## **Summary:**



## **Shape Representations and Statistics**

- Shape Representations
  - Local Properties
  - Shape Spaces
  - Object vs. Diffeomorphism representations



- Multi-entity objects, shape over time
- Shape statistics
  - Over Euclidean spaces
    - PCA, DWD, Permutation methods of hypothesis testing
    - Over diffeomorphism momenta
  - Euclideanization, esp. PNS, log (positive feature)
  - Over curved manifolds
  - Correspondence

### **Local Properties**

- Normal directions and tangent directions
- Fitted frames to boundary
  - Later: to interior via s-reps onion skins
  - Space curves: Frenet frames, curvature, torsion
- Curvatures: curves and surfaces
  - Esp. vertices and crests
  - Curvedness (C) and shape type (S)
- Manifolds and geodesics
- Distance measures
  - Riemannian metrics
  - Metric tensor: M<sub>II</sub>









# **Shape Representation Categories**



- Landmarks
- Objects
  - Boundaries
    - Points
    - Normals
    - Spherical harmonics
    - Signed distance images
  - Skeletal models
    - Multifigure models
  - Landcurves: currents
  - Multi-object representations

#### • Diffeos from a central example

- From boundaries of mean
- From s-reps of ellipsoid













#### **Shape Representation by Boundary Points**



- Points in correspondence (PDM); or Meshes
  - Correspondence produced by
    - Diffeomorphisms
    - Skeletal models
    - Entropy minimization
- Spherical harmonics
- Points with on landcurves (Currents)
- Normals with correspondence mod-ed out
- Signed distance images, esp. for 3D visualization
- Alignment by Procrustes
- Aligned PDMs on high-dimensional sphere









#### Shape Representation Designed for Correspondence

- Normals with correspondence mod-ed out [Srivastava, Kurtek]
- Skeletal models fit from ellipsoid
  - Interior positions correspondence
- ?? Diffeomorphisms based on boundaries
  - Points
  - Curves, e.g., crests



#### **Shape Representation by Skeletal Models**

- Medial and skeletal mathematics
  - Blum medial axis: bitangent spheres
    - Geometric relations among axis and width
    - Singularities: branching, ends, etc.
    - Radial shape operator  $S_{rad}$
    - Radial distance
      - Geometry of onion skins
    - Cm-reps based on Blum math
- Skeletal generalization: S-reps
  - Skeleton and spokes
  - Discrete s-reps
  - Deformation from ellipsoids
    - Alignment-free coordinates
    - Fitted frames
  - Slabular planar cross-section sweeping
    - Taheri s-reps: spine















#### Shape Representation by Skeletal Models

- S-reps
  - Fitting to boundaries
    - Optimization



Bdry implied by s-rep



- Cm-reps [2 lectures by P. Yushkevich]
  - Based on mesh and Blum conditions
    - Explicit: inverse skeletonization using biharmonic PDE
    - Implicit: deformation of boundary & medial locus preserving medial linkages to boundary
      - Like s-reps, starts from model with known branching topology and medial locus
    - Based on splines in  $\underline{x}$  and width



parametric medial model



### **Euclidean Statistics Methods**

- Means
- PCA: feature reduction and removal of noise
- Classification
  - Producing separation direction
  - Multi-entity analysis: DIVAS
- Hypothesis Testing
  - Permutation tests
  - Corrections for multiple tests
- Segmentation by posterior optimization
  - Priors via shape representation statistics
  - Likelihoods via shape-based coordinates
- Longitudinal methods

## **Euclidean Statistics Methods**, 2



- PCA: feature reduction and removal of noise
  - Eigenanalysis of covariance
  - Features via inner product with eigenvectors
  - And other related producers of modes of variation
- Classification
  - Producing separation direction
    - Distance-Weighted Discrimination
      - $-\Sigma 1/r + \Sigma$  misclassification penalties
    - Kernels, esp. radial basis functions
    - Multi-entity analysis: DIVAS
  - Producing & using histograms along separation direction

## **Euclidean Statistics Methods, 3**

- Hypothesis Testing
  - Permutation tests
  - Corrections for multiple tests
- Segmentation by posterior optimization
  - Priors via shape representation statistics
  - Likelihoods via shape-based coordinates
  - S-reps provide both
- Longitudinal methods
  - Variations on the Euclidean space
    - Curves over t for intra-subject distances
    - Inter-subject distances between intra-subject curves
    - Generalized linear models
  - Diffeomorphisms' momenta
    - Intra subject diffeos over t
    - Inter-subject diffeos



