Image-derived, Three-Dimensional Generative Models of Cellular Organization

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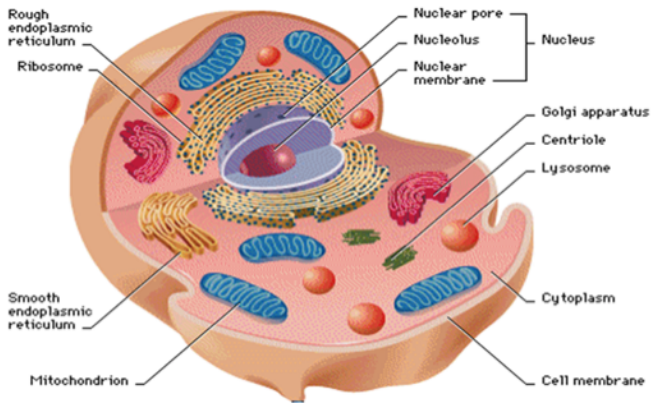
How do we learn and represent

- the number, sizes, shapes, positions of subcellular structures
- the distribution of proteins across those structures



High throughput image analysis

- Many groups imaging subcellular distributions by various tagging methods and microscopy methods
- Dominant approach to analysis uses classification or regression (with image features)
- However…

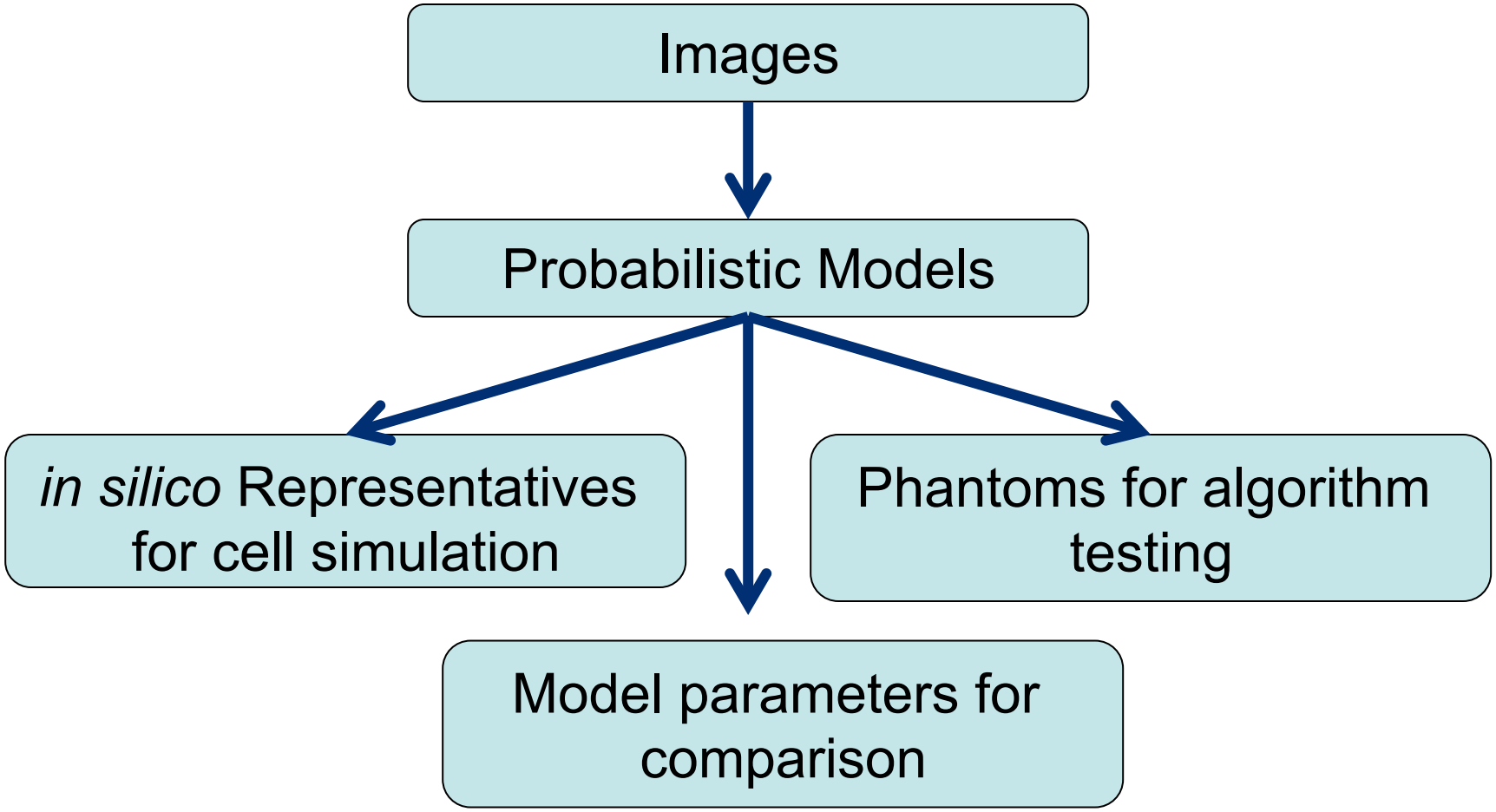
Assigning words not sufficient!

- Doesn't capture
  - new phenotypes
  - fractional distributions
  - suborganelle patterns
  - spatiotemporal distribution
  - cell type variation
  - conditional variation

