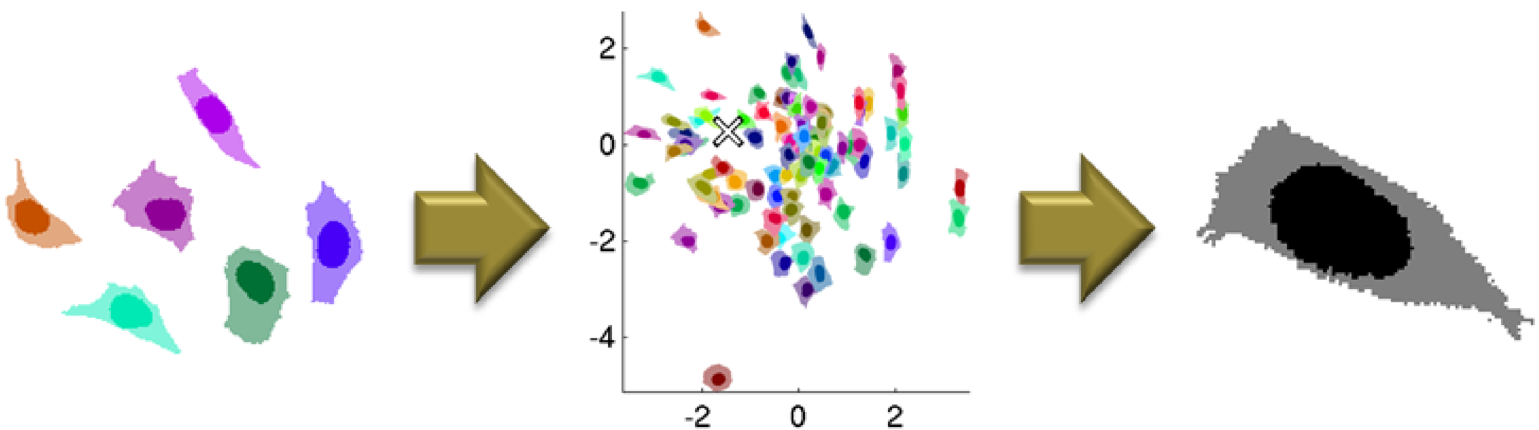
(A very fast primer for)

Diffeomorphic Modeling in CellOrganizer

Gregory Johnson

Diffeomorphic Models

- Uses Large deformation diffeomorphic metric mapping (LDDMM)
- Morph one shape to another
- Builds "shape space"
- Allows for walks through shape space that could be used to describe cellular dynamics



Cellular and nuclear shapes

Shape space

Synthetic shapes

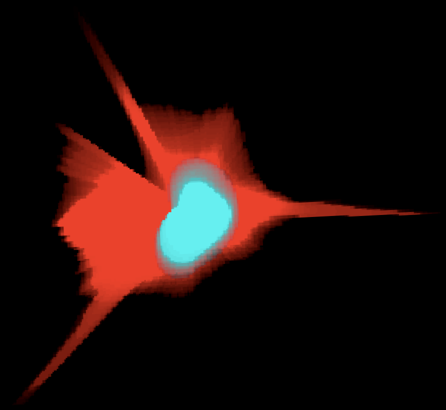
WHY?

Motivation

- Cells don't always satisfy assumptions of parametric models.