#### Applicability of Marchenko-Pastur Analysis on PNS modes [Choi]

- Our "eigenanalysis" is via PNS, i.e., on sphere
- Hyo Young Choi studied this problem
  - By producing derived features from the sphere that do follow the MP distribution
    - But she only studied great subspheres, whereas the common analysis uses small subspheres, when hypothesis test supports But the open problem remains: How to select the eigenmodesde by depolluting the MP-plot, given noise properties from high eigenvalues which show ~pure noise
  - Besides dealing with the actual subsphere approach

## **Euclidean Statistics Methods, 4**

- Multi-entity statistics (DIVAS, AJIVE)
  - Noise removal via PCA of each entity
  - Space of subjects: tuple of noise-removed features based on PCAs
    - Subspaces each specified by orthogonal linear combinations of subjects-space features
  - Subspace of joint features via Principal Angle Analysis
  - Subspaces of individual features for each individual
    - Orthogonal to joint subspace
    - Not necessarily orthogonal to subspace of other individuals



from Prothero et al.





# Shape Representation by Deformations

- Diffeomorphisms: velocities
  - Points data
  - Currents data
    - For landcurves
    - For surfaces
- Displacements
  - Thin-plate splines
  - B-splines
  - Elastic deformations





## **Thin Plate Splines Method**

- Fast: based on a solution to linear equations
  - Typically preceded by optimum affine transformation
- Elastic warp in each variable
  - $-\underline{\mathbf{x}'}(\underline{\mathbf{x}}) = \underline{\mathbf{c}} + A\underline{\mathbf{x}} + \sum_{\mathbf{j}} \underline{\mathbf{w}}_{\mathbf{j}} \mathbf{U}(|\underline{\mathbf{x}} \underline{\mathbf{x}}^{\mathbf{j}}|)$
  - Basis functions  $U(|\underline{x}-\underline{x}^{j}|)$  depend on moving image's landmarks  $\underline{x}^{j}$ 
    - Radial bases:  $U(d) = d^2 \log d$  for 2D,  $d^3$  for 3D
- Solve linearly for c, A, {<u>w</u><sub>j</sub>} based on {<u>Δx</u><sup>j</sup>}
  Minimizing Frobenius norm: ∫<sup>∞ space</sup> Σ<sub>all</sub> 2nd partial derivatives<sup>2</sup>, so smooth
  - 27 terms for 3D: 9 for  $\Delta x(x,y,z)$ , 9 for  $\Delta y(x,y,z)$ , 9 for  $\Delta z(x,y,z)$
- Not necessarily diffeomorphic; may produce folding Normally OK if displacements << inter-landmark spacing</li>
- Not symmetric, not affine invariant

#### Large Deformation Diffeometric Metric Mapping (LDDMM) Methods



- Consider the shape space of diffeomorphisms
- Let metric on that space measure spatial smoothness within a velocity image
- We want the shortest geodesic from Identity mapping to the diffeomorphism that maps the corresponding points onto each other
- Typically requires iterative optimization
- Implementations
  - Deformetrica
    - Can also use corresponding space curves
  - Joshi

#### Statistics on Curved Manifolds [Esp. Fletcher lecture]



- Exp<sub>p</sub> and Log<sub>p</sub>
- Fréchet and backwards means
- Geodesics
  - And other polynomial generalizations
- Shape spaces, esp. spheres and polyspheres: PNS
- Classification via separating directions
  - Esp. DWD
    - Advantage over SVM
- Longitudinal statistics
  - See later: longitudinal stats via diffeomorphisms



#### Statistics on Curved Manifolds, 2 [Esp. Fletcher lecture]



- Geodesics
  - Representation by point and direction
  - Generalization of line in Euclidean space
  - Yielding distances, thus Fréchet mean, princi directions
  - Polynomial generalizations
- Shape spaces, esp. spheres and polyspheres: PNS
- Classification via separating directions
  - Esp. DWD
    - Advantage over SVM
- Longitudinal statistics
  - Like Euclidean, but using geodesics, etc.
  - See later: longitudinal stats via diffeomorphism