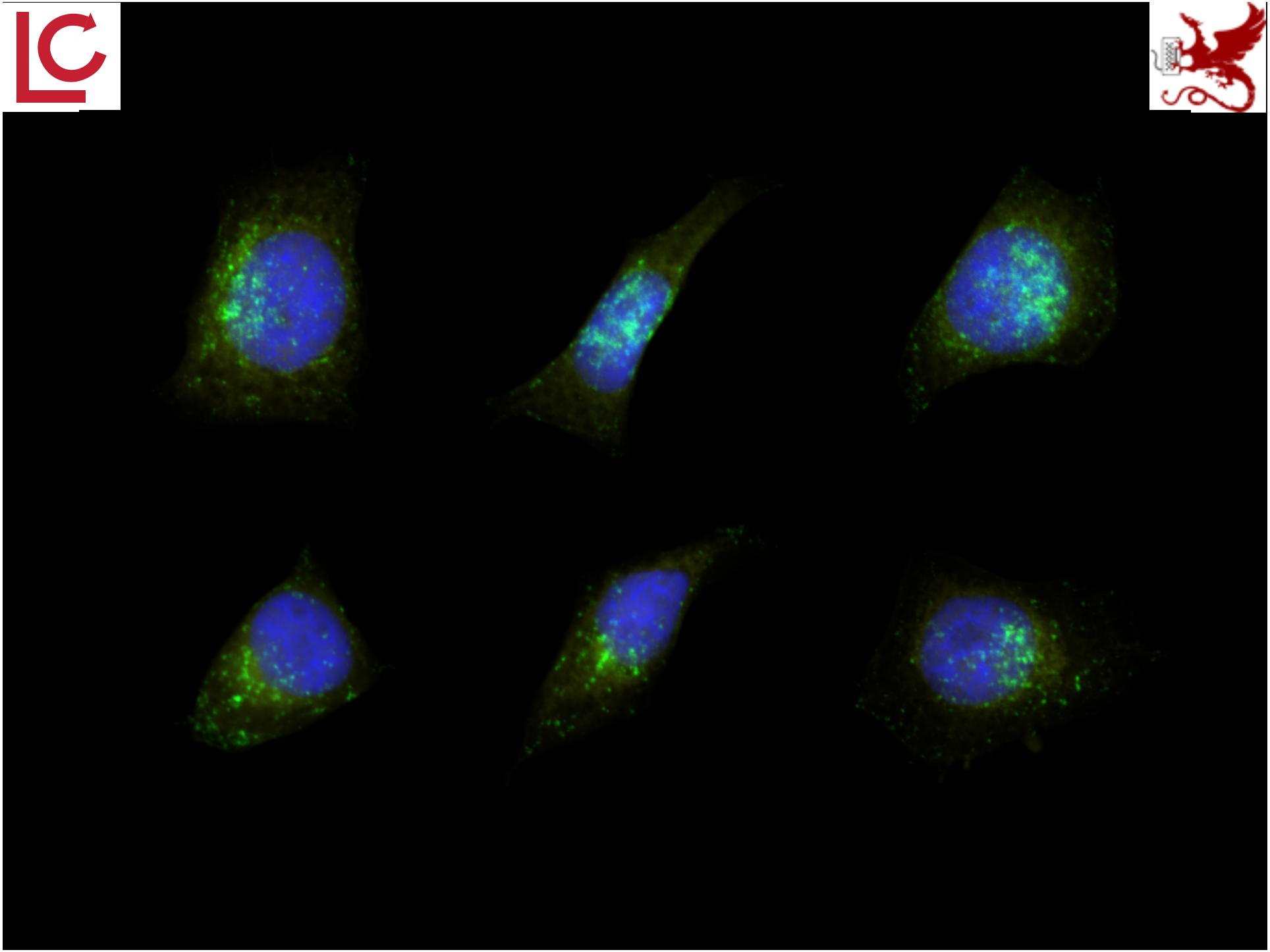
Want to Use Diverse Data

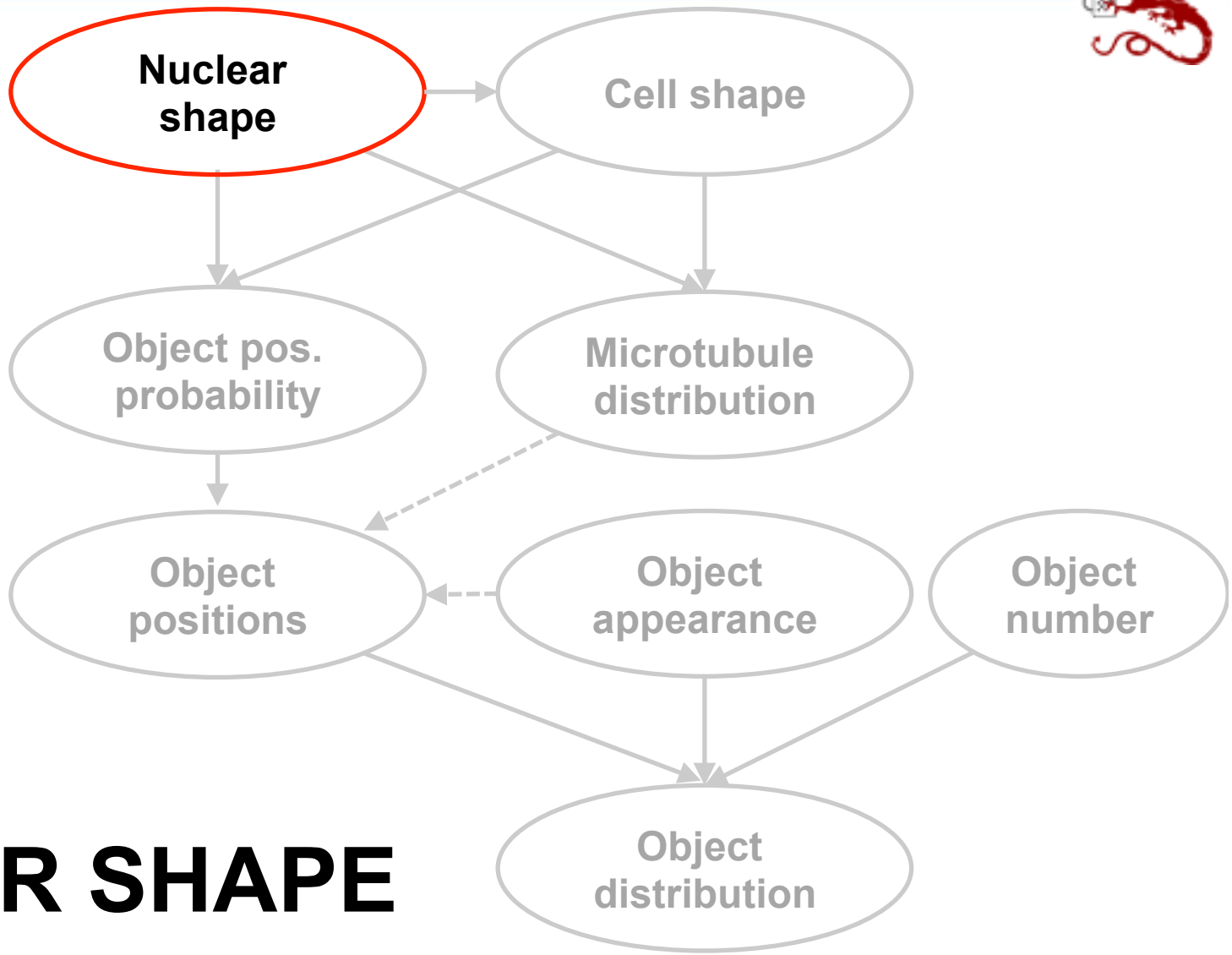
- From different:
  - Imaging systems
  - Cell lines
  - Protocols
- Feature values not “global”