Segmented PC12 cell

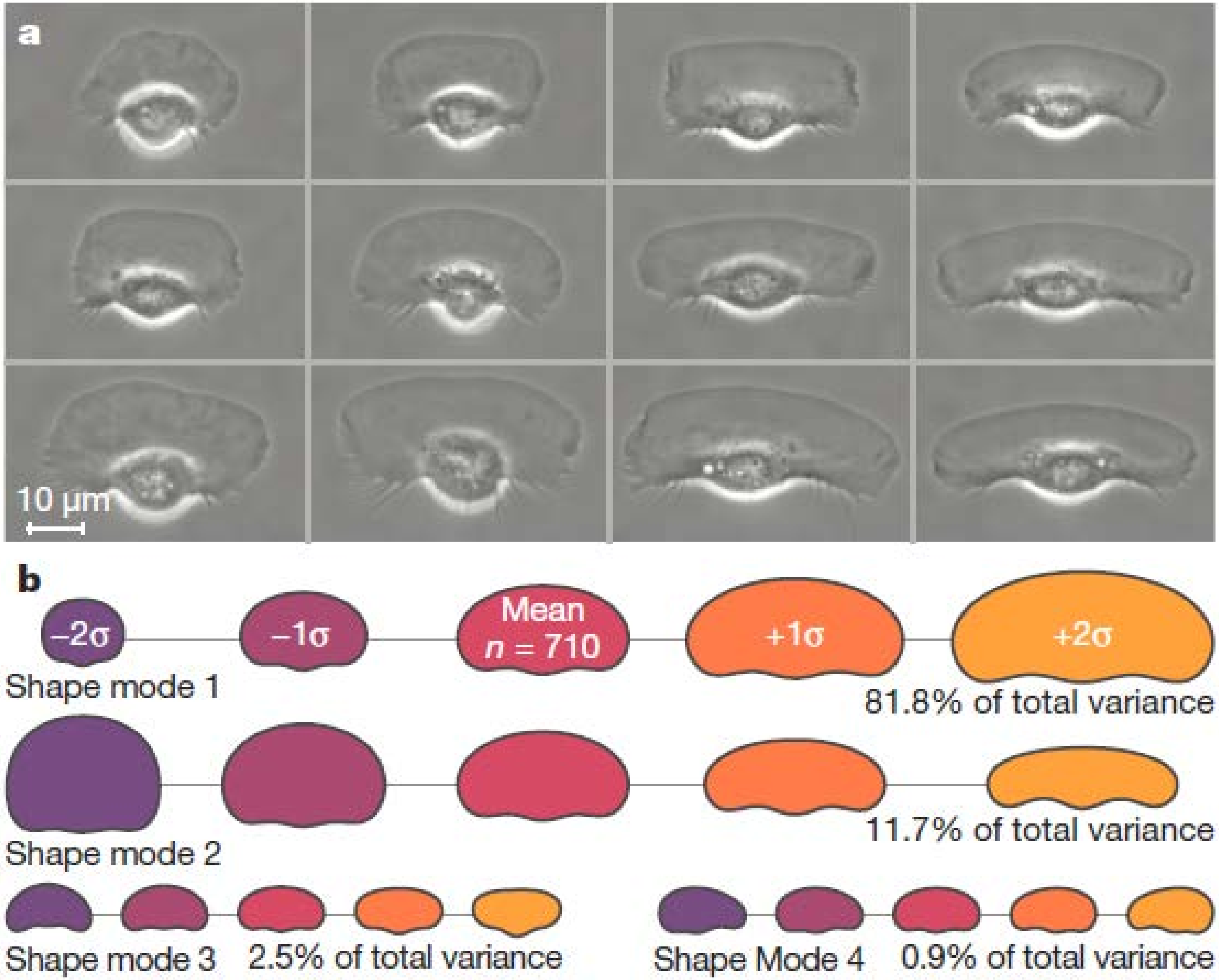
Star-polygon ratio model representation



Parametric shape space models

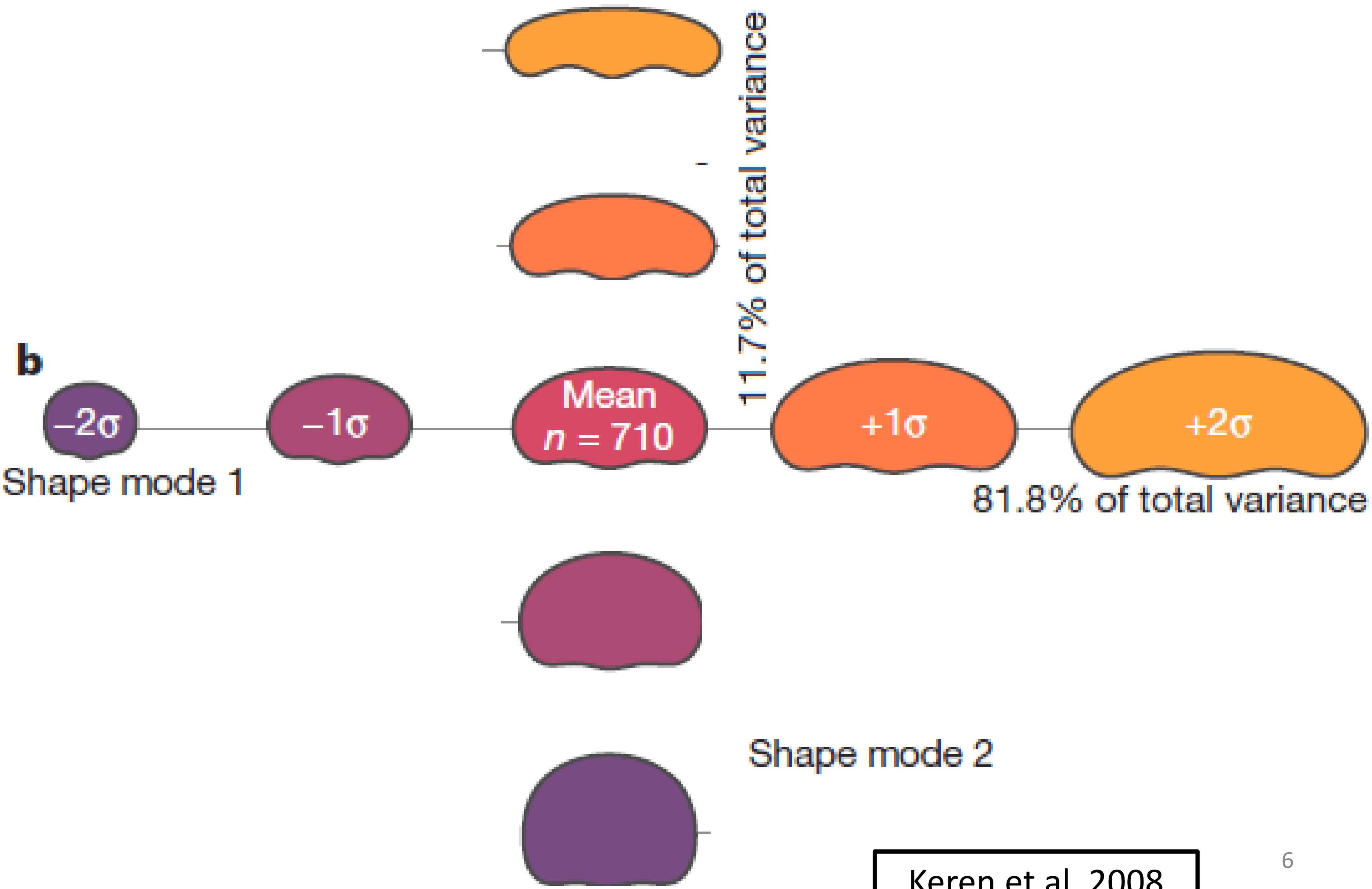
Images showing real shapes

Generative shape model



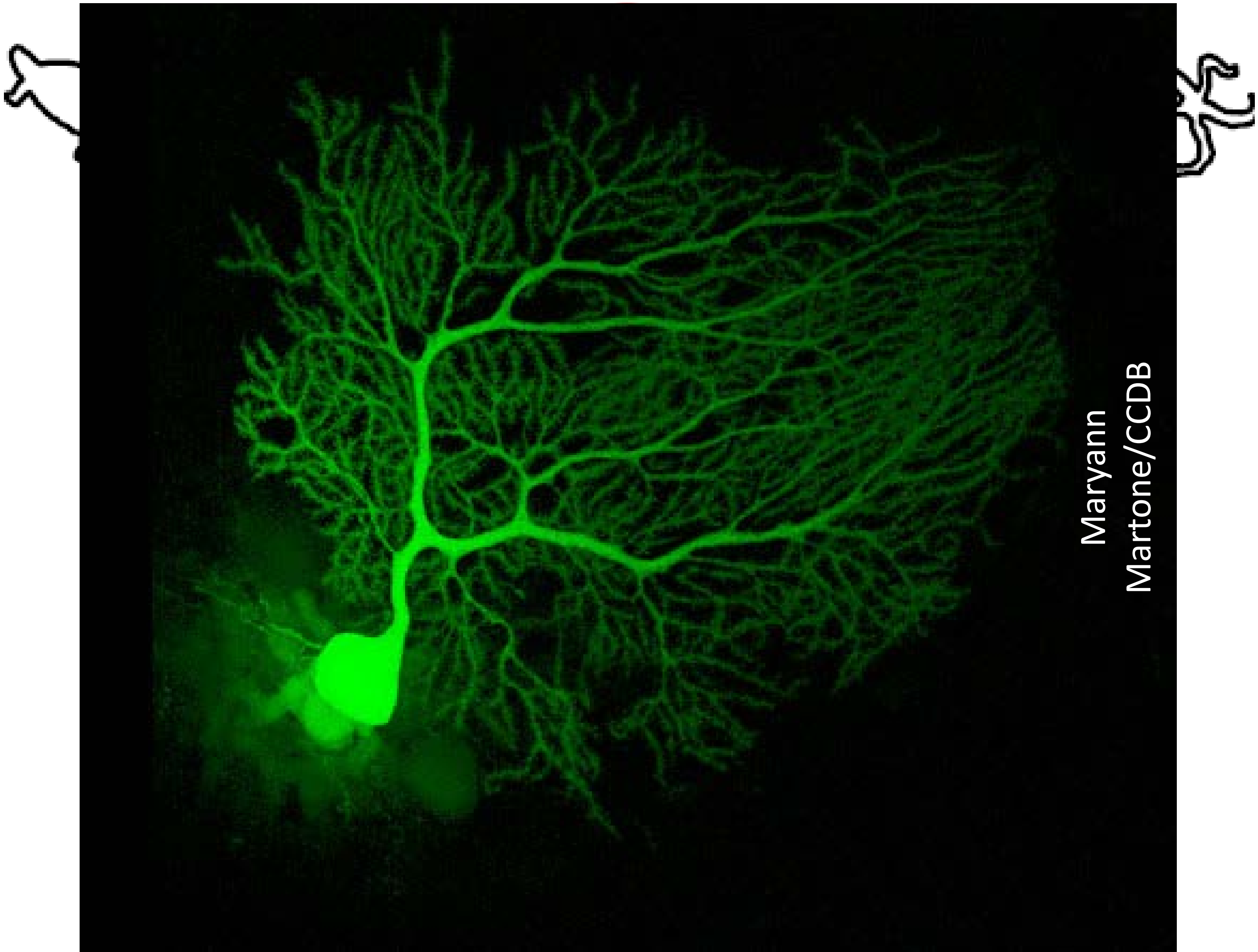
Keren et al. 2008

Shape space



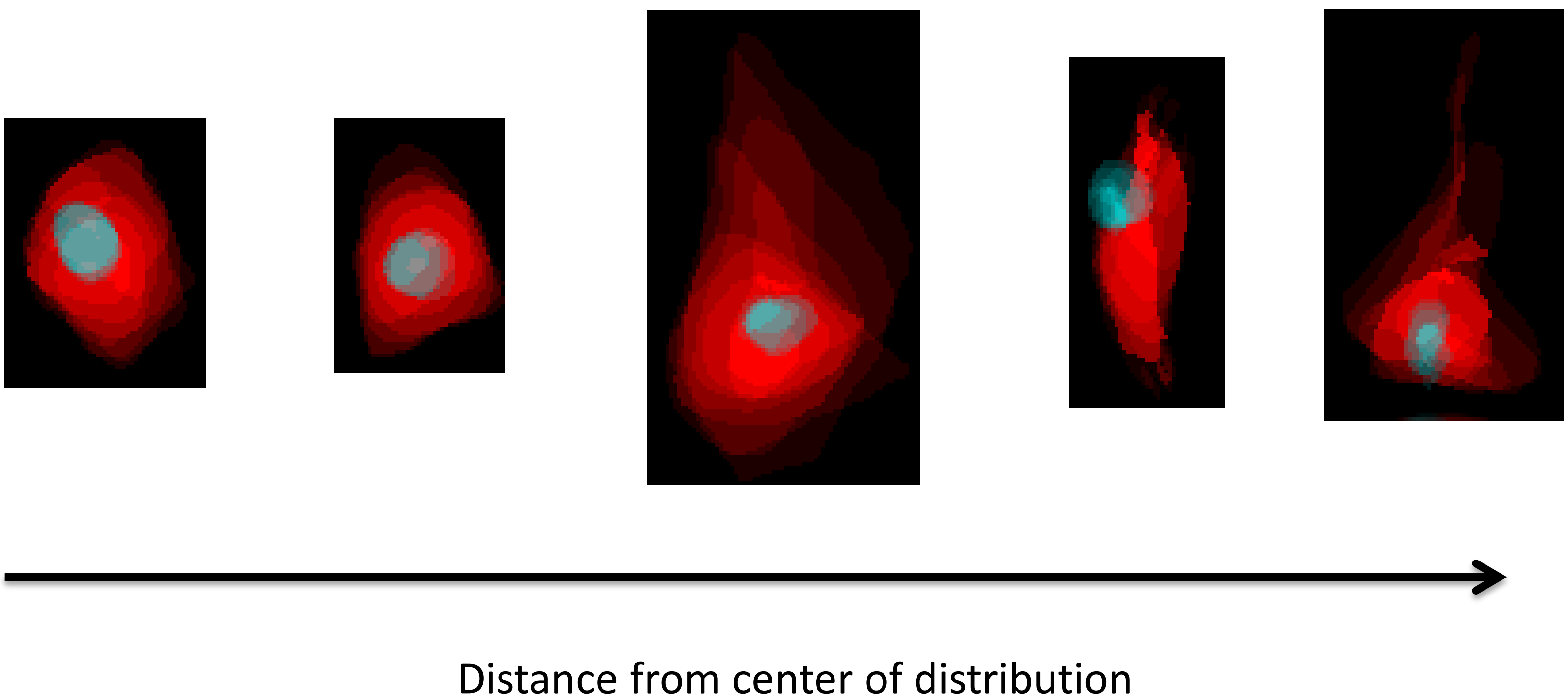
Keren et al. 2008

Limitations of common outline model



Srivastava et al.
2005

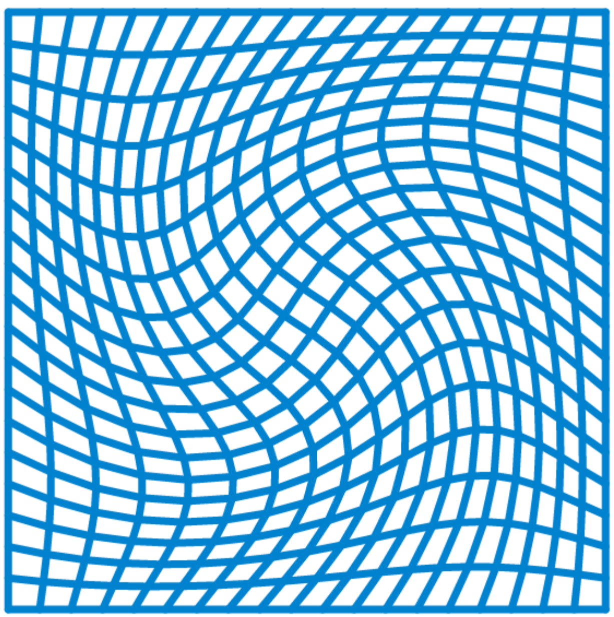
Limitations of common outline model



LDDMM - Large Deformation Diffeomorphic Metric Mapping