### **Statistics in Shape Spaces**



- Commensuration: scaling and weighting
- Euclideanization
  - -Positive scalars
  - -Directions
  - -Normalized PDMs
- Directly on curved manifold





- Importance
- Relation to PCA
- Production
  - Analytic form in Euclidean space
    - Given Principal frame R and eigenvalues  $\Lambda$
  - Diffusion:  $\partial f(\underline{x},t)/\partial t = \nabla^2 f$  with  $f(\underline{x},0) = \delta(\underline{x})$  with  $t = \sigma^2/2$
  - Brownian motion

#### • On curved surfaces, esp. spheres

- Wrapped Gaussian
- von Mises distribution
  - ~ wrapped Gaussian on sphere
  - With an analytic form not needing sums over wraps
  - Most commonly used due to its rather simple form
- Brownian motion (random walks)
  - Moving frames [Sommer]

#### **Statistics on PDMs**



- Procrustes alignment
  - Centering
  - Scaling via  $\Sigma$  squares
  - Rotation via 2<sup>nd</sup> moments
- Principal nested spheres for feature reduction
- Transformation to spherical harmonics coefficients





## Statistics on PDMs Transformed into Spherical Harmonics Coefficients

- Each object mapped from sphere:  $\underline{x}(\theta, \phi) = \sum_i \underline{b}_i \psi^i(\theta, \phi)$ 
  - Discretized with equal area spherical triangles
  - Can do Euclidean statistics of the <u>b</u> values over a population
  - <u>b</u> values are determined globally



- Object features: coefficients of basis functions on the sphere
  - Basis functions organized by frequency in latitude and longitude
  - From  $\underline{x}(\theta, \phi)$ , coefficients easily obtained by dot product w/ basis
  - For <u>any</u>  $(\theta,\phi)$ , <u>x</u> $(\theta,\phi)$  (e.g., mean) can be computed from coefficients
    - Correspondence via  $(\theta, \phi)$ , but empirically not always adequate

## How to get the point coordinates on the object onto the sphere



- Equal area mapping [Brechbuehler]
  - Or alternative of conformal mapping, which is angle preserving
- North pole and Greenwich meridian via best fitting ellipsoid
  - Might need straightening as a preprocessing



• Possible use of s-reps implied spacing

## Correspondence

Α В А B А High surface entropy



Non-tight distr'n (high ensemble entropy)

- Via entropy: produce tightest ensemble  $p(\underline{x})$ • Possibly also including C, S as features [Oguz] - Registration

Approaches

- Via landmarks
  - thin plate splines
  - diffeo guaranteeing methods
- Via transformation from basic object reflecting richer geometry, such as skeletal

Low surface entropy (uniformity)

А



# **Correspondence via Entropy of PDMs**

- Shapeworks [Cates, Whitaker]
  - Ensemble entropy H(ensemble) should be low (p(<u>x</u>) tight)
  - Entropy H(point positions along boundary for each case) should be high (uniformly distributed)
  - So  $\min_{\underline{x}} [H_{\text{training cases}}(\underline{\text{geometry}}) \Sigma_{\text{training cases}} H(\text{points on training case})]$
  - Entropy via PCA: H(nD Gaussian) = (n/2) [1+ ln( $2\pi$ ) + avg ln  $\lambda$ ]
  - Optimize by successively doubling number of points
    - Slow and often finds local optimum







#### Correspondence via Skeletal Mapping from Ellipsoid to Object

- Mapping via diffeomorphism such that
  - Vertices, crests map onto vertices
  - Crests map onto crests, crests
  - Straight spokes, radial distances map onto straight spokes, radial distances



 Defines a fitted frame at every sampled spoke point – i.e., on onion skins









[Pizer, *Skeletons, Object Shape Statistics*, Frontiers in Computer Science, 2023, on google drive for Pizer, Comp 790-6

#### Srivastava boundary geometry modulo correspondence



- Want representation independent of boundary parameterization
  - So inter-object distances are between equivalence classes over alignment in R<sup>n</sup> and reparameterization should be

$$- \left\| [q_1], [q_2] \right\| = \min_{0 \in SO^n, \gamma \in \Gamma} d_c (q_1, O(q_2 \circ \gamma)) / \sqrt{\dot{\gamma}},$$