Image-derived generative models of subcellular organization



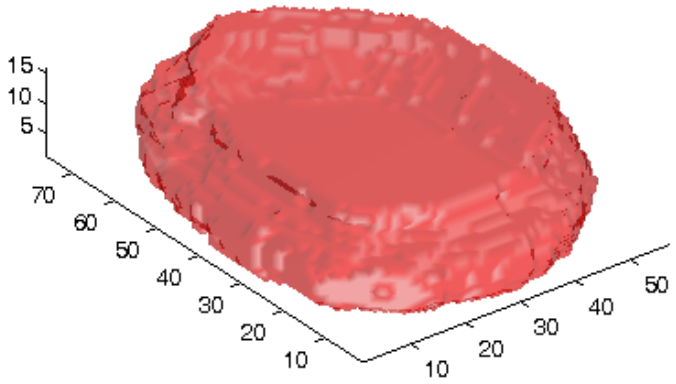
INPUTS: IMAGES



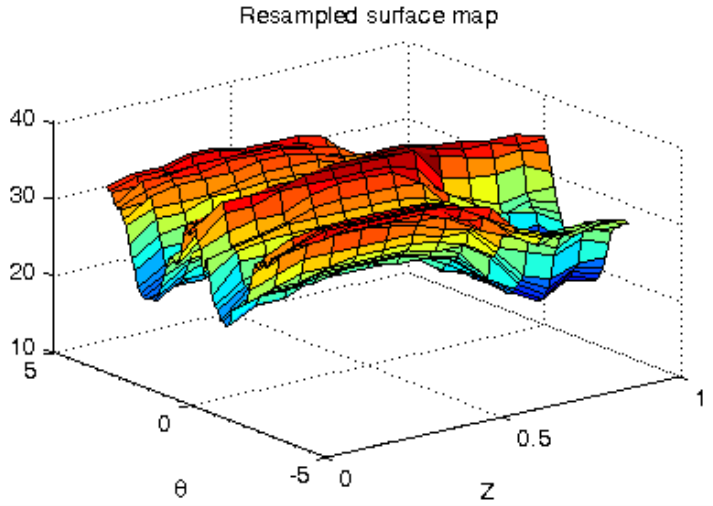


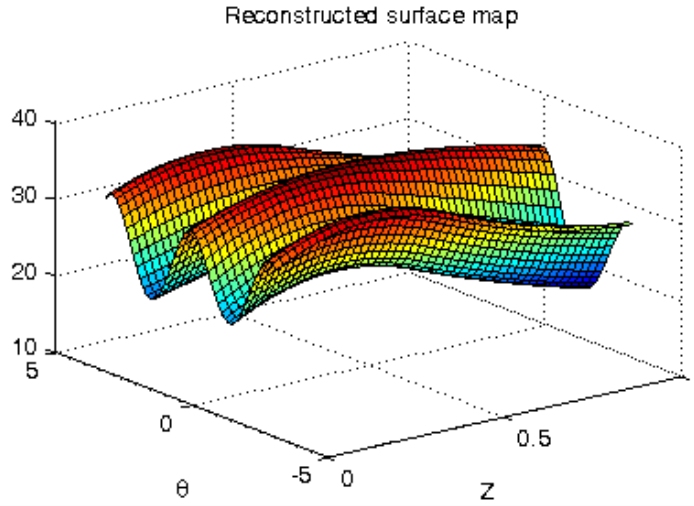
MODEL: NUCLEAR SHAPE

3D nuclear model: cylindrical spline surface