What is a diffeomorphism?

- Essentially a smooth and invertible mapping from one coordinate space to another

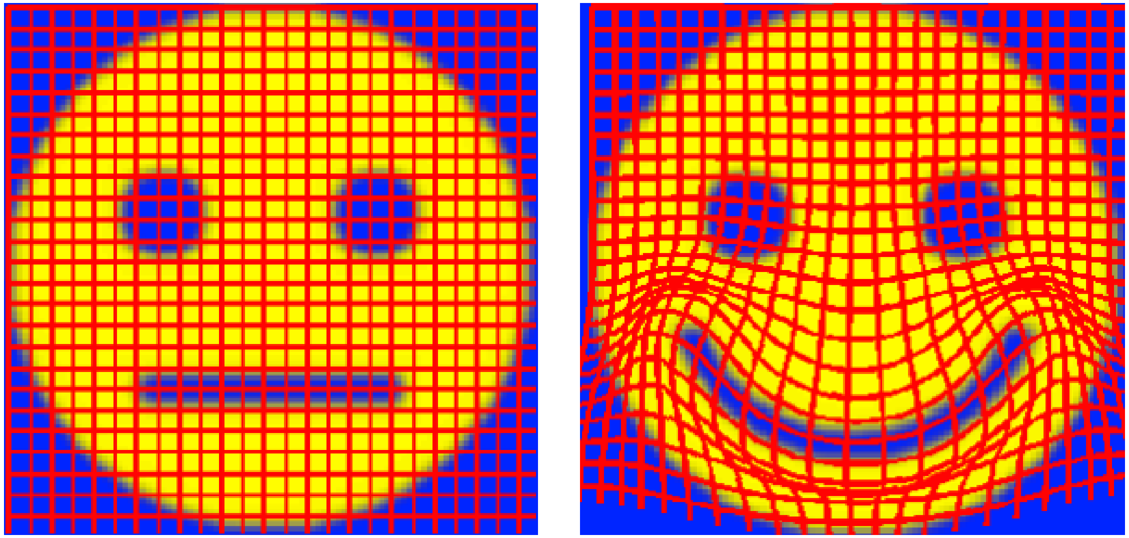


A diffeomorphic mapping from a regular rectangular grid.

https://en.wikipedia.org/wiki/Diffeomorphism

Diffeomorphic mappings of continents to a 2D projection of a globe

http://wwwx.cs.unc.edu/~mn/classes/comp875/doc/diffeomorphisms.pdf



A diffeomorphic mapping from one image to another.

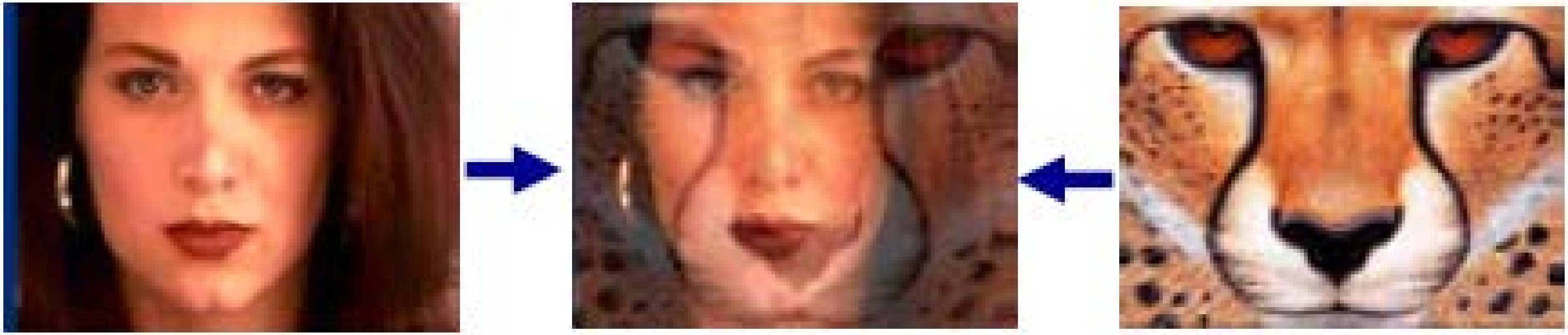
http://wwwx.cs.unc.edu/~mn/classes/comp875/doc/diffeomorphisms.pdf