- $||A,B|| = distance^2$  between A and B
- $[q_i]$  = equivalence class of  $\Gamma$  = rep'ns  $q_i$  that are reparameterizations  $\gamma$  of boundary of object i
- $d_C$  is  $L^2$  norm on boundary representation (normal)
- *O* is orbit over reparameterizations
- $-= \min_{0 \in SO^{n}, \gamma \in \Gamma} d_{c}(q_{1}, O(q_{2} \circ \gamma)) / \sqrt{\kappa(\gamma)}$

#### Kurtek 2D boundary geometry in 3D modulo correspondence, 3



- Want representation independent of boundary parameterization
  - So inter-object distances are between equivalence classes over alignment in  $R^n$  and reparameterization

 $- d([q_1], [q_2]) = \min_{O \in SO(3), \gamma \in \Gamma} // q_1 - O_{\gamma} q_2 //$ 

- d(A,B) = distance between A and B
- $[q_i]$  = equivalence class of  $\Gamma$  = rep'ns  $q_i$  that are reparameterizations  $\gamma$  of boundary of object i
- $O_{\gamma}$  is orbit over reparameterizations
- In  $q_1$  and  $q_2$  scaled versions of the objects are used
- Minimization of the reparameterizations needs to use its Jacobian, which captures the geometry through its fitted frames



# **Skeletal Representations**

- Conceptually, skeletal representations have the following major advantages over other representations:
  - For correspondence reflect
    - Object width
    - Curvature and direction of the object *interior*
  - Ideally, capture division of object into a tree of protrusions and indentations
  - Separate width and bending features





#### **Medial and Skeletal Mathematics**

- Blum Medial representation
  - Skeleton (medial locus)  $\underline{x}(u,v)$ , spoke length r(u,v)
    - Bitangent spheres entirely in object interior with centers <u>x</u>, radii r
    - Implies spoke rU, orthogonal to boundary where U gives spoke direction – Computed by grassfire
- Folded skeleton: (u,v) spherical
- Interior and boundary positions are parameterized by figural coordinates  $(u,v,\tau_2)$ , with  $\tau_2 =$  (radial distance) fraction of spoke from <u>x</u>(u,v)

$$-\underline{\mathbf{b}}_{\tau 2} = \Psi(\underline{\mathbf{x}}, \tau_2) = \underline{\mathbf{x}} + \tau_2 \mathbf{r} \mathbf{U}$$

• Branch  $(A_1^3)$  and endpoints  $(A_3)$ 















# Blum Ends (Folds) in 2D

- Fold (end) atom
  –Zero object angle
  - -Multiplicity 3 tangency, i.e., osculation
  - $-\theta = 0$ , so  $dr/dx = -\cos(0) = -1$
  - -Infinitely fast spoke swing in limit



## **Medial Mathematics in 3D**

- Medial representation singularities
  - Normal point (no singularity; 2D or 3D):  $A^{2}$  (bitangent)
    - $A_1^2$  (bitangent)
  - Point on branch curve (point for 2D):  $A_1^3$  (tritangent)
  - Point on fold curve (point for 2D):
     A<sub>3</sub> (tangent of order 3 at 1 point)
    - Surprisingly 3<sup>rd</sup> order touching at crest
  - 4 point contact not generic in 2D but is generic in 3D:  $A_1^4$
  - Ends of branch curves in 3D mix normal point and fold of branch :  $A_1A_3$









# **B**

## **Radial Shape Operator [Damon]**

- $S_{rad} = 2 \times 2$  matrix of negative of orthogonal ( $e_u, e_v$ ) coefficients for walking directions
  - $-S_{rad} \underline{w}$  analyzes swing of spoke direction U for any walking direction  $\underline{w}$  on the skeletal tangent plane
- Radial curvatures  $\kappa_r$  are eigenvalues of  $S_{rad}$ 
  - $-r < 1/\kappa_{r_i}$  for all positive radial curvatures and all skeletal points to prevent spoke crossing in closed object interior
  - Boundary curvatures:  $\kappa = \kappa_r / (1 \kappa_r)$
  - Similar formula for onion skins (which have same skeleton)



#### Among Objects with with Spherical Topology, The Ellipsoid: The Primordial Shape

- Ellipsoid with principal radii  $r_x > r_y > r_z$  is simplest shape with a skeleton in the form of a folded surface
  - Blum skeleton is ellipse in (x,y) plane with principal radii:  $(r_x^2 + r_z^2)/r_x$  in x direction ;  $(r_y^2 + r_z^2)/r_y$  in y direction
  - Crest of boundary
    - Medial spokes are from fold
    - Relative max of  $\kappa_1$  in  $\mathbf{p}_1$  direction
    - On ellipsoid is an ellipse in the (x,y) plane
      - It has two opposing vertices