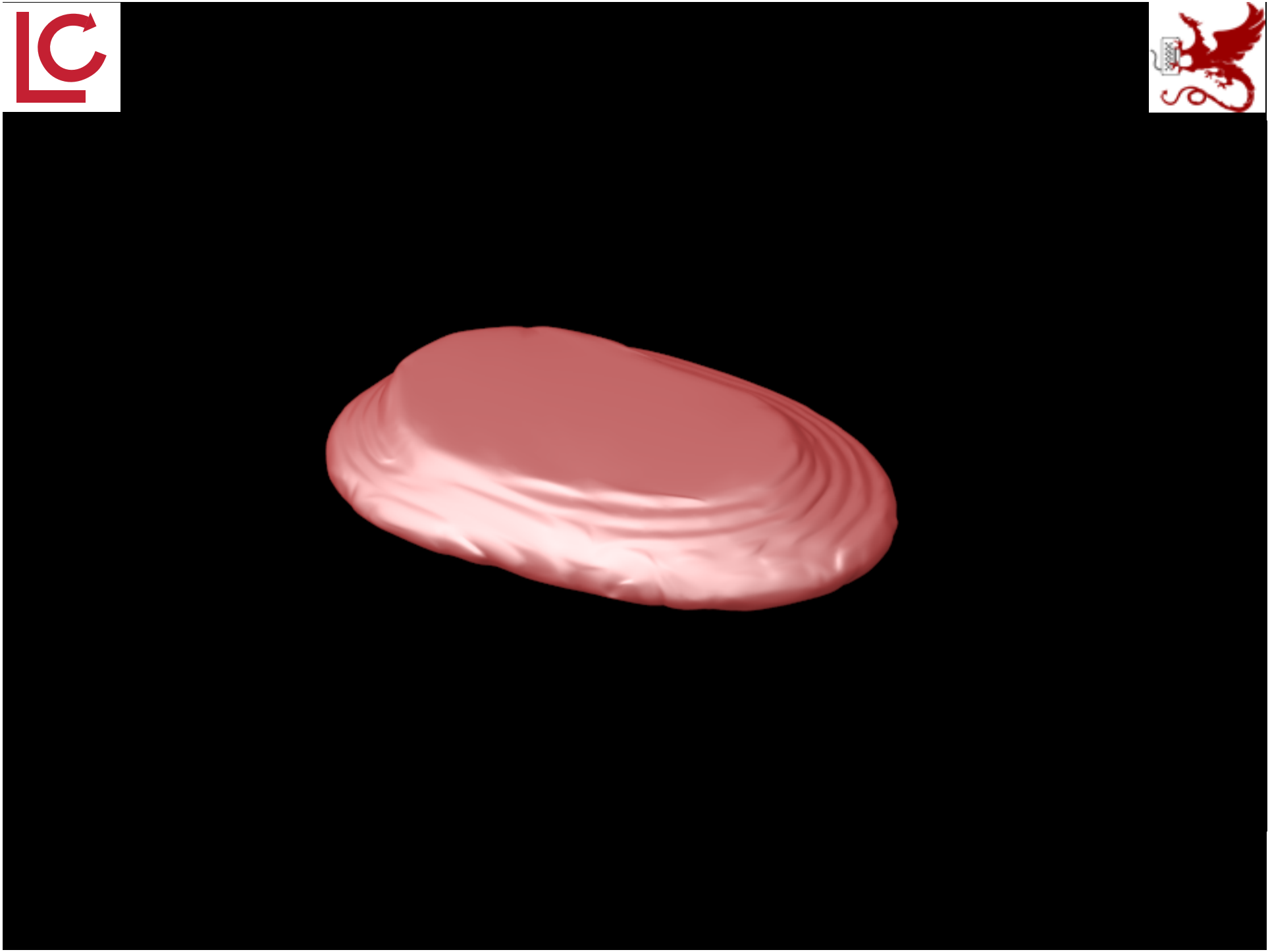


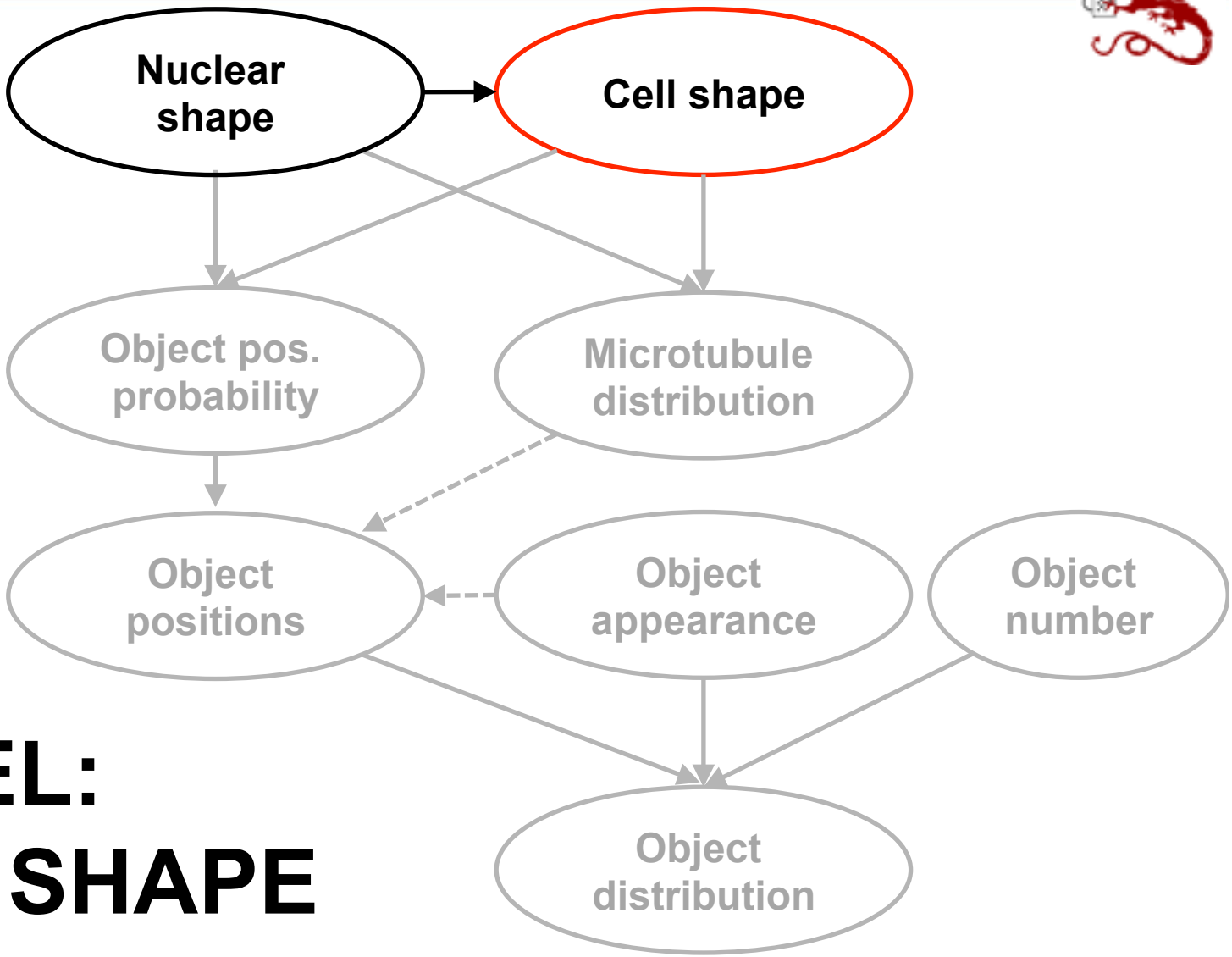
Tao Peng



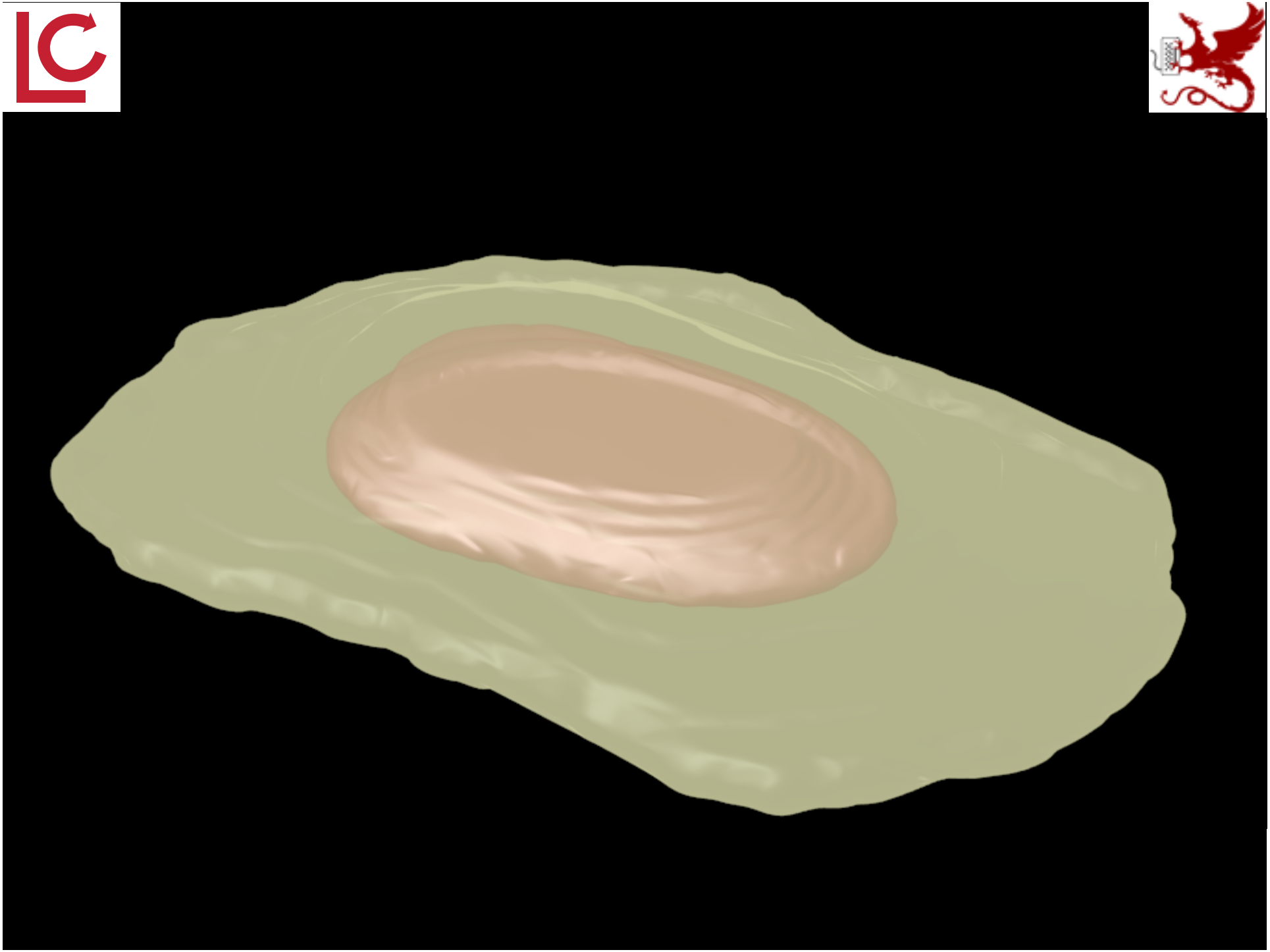


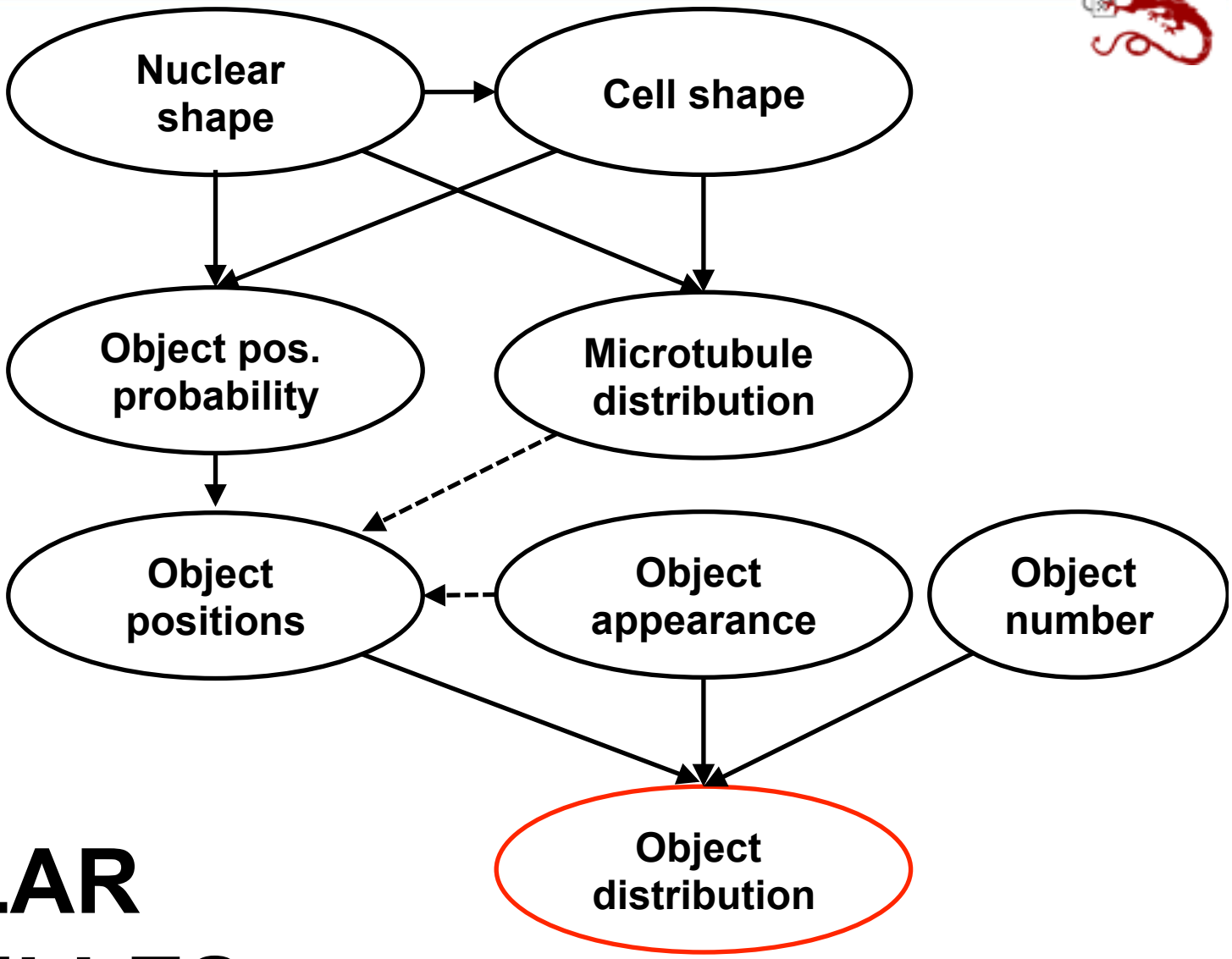
32 parameters for spline coefficients, 1 for height