Nonparametric shape image-based models

Real 2D nuclear shapes

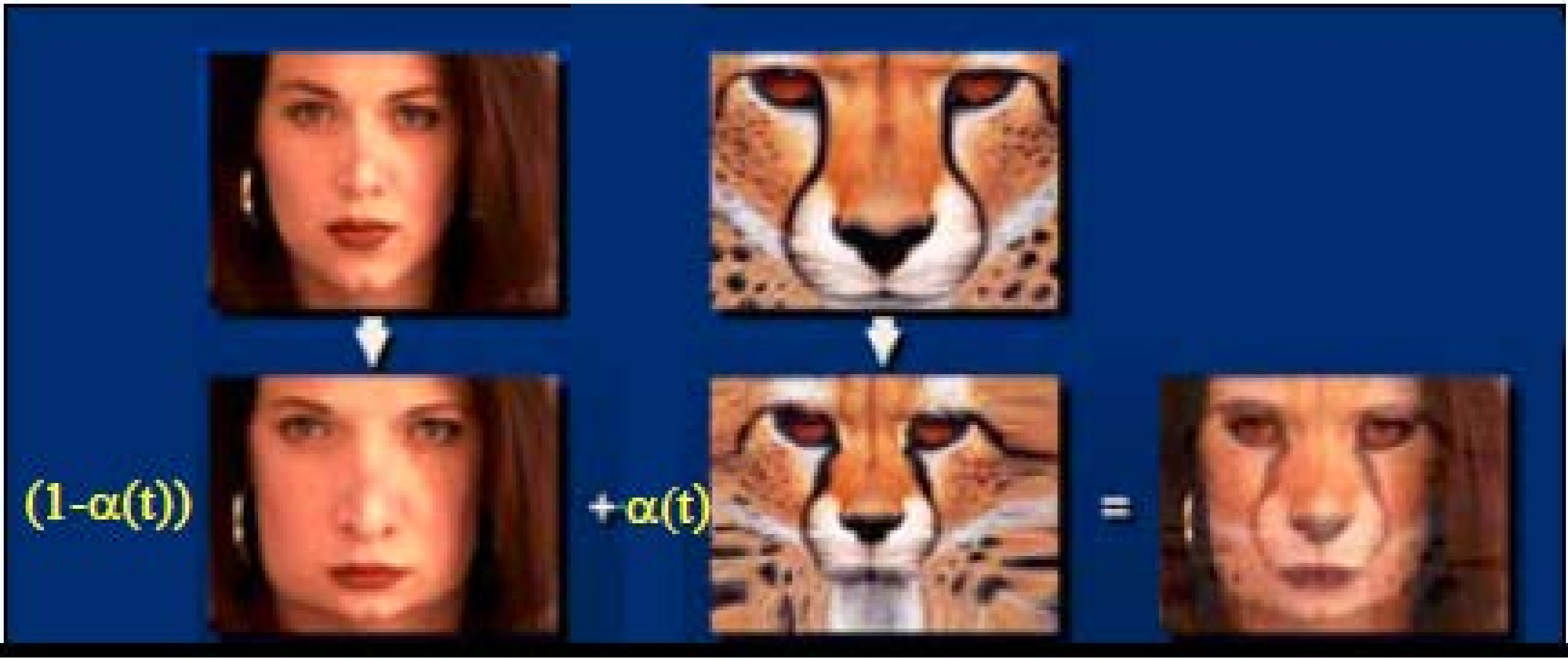
Peng et al. 2009

Cannot just interpolate images as if they were vectors



http://alumni.media.mit.edu/~maov/classes/comp_photo_vision08f/

Morphing to interpolate images



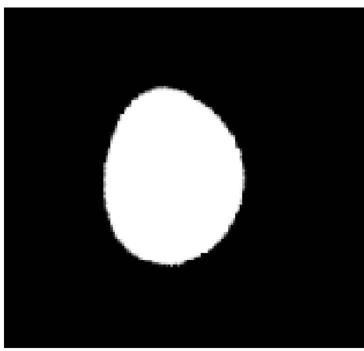
http://alumni.media.mit.edu/~maov/classes/comp_photo_vision08f/

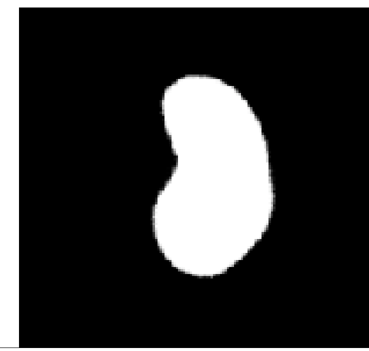
Distance between two shapes

Work so far   Distance

Shape A   Shape B

0   0.0195





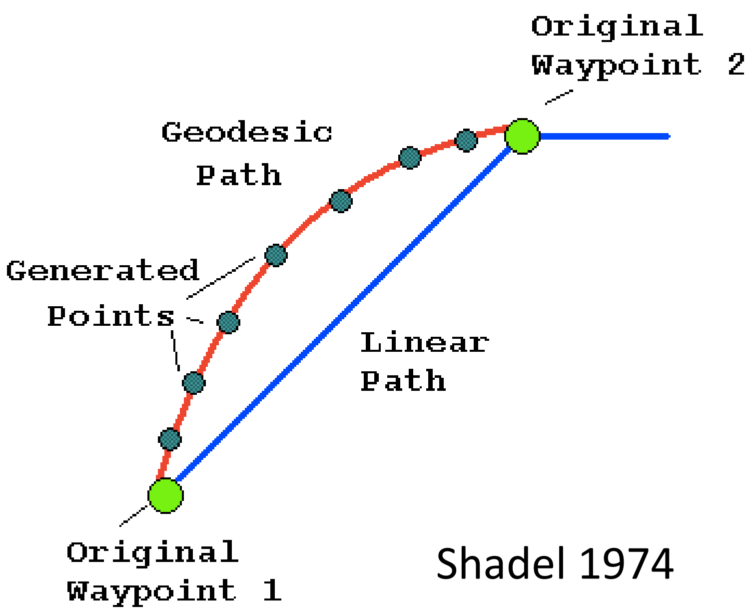
Iterative reduction in difference between deformed shape A and B

Distance = total work across all iterations

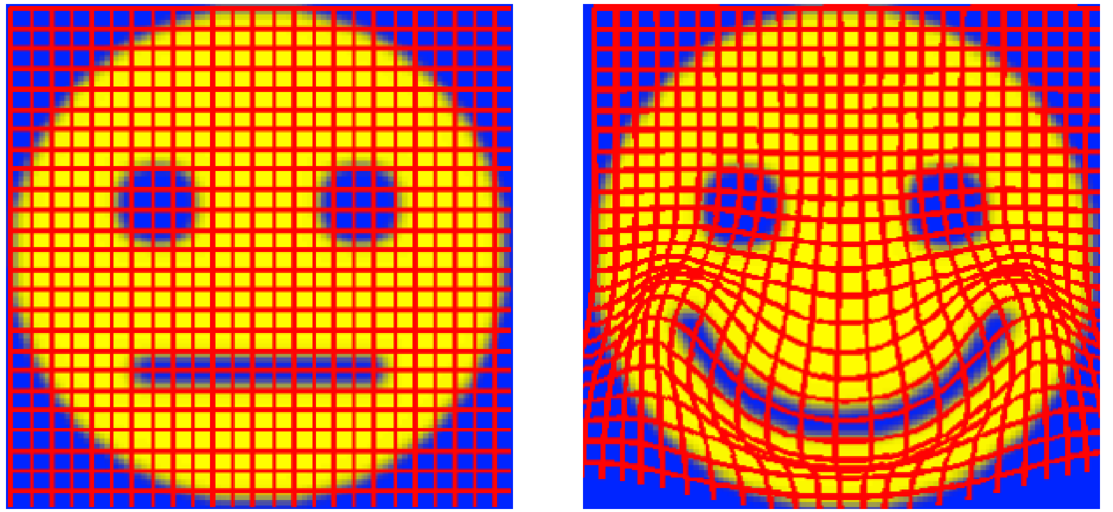
Peng et al. 2009

LDDMM - Large Deformation Diffeomorphic Metric Mapping

- Minimal energy transformation with respect to the gradient of the deformation field i.e. Geodesic distance



Shadel 1974



A diffeomorphic mapping from one image to another.

