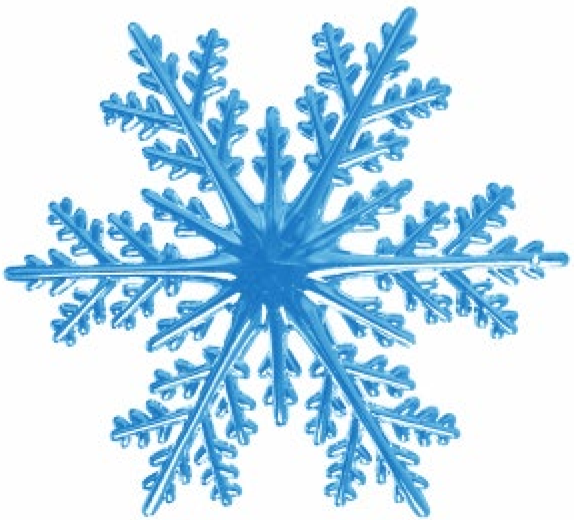
- **NIH-NIBIB**: SlicerSALT, **Shape** Analysis Toolbox
- **NIH-NICHD**: ACE-IBIS (**Autism** Center)
- **NIH NINDS**: **Down's** Syndrome
- **NIH-NIDA:** Brain dev. of offsprings of **cocaine abusing** mothers
- **NIH-NEI**: AMD: Age-related **Macular Degeneration**
- **NIH-NEI:** Novel **Glaucoma** Diagnostics for Structure & Function
- **NYC CATT:** NY Center for Advanced Technology in Telecomm.
- **Kitware Inc.**

Kitware itk vtk CMake

Quotation of the Day

"The perfection of mathematical beauty is such ….. that whatsoever is most beautiful and regular is also found to be the most useful and excellent."

D'Arcy Wentworth Thompson



Are you still in “Good Shape”?

Bob Dylan & the Band:
The Shape I'm In

Go out yonder, peace in the valley
Come downtown, have to rumble in the alley

Oh, you don't know the shape I'm in

Has anybody seen my lady
This living alone will drive me crazy

Oh, you don't know the shape I'm in

I'm gonna go down by the wa - ter
But I ain't gonna jump in, no, no
I'll just be looking for my mak - er
And I hear that that's where she's been? oh
Out of nine lives, I spent seven
Now, how in the world do you get to heaven

Oh, you don't know the shape I'm in

Conclusions

- "Shape" is a fundamental concept of human perception.
- "Shape" is an essential concept for Medical Image Analysis.
- Many routine applications exist, e.g. selection of optimal implants.
- Foundational mathematical & statistical concepts help to make the field much more mature, but:
  - Need to bridge the gap between the **"Beauty of Math"** and **"Biological Shape".**
  - Biological shapes come with sets of **covariates,** not just two groups.
  - Biological shapes are **deformable** and show **changes over time**.
  - **P-values** are common, but we need to explain shape changes to clinical researchers → **Interpretability**.