#### **Objects with Spherical Topology and No Protrusions or Indentations**

- Can be understood as diffeomorphism of the ellipsoid
  - It will have at least two opposing vertices and at least one closed crest
- Want to carry all the basic skeletal geometry into the object throughout the diffeomorphism
- Designed to yield a strong correspondence in and near objects' interiors across objects in a population via (θ, τ<sub>1</sub>, τ<sub>2</sub>)











#### Single Figure Objects with Spherical Topology via Diffeomorphism of Ellipsoid

- For correspondence, want the diffeomorphism to carry the basic skeletal geometry of the ellipsoid into the target object
- Because the skeleton is designed to carry the curvature of the interior of the object, it appears not possible for the spokes across the skeleton (with their radial distance τ<sub>1</sub>), which are straight in the ellipsoid's skeleton to remain straight in target object skeleton.
  - But in Taheri's swept plane skeleton coplanar spokes from skeleton with common spine point









#### Single Figure Objects with Spherical Topology via Diffeomorphism of Ellipsoid, 2

• Computation of diffeomorphism from ellipsoid to object can be initialized with curvature-smoothing flow of target object boundary, which will approach ellipsoid



- Before it approaches its limiting sphere
- By conformalized mean curvature flow [Kazhdan]
  - But produces poor correspondence for skeletal geometry maintenance
- Will collapse protrusions and indentations early (see subfigure discussion)
- Its inverse, the desired diffeomorphism, needs to be modified to maintain the basic ellipsoidal skeletal geometry for the object





#### Conformalized Mean Curvature Flow of an Object Boundary

- Original idea was mean curvature flow:
  - $d\underline{b}/dt = H(\underline{b}, t) \mathbf{N}(\underline{b}, t)$ 
    - t is time of flow
  - Though it does deform boundary into a near ellipsoid, it collapses regions of high curvature into a point,
    - i.e., has singularities
- Improved method does not have singularities: conformalized mean curvature flow [Kazhdan]
  - Changes the metric for the flow:
    - Metric is in principal coordinates
    - Metric changes with deformation time t



$$\tilde{g}_t = \sqrt{|g_0^{-1}g_t|}g_0.$$



#### Fitted Frames for Single-Figure Objects

- Objective
  - Like fitted frames for boundary (Cartan), carry local geometry,
    - But here of the closure of interior, not just the boundary
    - Like boundary fitted frames, capture local curvatures,
  - Provides a coordinate system for inter-point geometry
    - Rotations: curvature
    - Inter-point vectors
  - Do it with good correspondence across the object population
- Avoids need for alignment

   No dependence on alignment scale







## Fitted Frames for Ellipsoid, 3

#### • On onion skins

- Thus on skeleton ( $\tau_2=0$ )
  - Respecting side of fold, dependent on  $\theta$
  - And thus on spine ( $\tau_1 = \tau_2 = 0$ )
- Thus on boundary ( $\tau_2=1$ )
- In 2D normal and tangent to onion skin form frame

– In 3D

- Third frame vector **f**<sup>3</sup> is normal to onion skin
- Second frame vector f<sup>2</sup> is along fixed τ<sub>1</sub> as θ varies
   f<sup>1</sup>
- $\mathbf{f}^1 = \mathbf{f}^2 \times \mathbf{f}^3$
- Allows spoke interpolation
  - Rotations of frame
  - r interpolation recognizing dr properties





## Fitted Frames for 3D, Single Figure Object of Spherical Topology

- With proper diffeomorphism, same definition as from ellipsoid
  - In 3D
    - Third frame vector **f**<sup>3</sup> is normal to onion skin
    - Second frame vector f<sup>2</sup> is along fixed τ<sub>1</sub> as θ varies
    - $\mathbf{f}^1 = \mathbf{f}^2 \times \mathbf{f}^3$
- Approximation by carrying f<sup>1</sup> and f<sup>2</sup>
   by diffeomorphism from ellipsoid