MODEL: CELL SHAPE

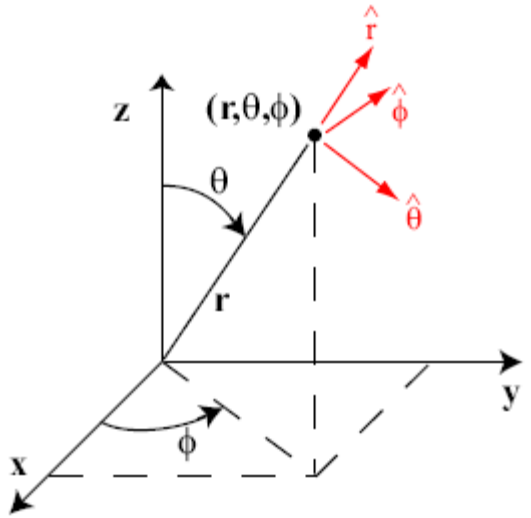




MODEL: VESICULAR ORGANELLES

Protein Objects Model: Position

3D

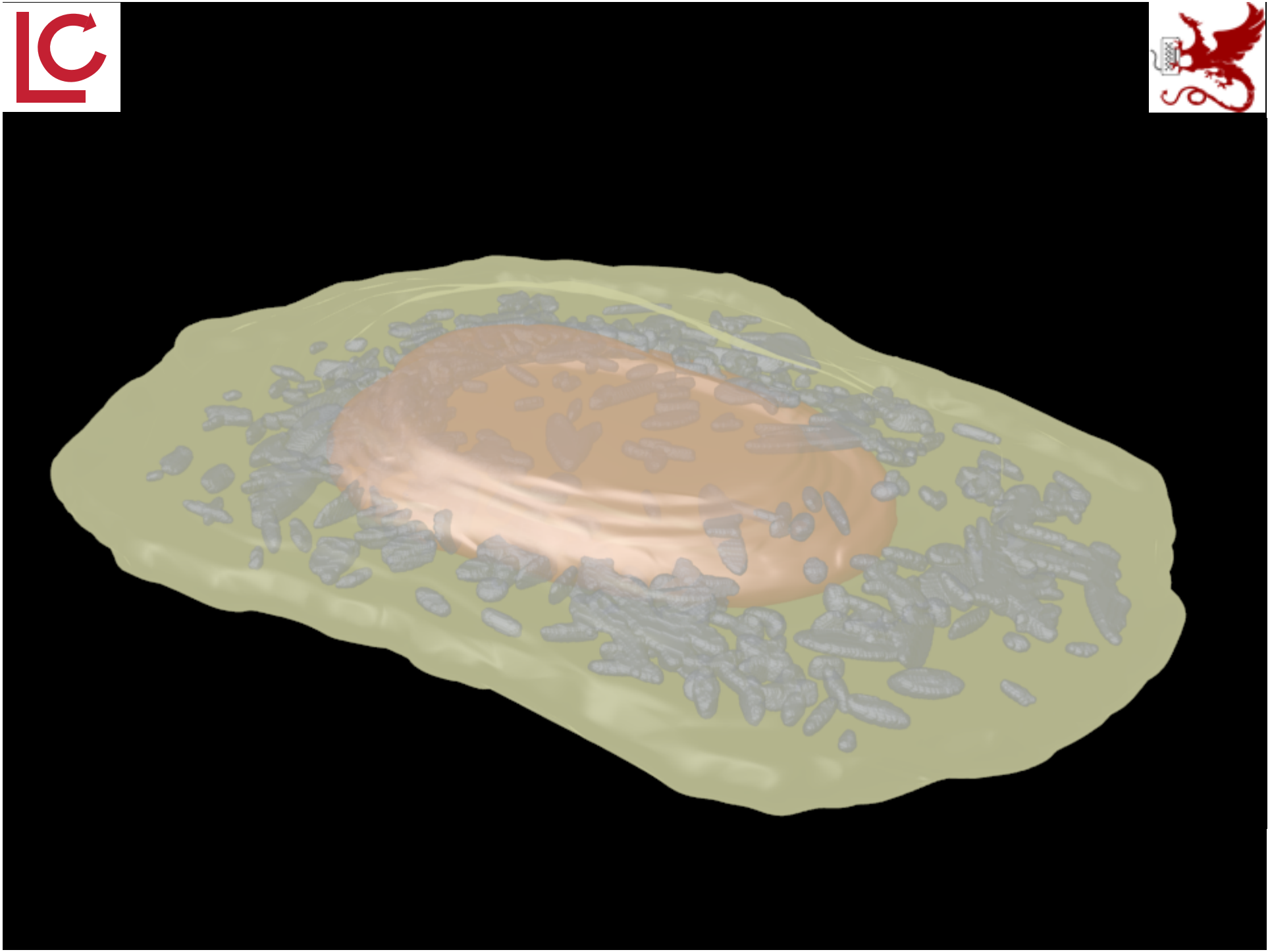


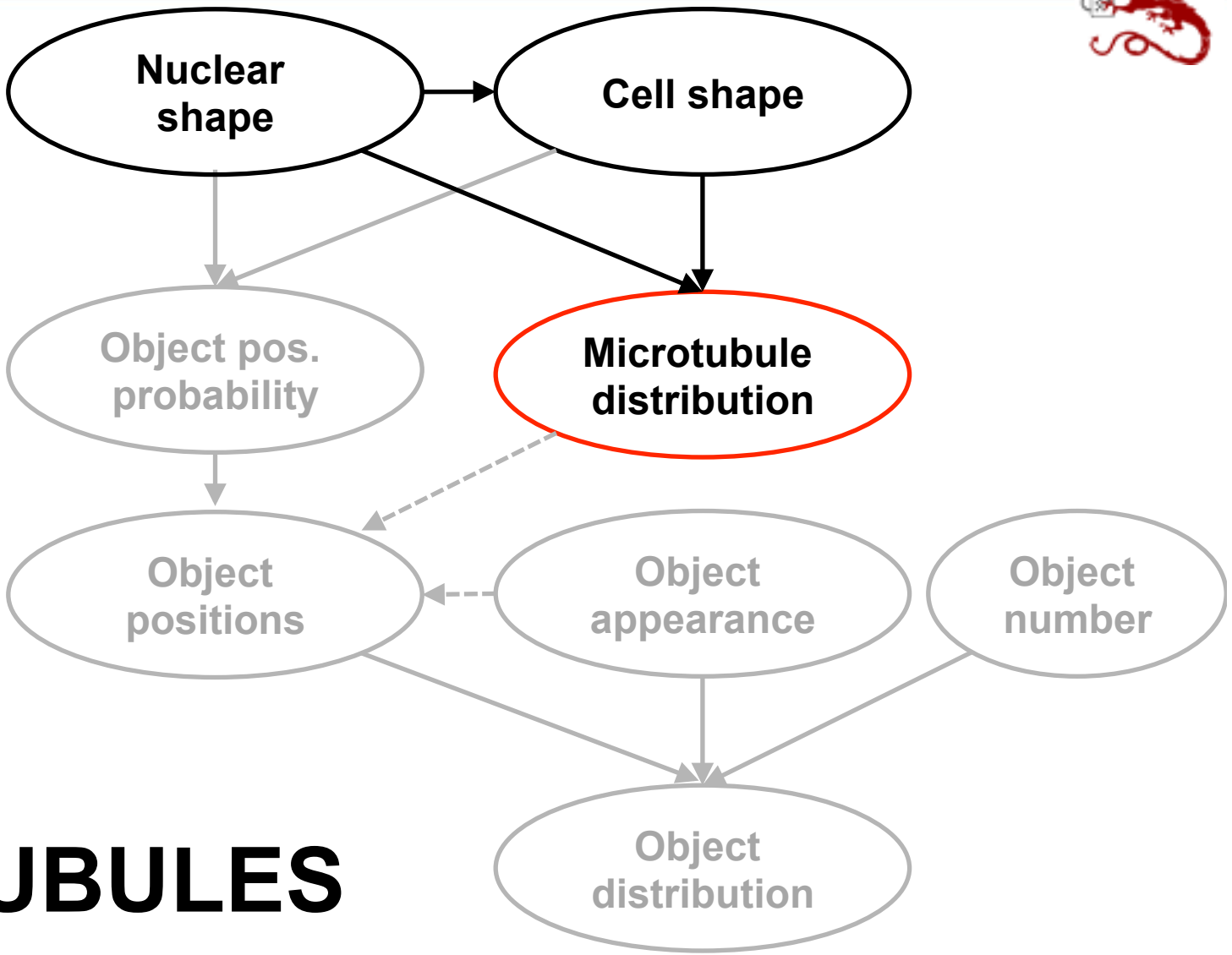
$$P(r,a) = \frac{e^{\tau(r,\theta,\varphi)}}{1+e^{\tau(r,\theta,\varphi)}}$$

$$\tau(r,\theta,\varphi) = \beta_0 + \beta_1 r + \beta_2 r^2 + \beta_3 \sin\theta\cos\varphi + \beta_4 \sin\theta\sin\varphi + \beta_5 \cos\theta$$