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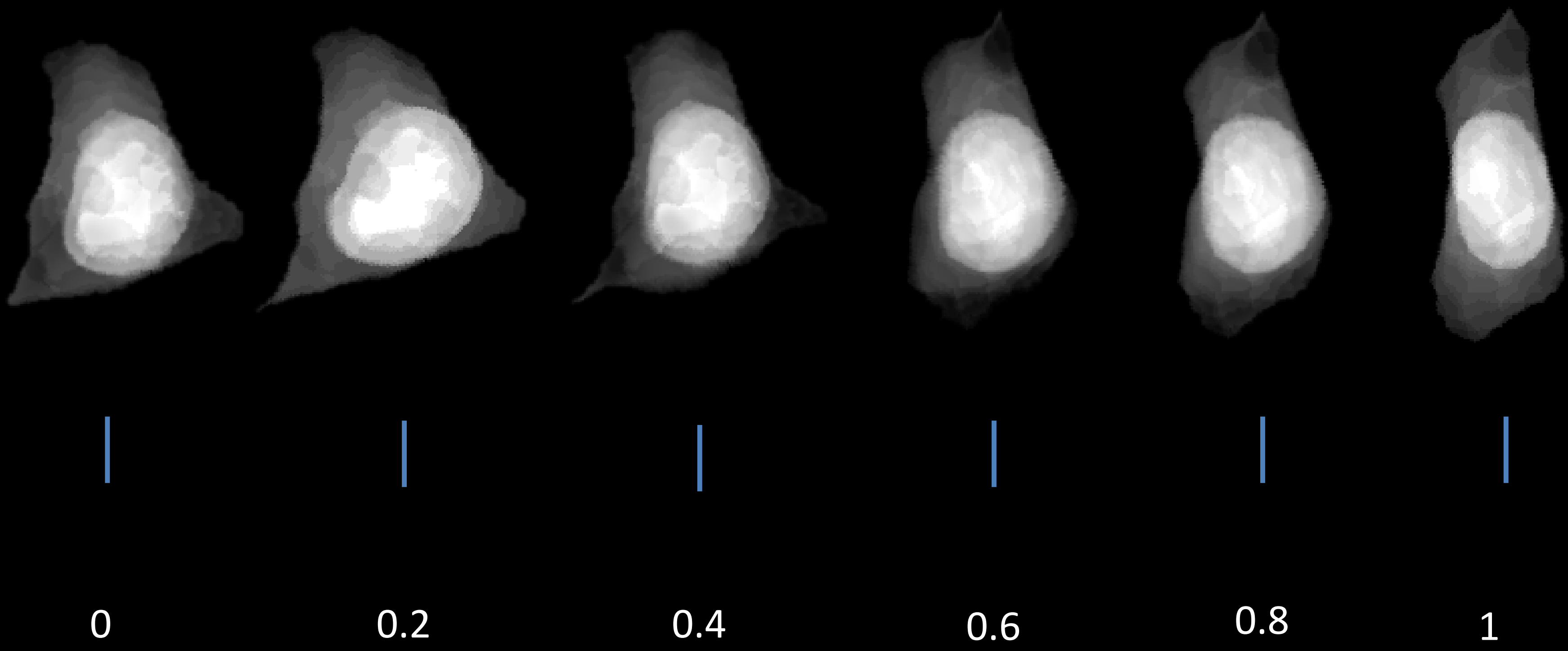
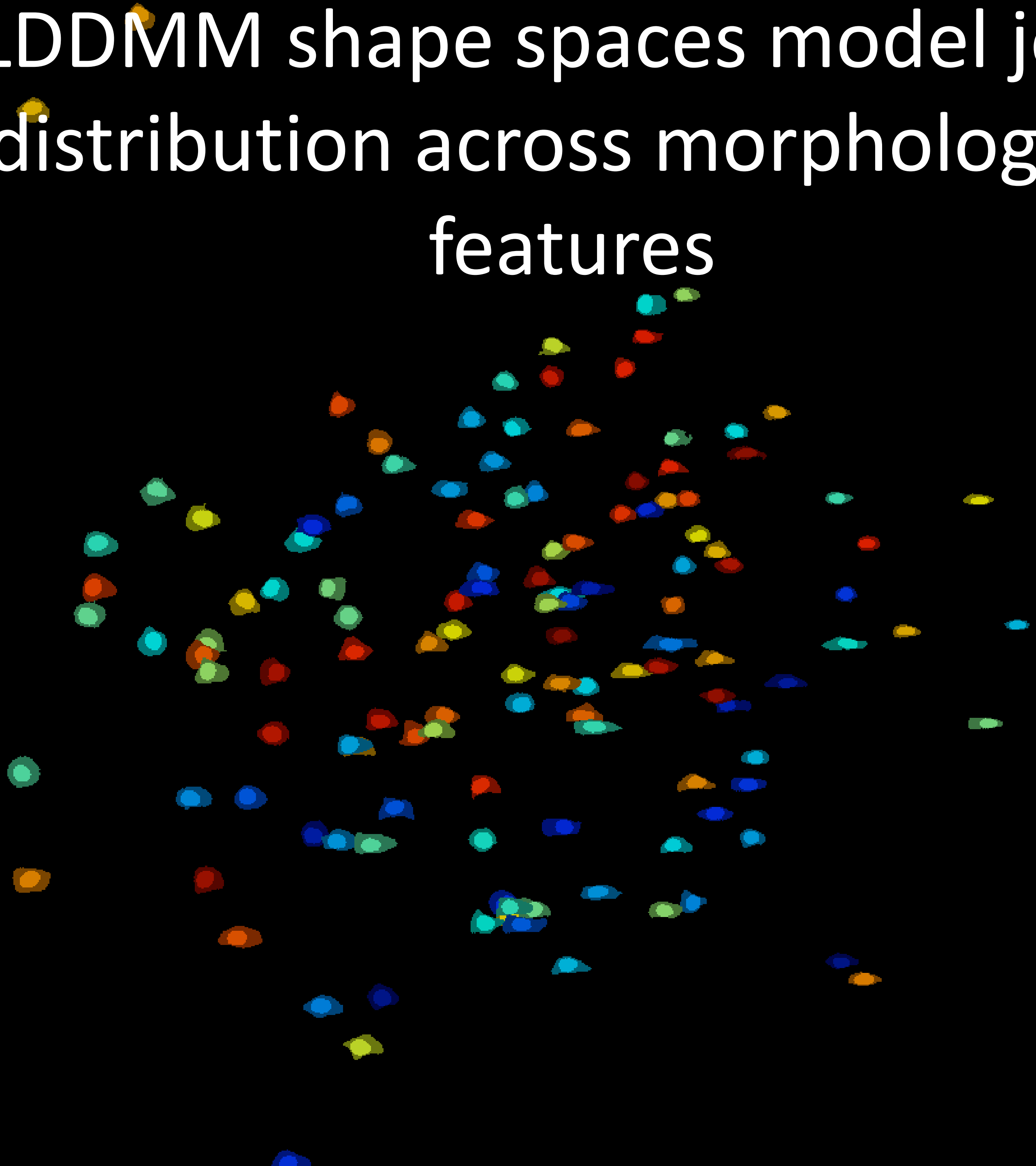
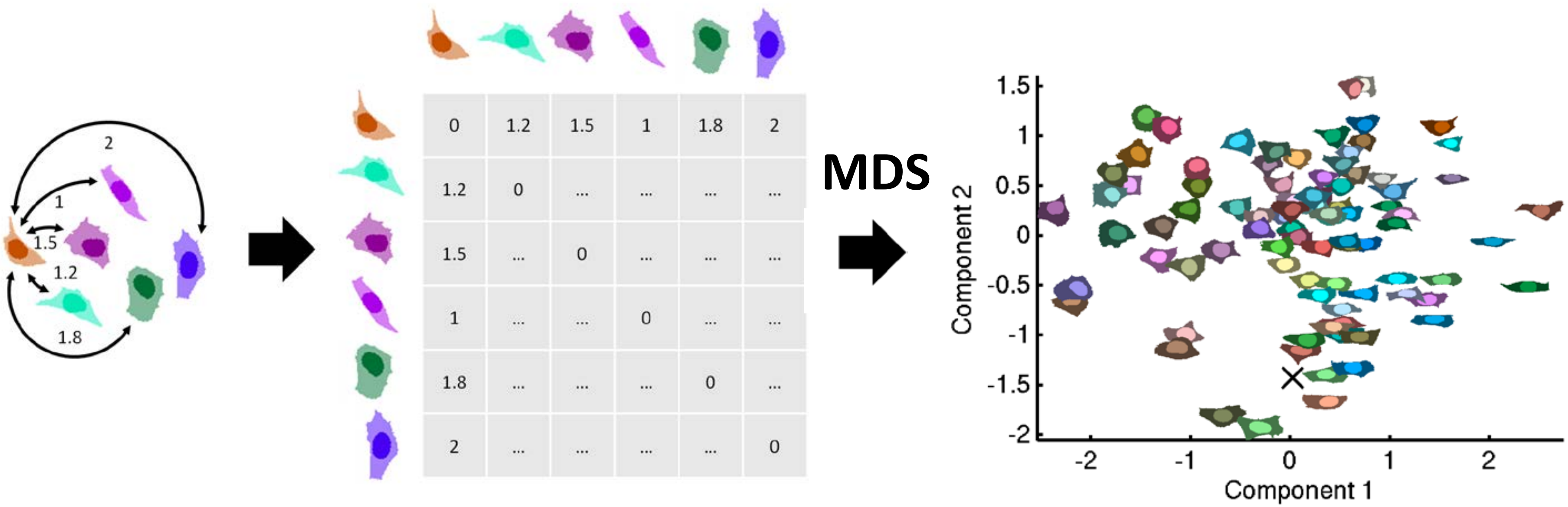