# Affine Fitted Frames for 3D Single Figure Object of Spherical Topology



- Carry **f**<sup>1</sup>, **f**<sup>2</sup>, and **f**<sup>3</sup> by diffeomorphism from ellipsoid
  - Will no longer have unit lengths
    - Lengths form features
  - Will no longer be mutually orthogonal
    - Angles form features



Affine fitted frames to a hippocampus skeleton [Z Liu]







## **Skeletal Features for Single Figure Object**

- Skeletal positions
  - Ideally relative to
    - Center point frame, or
    - Neighbor skeletal position frame
- Spoke lengths
- Affine frame lengths
- Directions
  - Frame vector directions
  - Affine frame directions
  - Ideally, all relative to local frame
- For statistics, spoke directions and frame rotations are Euclideanized using PNS





Affine fitted frames to a hippocampus skeleton [Z Liu]

## Summary of Production of Skeletal Features with Correspondence

- Let rep'n of each training sample come from diffeomorphism of the same ellipsoid, recognizing
  - Vertices and crests
  - Boundaries, using CMC flow
  - Spoke loci and radial lengths
    - From skeleton to boundary
    - From spine to skeletal fold
- And producing correspondence via skeletal coordinates (θ, τ<sub>1</sub>, τ<sub>2</sub>)
  - Achieved by fitted frames via onions skins
    - With directions and positions measured via local frames
- Avoids alignment by use of frames fitted to onion skins





# Fitting an S-rep to a Boundary Mesh

- Fitting rather than generated from boundary to fix branching topology
- Fitting to boundaries
  - Optimization [Z Liu]



- Stage 1: approximate diffeomorphism to yield correspondence
- Stage 2: Refinement optimization: Penalties:
  - 1) foremost, a term heavily penalizing crossing of the spokes, via  $\kappa_{r_i}$ 
    - » Could be a hard constraint
  - 2) the deviation of the implied boundary from the target object boundary;
  - 3) the deviation of the angle of the spokes from the corresponding boundary normal
  - Could use the difference in corresponding spoke lengths
- Code at slicersalt.org
- Alternatives on next slides



## Fitting an S-rep to a Boundary Mesh, 3

• By temporal stages producing reverse diffeomorphsisms to yield stage to stage small deformations





- Each of these is an optimization: Penalties:
  - 1) foremost, a term heavily penalizing crossing of the spokes, via  $\kappa_{r_i}$ 
    - Could be a hard constraint
  - 2) the deviation of the implied boundaries between stages
  - 3) the deviation of the angle of the spokes from the corresponding boundary normal
  - 4) the deviation of the implied crest to the later stage crest – Also for vertices
  - 5) the difference in corresponding spoke lengths
- In late stages of development [Tapp-Hughes]

## **Taheri Computing a Plane-Sweep S-rep from a Boundary Mesh**

- Find shortest spokes to boundary from each interior point

   Find pairs with largest angles
- Classify paired spokes into top and bottom
  - Straighten and fit planes
- Compute spine
  - Requiring relative curvature criterion
- Optimize volume coverage, skeletal symmetry, and lowered curvature







#### **Cm-reps via PDE [Yushkevich]**



# Biharmonic (Laplace-Beltrami)<sup>2</sup> operator offers an elegant solution



Laplace-Beltrami Operator (LBO)

$$\nabla_{\mathbf{x}}^{2} f = \operatorname{div}_{\mathbf{x}} \nabla_{\mathbf{x}} f = \frac{1}{\sqrt{g}} \frac{\partial}{\partial u^{\eta}} \left( \sqrt{g} \, g^{\mu\eta} \frac{\partial f}{\partial u^{\eta}} \right)$$

- The 4<sup>th</sup> order PDE admits <u>two</u> boundary conditions
  - Dirichlet and von Neumann
- The non-linear constraint can be made linear w.r.t. the unknown function *R* by introducing new parameter function *R*<sub>0</sub>



# Cm-reps via PDE [Yushkevich], 2

#### Example of medial model fitting (hippocampus)



### **Cm-reps via PDE [Yushkevich], 3**

#### Limitations of the PDE-based approach

- Computationally expensive
  - Must solve a PDE (large sparse linear system) every iteration
  - -R, y depend on  $\rho$  globally (lots of derivatives to compute)
- Does not handle tubular structures in 3D
- Limited to simple branching configurations
  - How to handle seam-edge and seam-seam intersections?