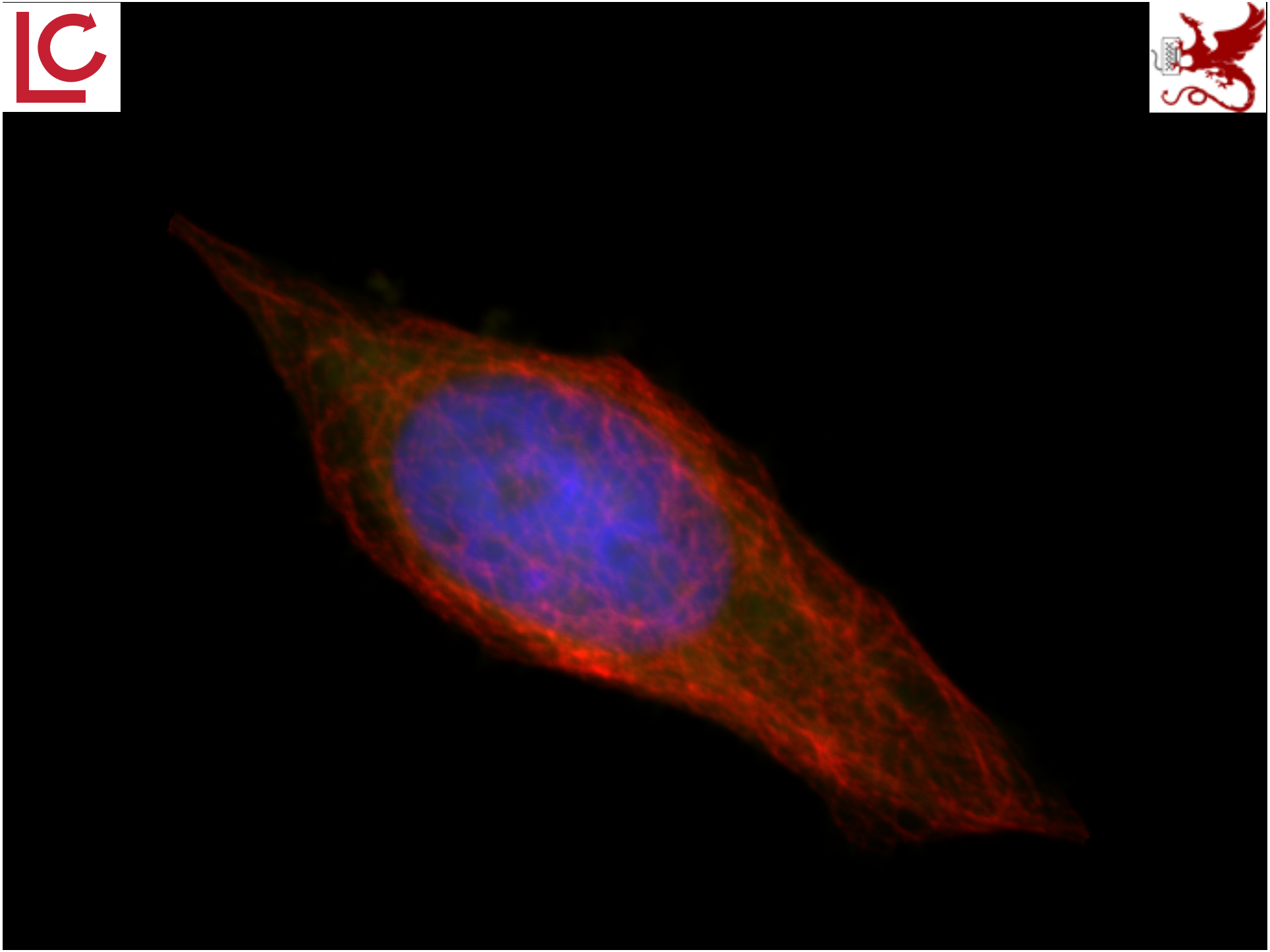
Radial preference

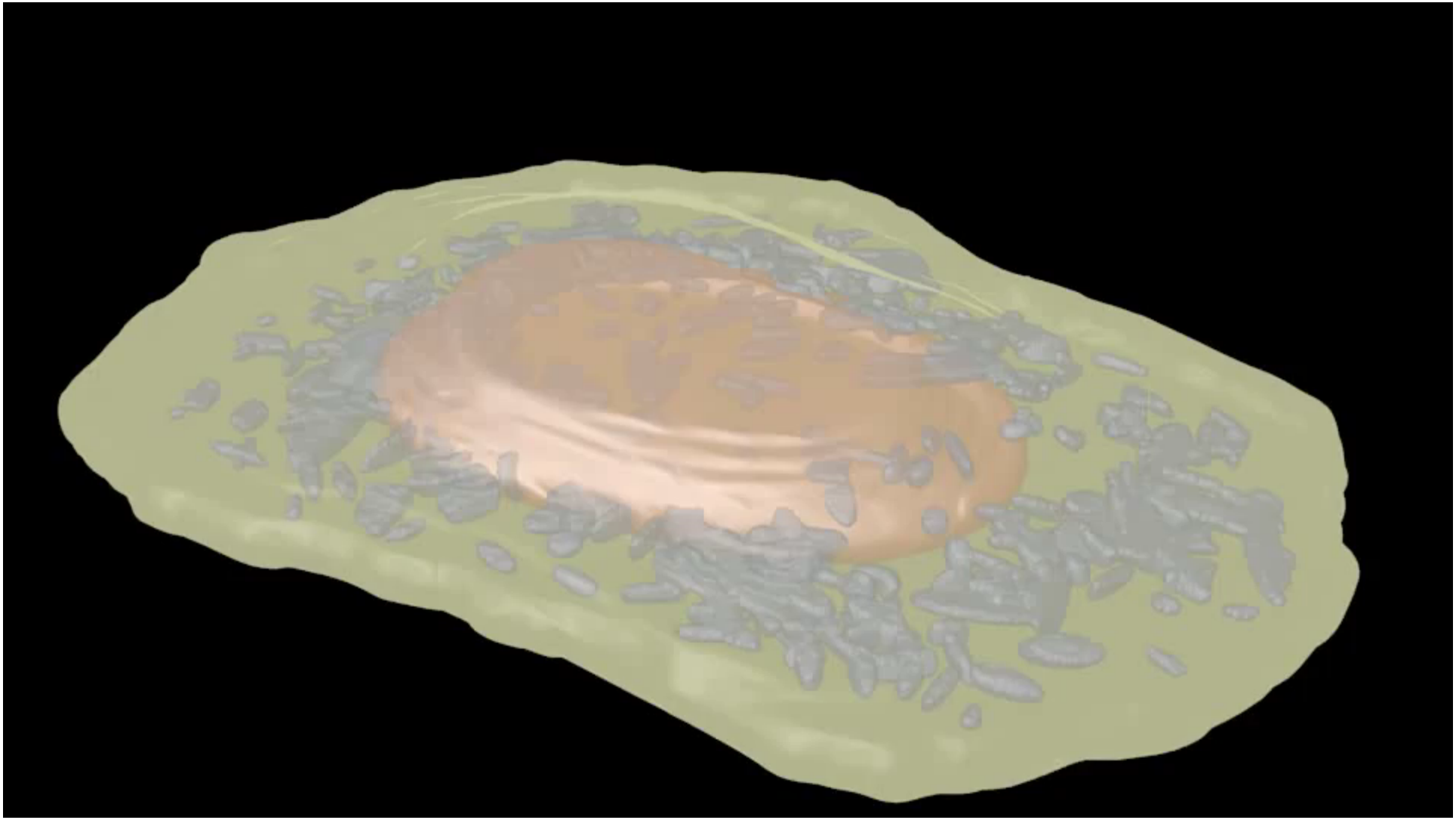
Angular preference





MODEL: MICROTUBULES

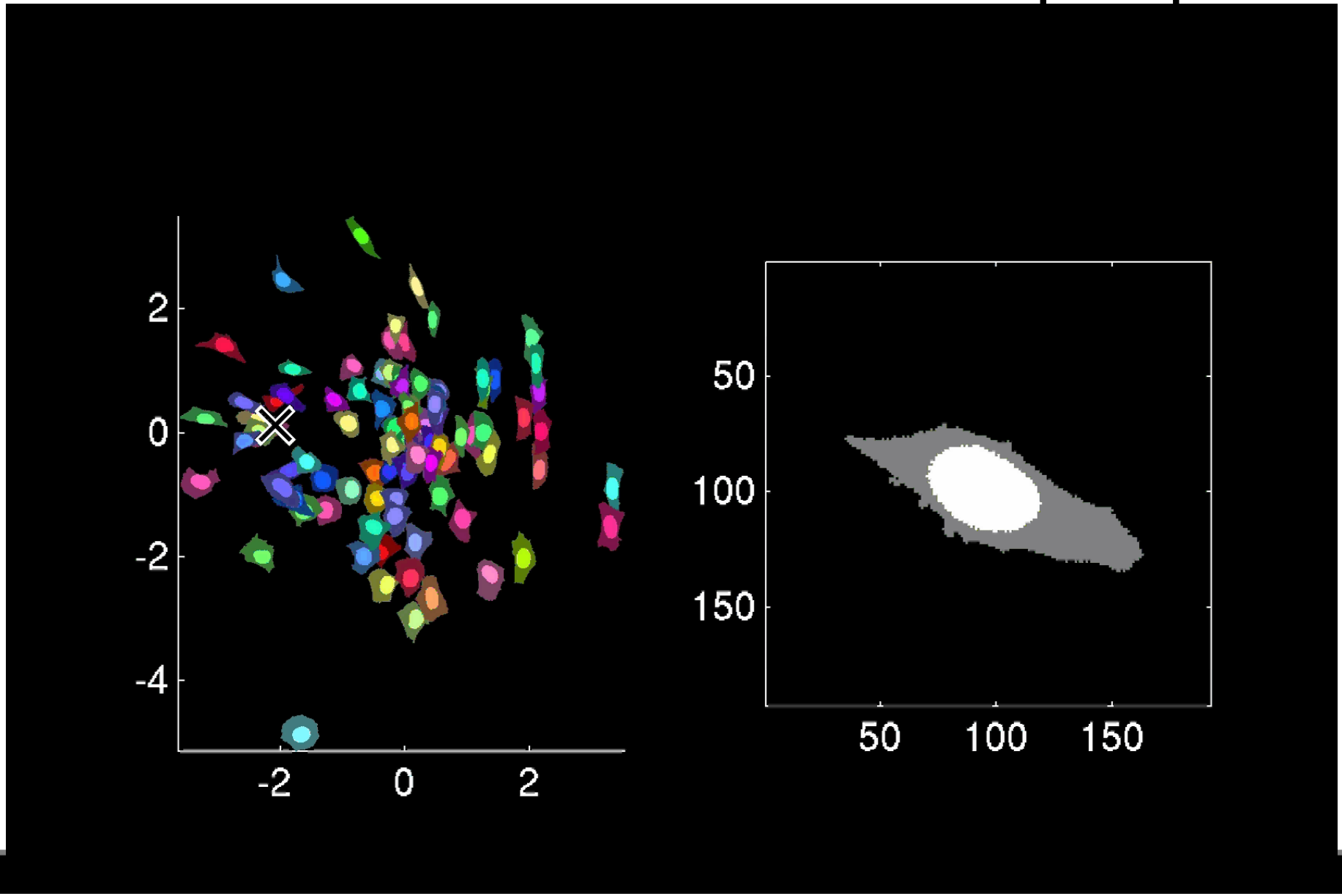


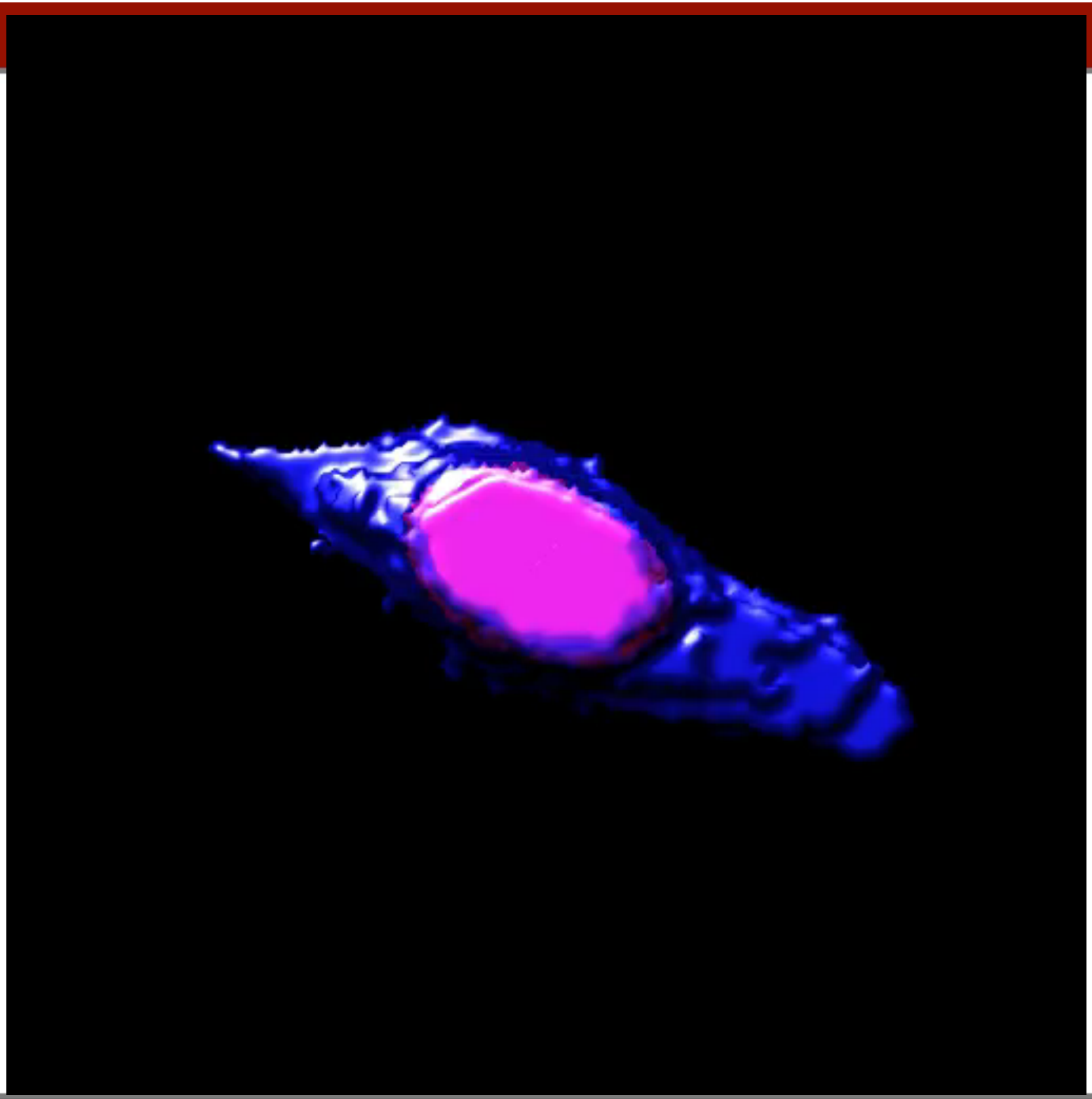



Shape space

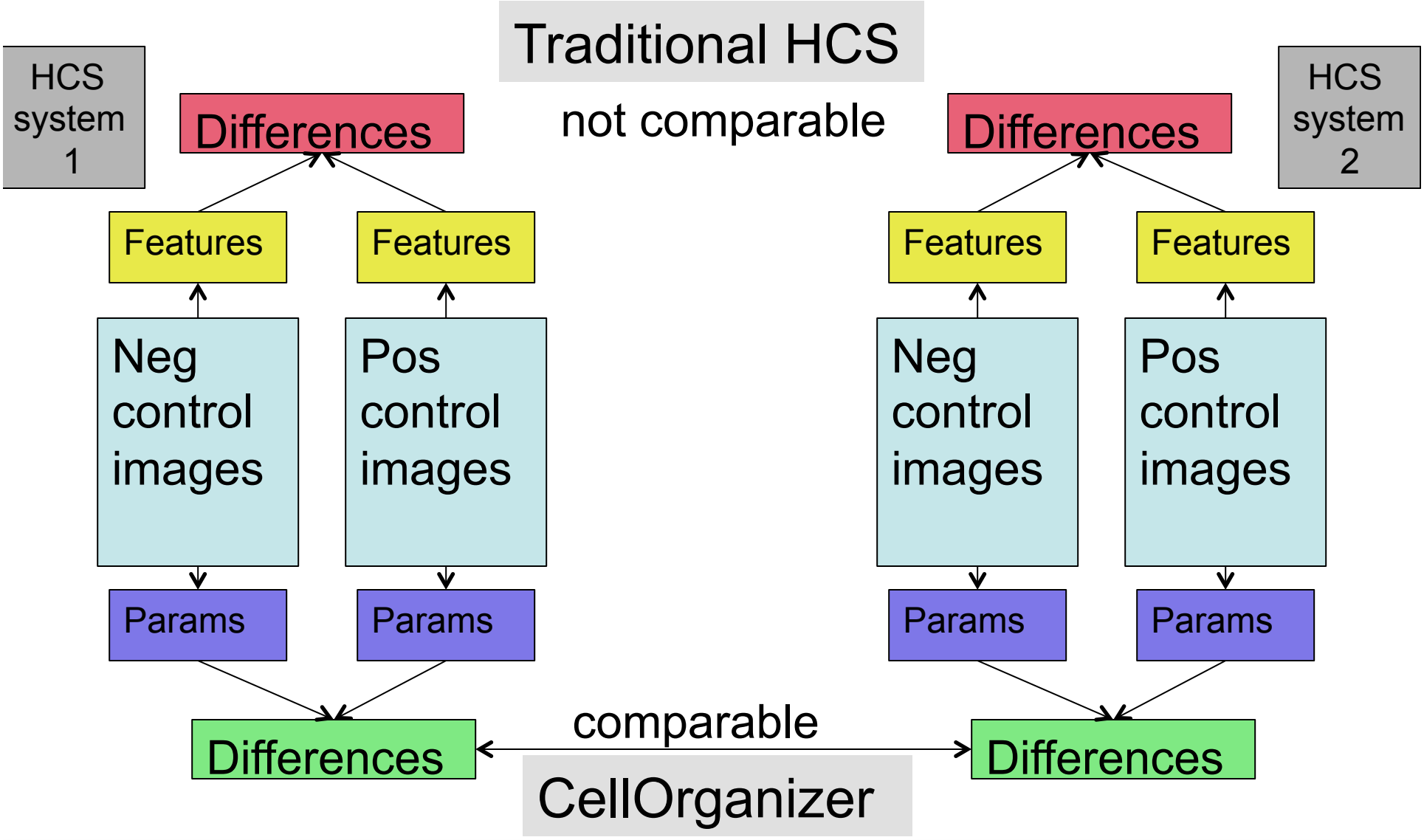
- Can measure distance between all pairs of shapes to construct a “shape space”
- Captures essential aspects of how shapes vary
- Can be applied in 2D, 3D, 4D and to more than one component at a time

Random walk in cell/nuclear shape space





CellOrganizer vs. traditional HCS



CellOrganizer.org

CellOrganizer
Images ↔ Models

People

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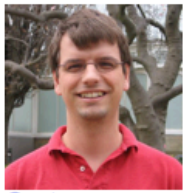
Project leaders


Robert F. Murphy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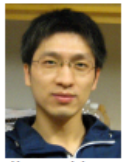
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Support for *CellOrganizer* has been provided by grants GM075205 and GM090033 from the National Institute of General Medical Sciences, by a ForschungPreis from the Alexander von Humboldt Foundation, and by the School of Life Sciences of the Freiburg Institute for Advanced Studies.