0
0.2
0.4
0.6
0.8
1

LDDMM shape spaces model joint distribution across morphological features



Diffeomorphic Training

Shapes to Space

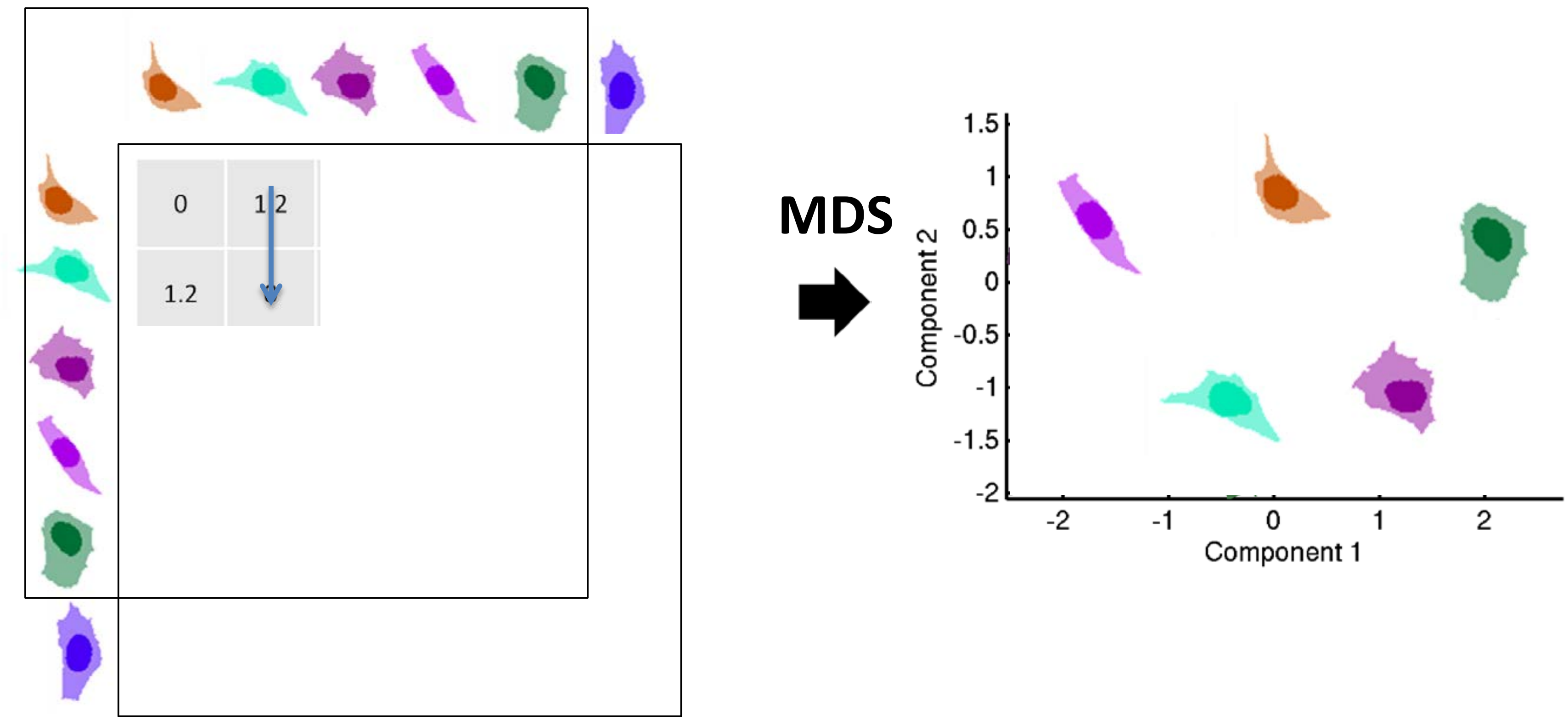


0	1.2	1.5	1	1.8	2
1.2	0	...	...	...	...
1.5	...	0	...	...	...
1	...	...	0	...	...
1.8	...	...	...	0	...
2	...	...	...	...	0

But this takes a lot of time

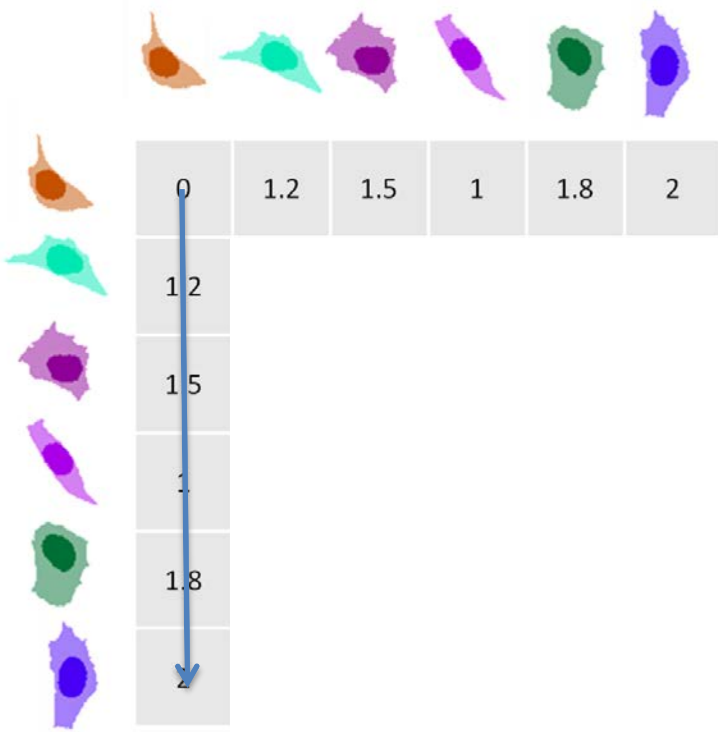
Partial Distance Matrix Learning

- Most complete shape space



Partial Distance Matrix Learning

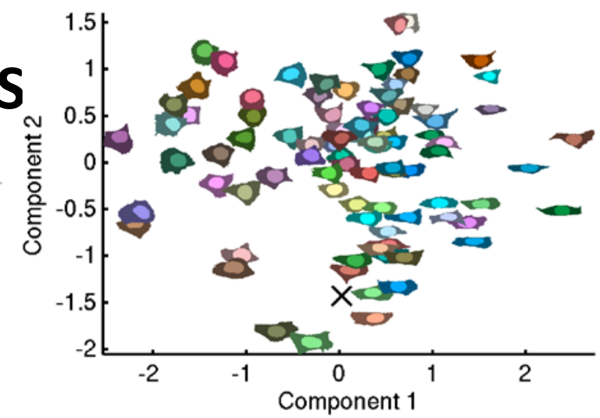
- Landmark MDS



Nystrom Approximation

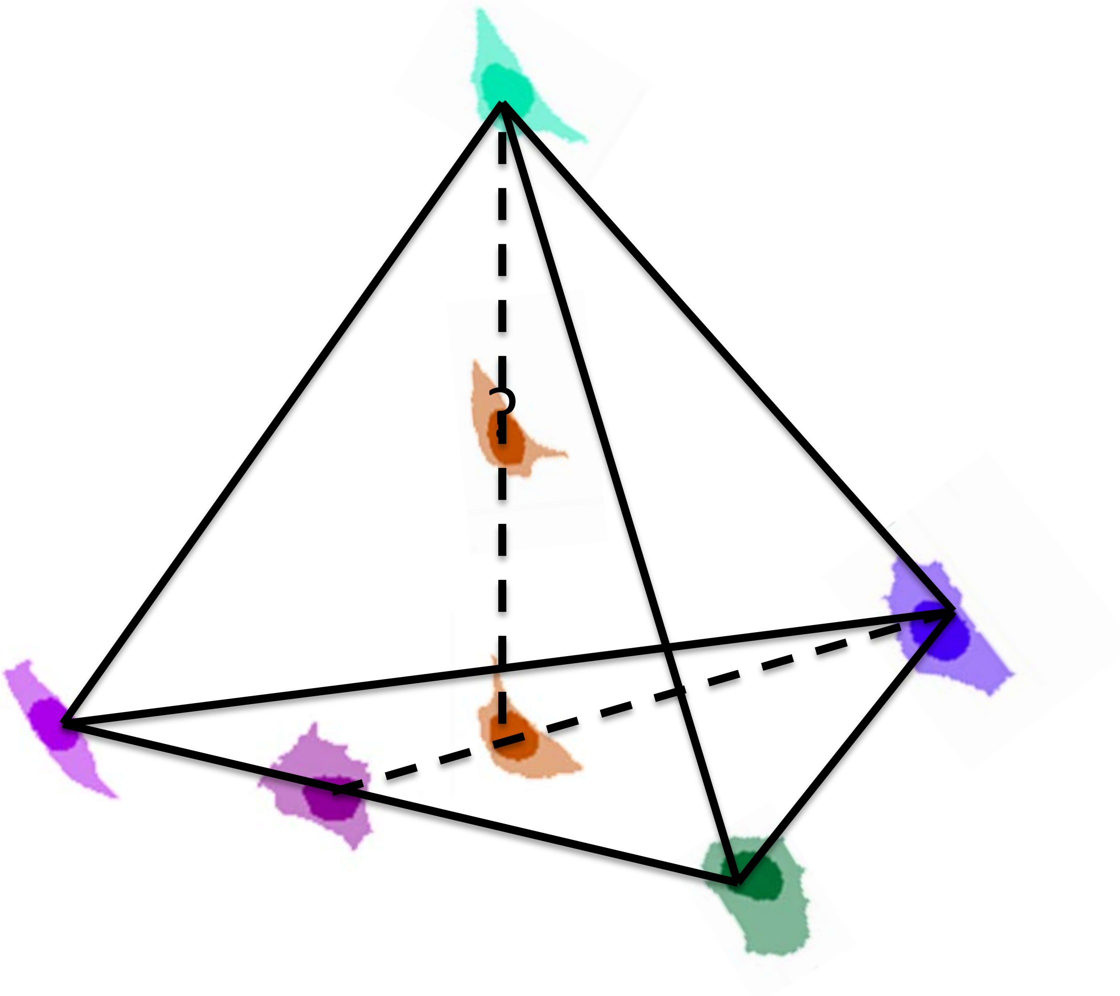
$$\tilde{\mathbf{K}} = \begin{bmatrix} \mathbf{A} & \mathbf{B} \\ \mathbf{B}^T & \mathbf{B}^T\mathbf{A}^{-1}\mathbf{B} \end{bmatrix}$$