#### **Cm-reps via Medial Linkage Preservation [Yushkevich]**



The boundary-first approach, for the first time, allows deformable medial modeling of objects with **branching** Blum medial axis



It also has the potential to model tubular and part-sheet/part-tube objects



# Univariate Hypothesis Testing on a Curved Surface

- Test is by DOUBLE NEGATIVE: *Reject* (null) hypothesis *that* the two classes are *not different*
  - I.e., reject hypothesis that two classes are the same, i.e., observed differences come from random sampling
- Typically tests on magnitude of differences between class means: m<sub>A</sub> and m<sub>B</sub>

$$- T_0 = d(\mu_A, \mu_B | / (s_A^2/n_A + s_B^2/n_B)^{\frac{1}{2}})$$

- Create distribution of T under null hypothesis empirically
  - Under null hypothesis groups are not different, any permutation produces an equivalent T (normalized
  - Over all permutations produces empirical T distribution
  - With that distribution see percentile of T<sub>0</sub> in that distribution: p-value =
     #Perms larger / #Perms total





# Hypothesis Testing of Shape with Locality

- Goal: given training data sets of objects <u>z</u><sup>k</sup> in two classes, determine whether there are significant differences between the classes and if so, where
  - Where (locality): positions or other parameters
  - Training data:  $\{\underline{\mathbf{z}}^k | 1 \le k \le n_{A;} n_A + 1 \le k \le n_A + n_B\}$
- Method: Hypothesis test with initial Geometric Object Property(ies) (GOPs) at each location
  - A GOP may be a tuple, e.g., object normal direction
  - With corrections for multiple comparisons, which will lead to a different threshold for each location × GOP
    - Commensuration by turning T values into p values
    - Making p values for each feature std Gaussian
    - Then decorrelation via PCA

## Permutation Tests on >1 Variable µ-diff fixup

- Commensurate by transforming each mean difference into a probability via its histogram
- Make distributions same and joint distribution Gaussian by turning each distribution into a standard Gaussian
  - Two cumulative histogram transformations: quantiles have uniform probability
    - Cumulative dist. of v'ble  $\rightarrow$  uniform
    - Quantile f'n of normal  $\rightarrow$  st'd Gaussian
- What's left is handling covariance of transformed variables



### Decorrelating the Standard Normal Variables

- Note that all hyperplanar (including dimension 1) crosssections through the mean of a Gaussian are Gaussian
  - Also, the principal dimension-1 cross-sections yield uncorrelated variables
- $\Sigma_{\rm U}$  is made up or correlated standard 1-dimensional Gaussians
  - So the cross-sections are not principal (nor orthogonal)
- Use PCA on  $\Sigma_U$  to produce new, uncorrelated variables formed as the eigenvector directions
  - Multiple test correction assuming non-correlation is applicable
  - For shapes (U formed from GOPs) there will be few such variables (ones with low eigenvalues can be cut out)

#### **P-value correction via FDR or FWER**

- False Discovery Rate (FDR)
  - More relaxed assumptions
    - More power than Bonferroni, higher specificity than uncorrected
  - Used in fMRI, VBM and Deformation field analysis
- FDR: Proportion of false positive tests among those test for which H<sub>0</sub> is rejected
  - Bounds expected rate among those tests that show significance only.
- FWER correction: Rate of false positives among all tests, whether or not  $H_0$  is rejected
  - 1. Controlling False Discovery Rate: A practical and powerful approach to multiple testing, Y Benjamini, Y Hochberg, J.R. Stat Soc Ser B 57 1995
  - 2. Thresholding of Statistical Maps in Functional Neuroimaging Using the False Discovery Rate, CR Genovese, NA Lazar, T Nichols, NeuroImage 15 2002

Slide: M. Styner

#### **Corrected Multivariate Hypothesis Testing: by Permutation Tests [Pizer]**



# **ROC Analysis**

- An important means of evaluating any medical procedure involving a detection of a signal
  - Signal can be classification of voxel as the object to be segmented
- True positive rate (*sensitivity*) plotted against false positive rate (1-*specificity*)
  - TPR: P(correct decision | signal present)
  - FPR: P(wrong decision | signal absent); a measure of conservatism
  - Common measure: area under ROC (AUC)
    - Equivalent to 2-alternative forced-choice fraction correct