MDS



Diffeomorphic Synthesis

Space to Shapes

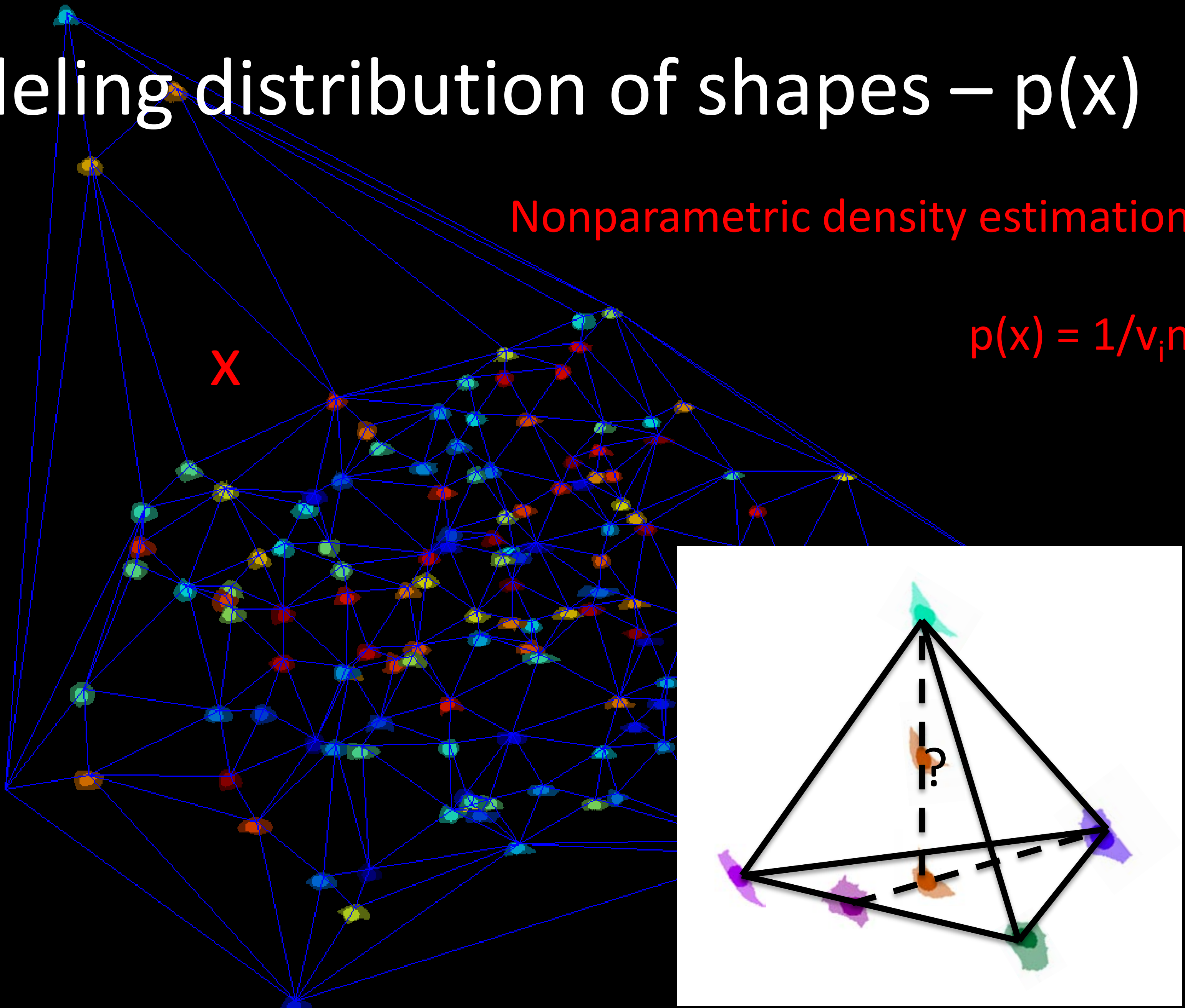


Synthesis strategy for new points

Modeling distribution of shapes – p(x)

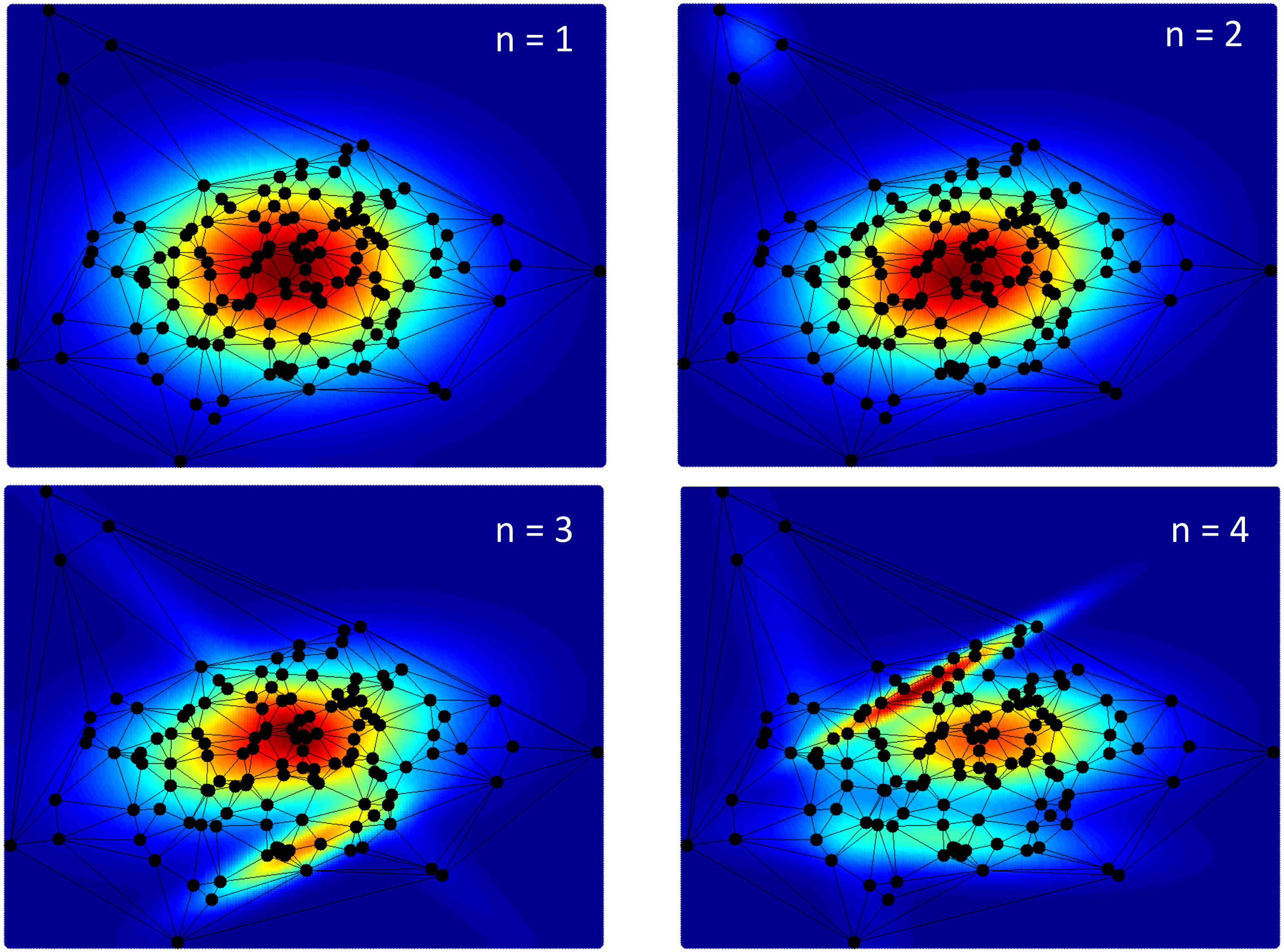
Nonparametric density estimation

$p(x) = 1/v_i n$



Modeling distribution of shapes – p(x)