#### **AUC by Random Holdouts**

- Assume data has N<sub>i</sub> in class i
- Pick a subdivision fraction:
  - f = # training cases / N = # all cases, e.g., 80%
    - # test cases is complement
    - In each holdout # of test cases is (1-f)  $N_1$  in class 1 and (1-f)  $N_2$  in class 2, with the cases chosen at random
- Run the experiment many times
  - Each test case yields a d value, leading to a class choice, given a threshold
  - Yield TPR and FPR for various thresholds
- Two options for combining trials
  - Average AUCs per random set
  - Combine FPR, TPR data over sets, to yield a single AUC



#### Combining random holdouts results into an AUC

- Each test case yields a d value along separation direction
- But d values are not commensurate across random holdouts
  - They have different separation directions
- So turn d values into p values via Bayesian analysis



 Then the set of p values for each class can be coalesced to produce 2 histograms, which can yield an ROC and thus an AUC



### Going from histograms on d to P(schizo | D) function

- Bayesian formulation
  - Two histograms are Gaussians
     with common variance from histo's
     P(d | schizo) and P(d | control)
    - P(schizo|d) =

 $p_s p(d|schizo)$ 

 $\overline{p_s \, p(d|schizo) + (1 - p_s) \, p(d|control)}$ 

- There is a parameter, P<sub>s</sub>, the prior probability of being schizo
  - Each value of P<sub>s</sub> yields a different P(schizo | d) function
  - Applied to test data, each value of  $P_s$  yields a different true positive rate and true negative rate
  - These rate curves yield an ROC





#### **Longitudinal Analysis of Shape**



- How does shape change over time?
- Longitudinal data set:
  - Set of homologous objects (e.g., anatomical structures), each object being observed repeatedly at several time points; for now non
    - cyclic, e.g., aging
  - Shape varies across individuals
  - For each individual shape temporal paths differ
    - Temporal sampling may differ among individuals
    - Initial times and rates of changes of shape longitudinal changes may differ among individuals

#### • Two approaches

- Use object features  $\underline{z}$  on curved manifold and study  $\underline{z}(t)$ 
  - See Fletcher lectures in this course and his papers
  - Schiratti, ..., Durrleman, for mixed effects models on manifolds: "Learning spatiotemporal trajectories from manifold-valued long'l data"
- Study deformations in time:  $\phi(\underline{x},t)$ . See upcoming slides

#### Longitudinal Analysis of Shape via Space Deformations

• Data



- Need to do subject by subject deformations across time:
- Need to do subject by subject temporal deformations from atlas
  - Time passes on differently for different subjects
- Need to do inter-subject deformations from atlas
  - Thus need an atlas, M(t), typically a kind of mean
- Want to include covariates such as age (especially) and gender in the analysis





#### Longitudinal Analysis of Shape via Space Deformations, 3



- Issues
  - Need to do subject by subject deformations across time: S<sub>i</sub>(t)
  - Need to do subject by subject temporal deformations from atlas



- Time passes on differently for different subjects
- Need to do inter-subject deformations from atlas
  - Thus need an atlas, M(t), typically a kind of mean



#### Subject-specific Longitudinal Analysis of Shape via Space Deformations



of subject j





• Via LDDMM approach minimize

$$E(\chi) = \sum_{t_i} \mathrm{d}(\chi_{t_i}(M_0),S_i)^2 + \gamma^{\chi}\mathrm{Reg}(\chi)$$

#### Subject-specific Longitudinal Analysis of Shape via Space Deformations



- Let  $\chi(t)$  be deformation of shape across time of atlas - Let  $\chi_j(t)$  be deformation of shape across time of subject j
- But time runs differently for each subject - Let  $\psi(t)$  deform time:  $\Phi(x, y, z, t) = (\phi(x, y, z, \psi(t)), \psi(t))$

where the geometrical part has the form

 $\phi(x,y,z,t) = \chi_t {\bigcirc} \phi_0 {\bigcirc} \chi_t^{-1}(x,y,z)$ 

• Via LDDMM approach minimize

$$E(\phi,\psi) = \sum_{t_j} \mathrm{d}(\phi(S(\psi(t_j))), U_{t_j})^2 + \gamma^{\phi} \mathrm{Reg}(\phi) + \gamma^{\psi} \mathrm{Reg}(\psi)$$



– where  $U_{tj}$  is the shape of object j at time t

subject-specific approach