Shape space modeled as a Gaussian Mixture Model

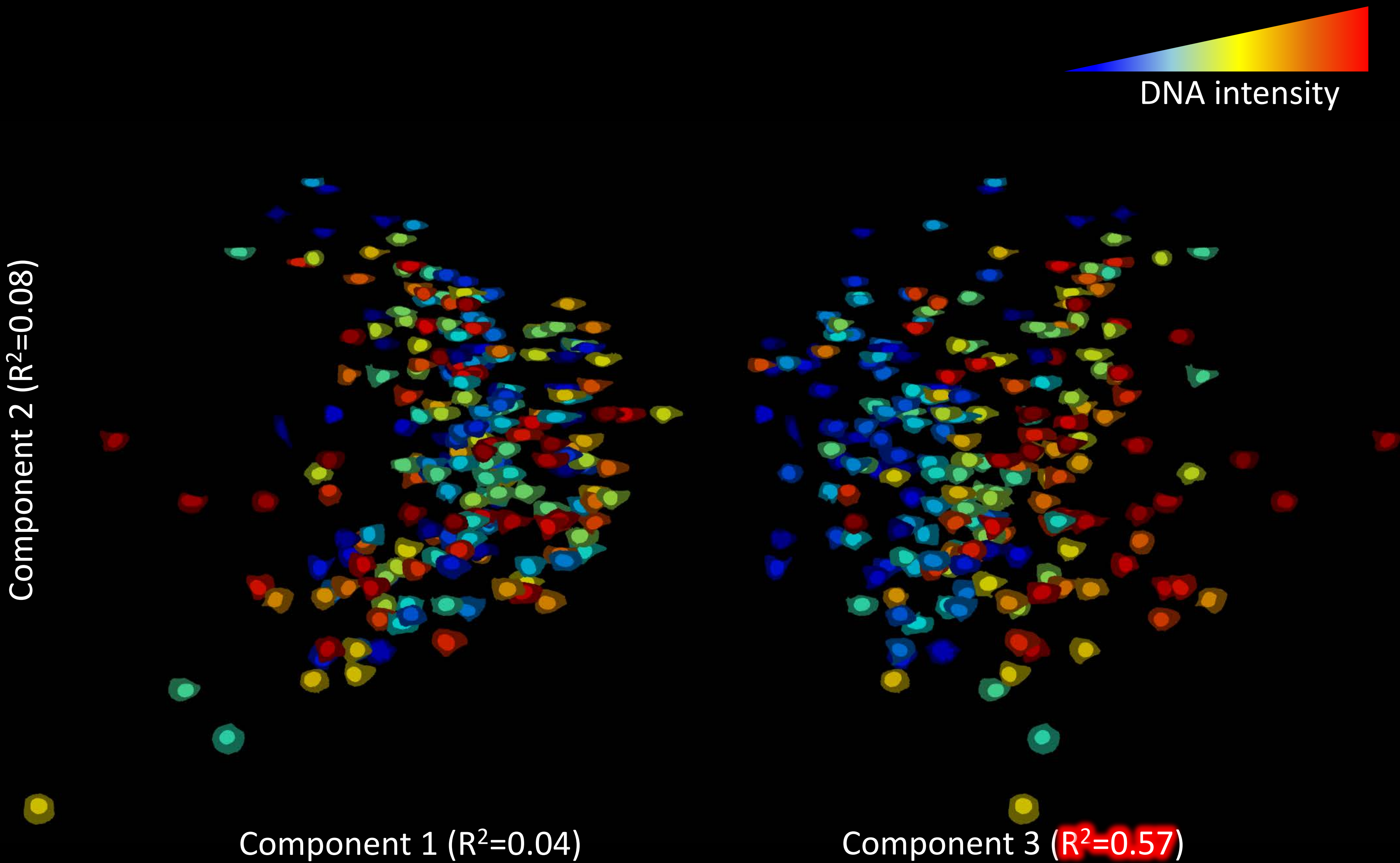


Diffeomorphic space

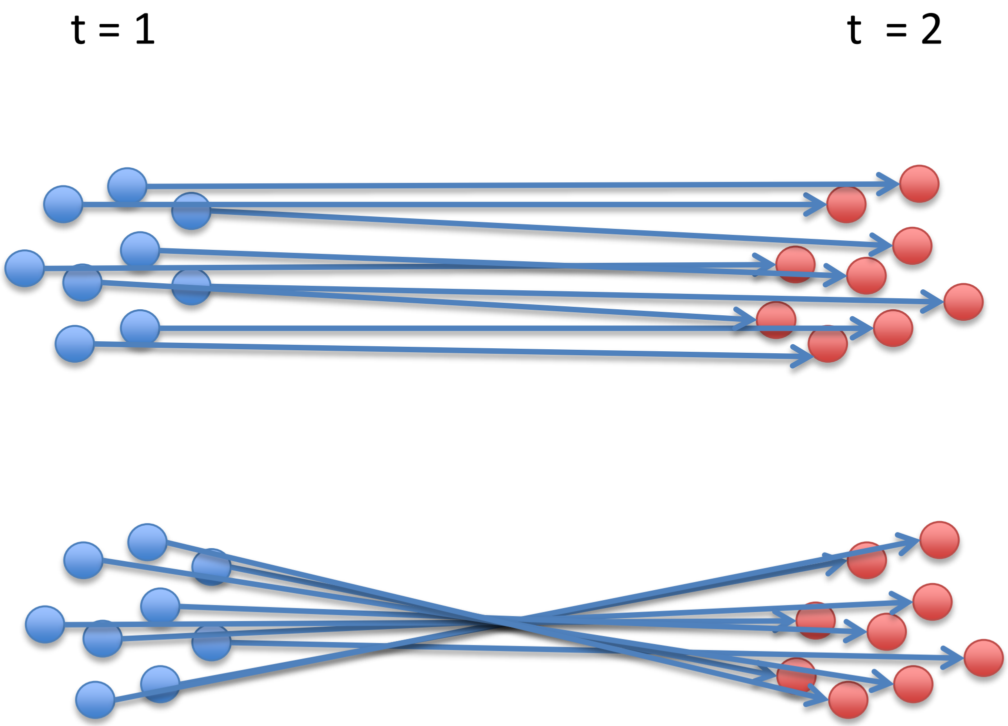
- New feature space
  - Positions in space correspond to a real image
  - Feature dimensions correspond with dimensions that with highest eigenvalues

  - Can be treated exactly like a normal feature space

HeLa shape space with DNA intensity



Minimum energy pathway reconstruction example



Plausible

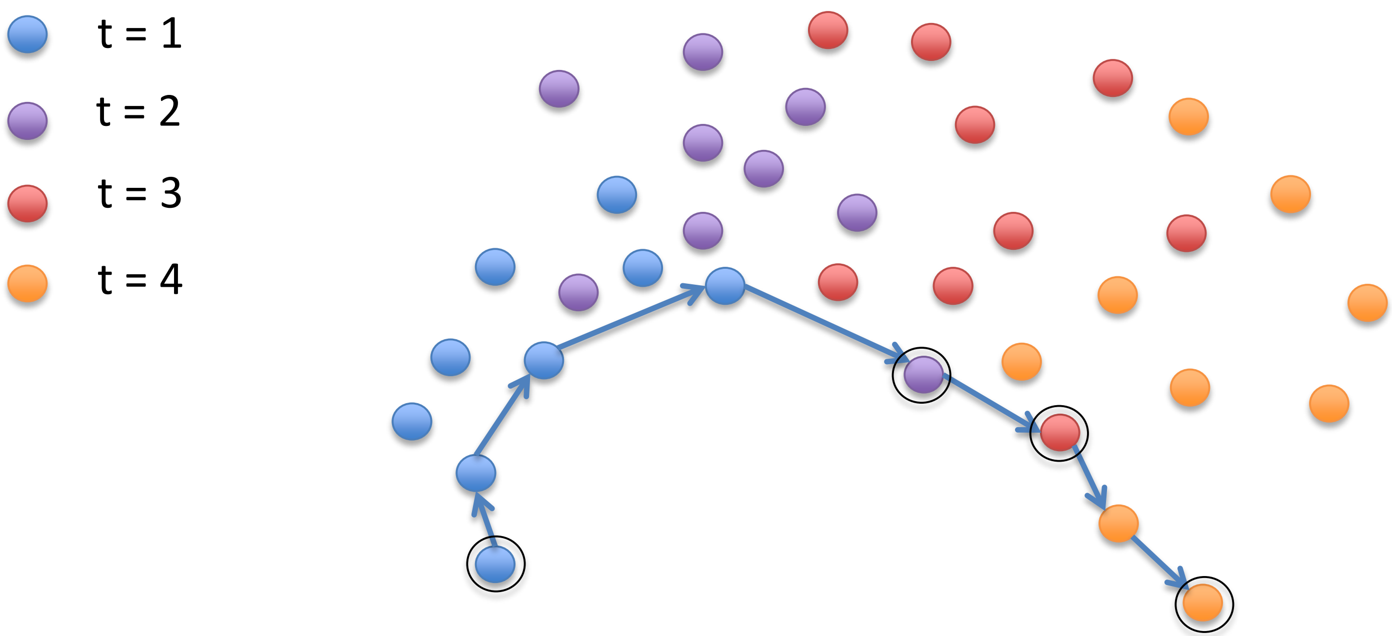
- Lower net distance traveled
- Matched points are more similar

Less Plausible

- Greater net distance traveled
- Matched shapes less similar

Solution: Minimum global weight bipartite matching

Minimum energy pathway reconstruction example



Minimize net flow

while

min(max(w) - min(w))

Constraints

Travel along shortest path on d^2

Procedure

- Construct distance matrix
- Construct neighbor graph
- For each interval: t_i to t_{i+1}

  Find shortest path from each observation in t_i to every other cell in t_{i+1}

  Find transition pairs via minimum weight bipartite matching
- Construct transition pathways