# Exploring biological shape analysis through topology, geometry and statistics

Ph. D. summer school: Biomedical image analysis, 2024/03/20

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Department of Computer Science

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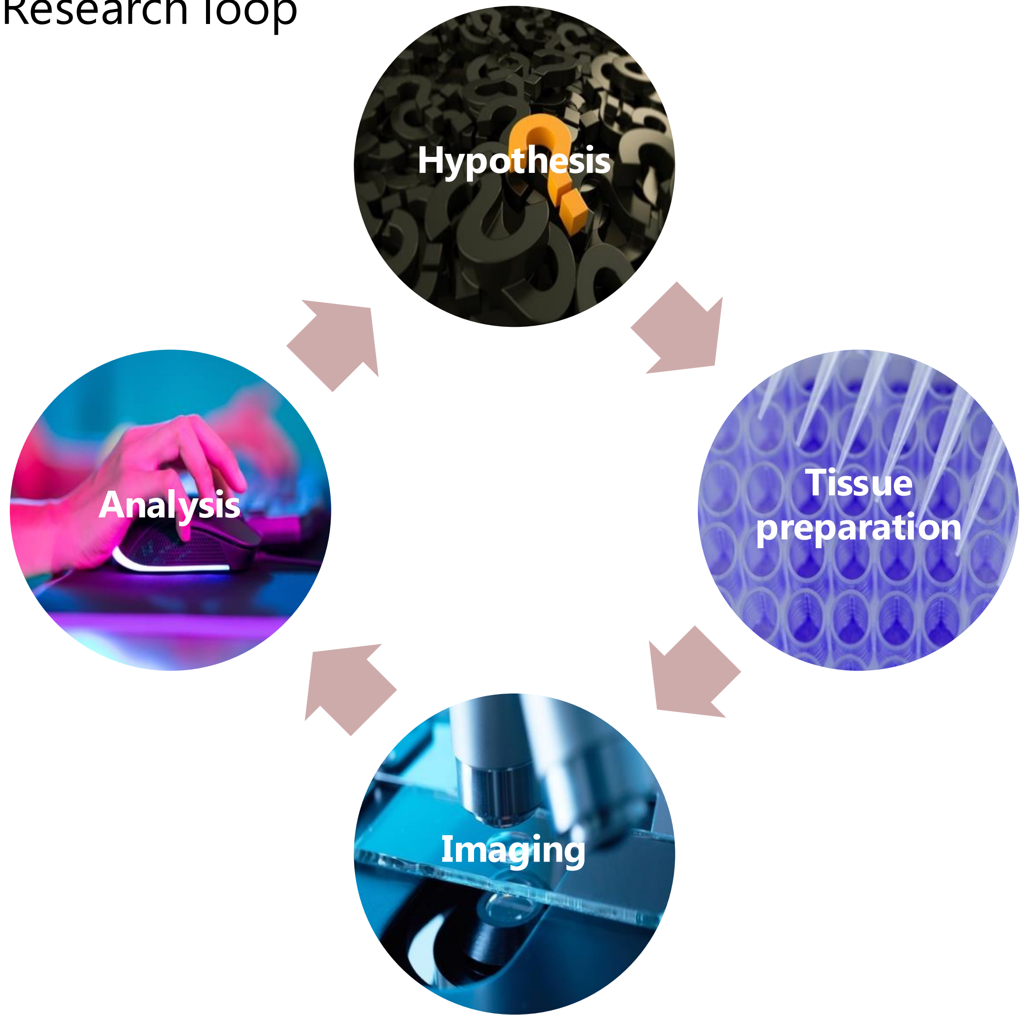
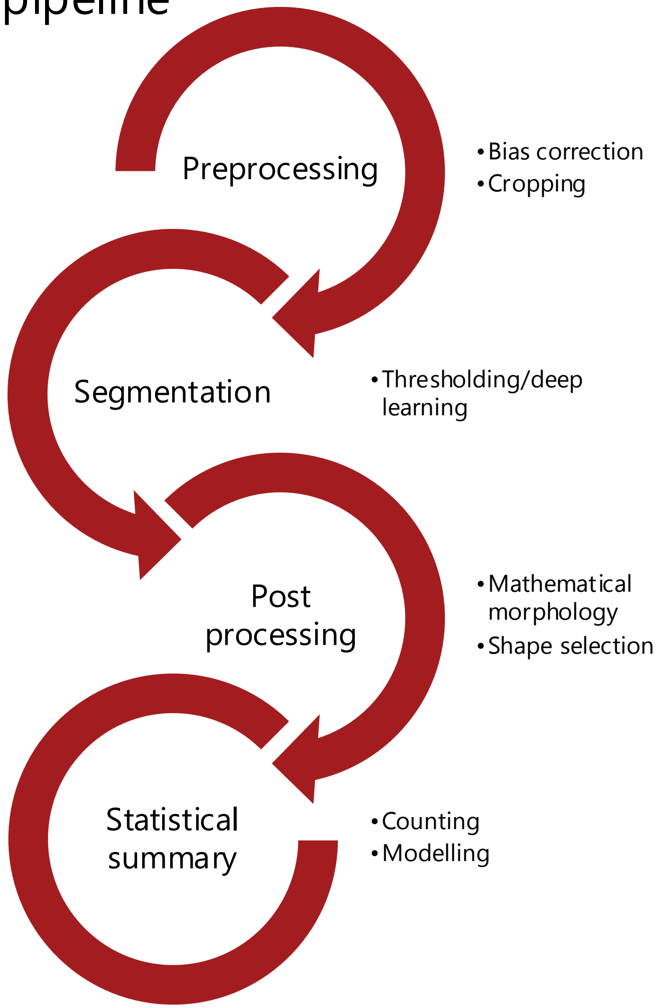
# Imaging research and pipeline

## Research loop




## Image analysis pipeline



# AI is pretty good at segmenting stuff, what’s next?

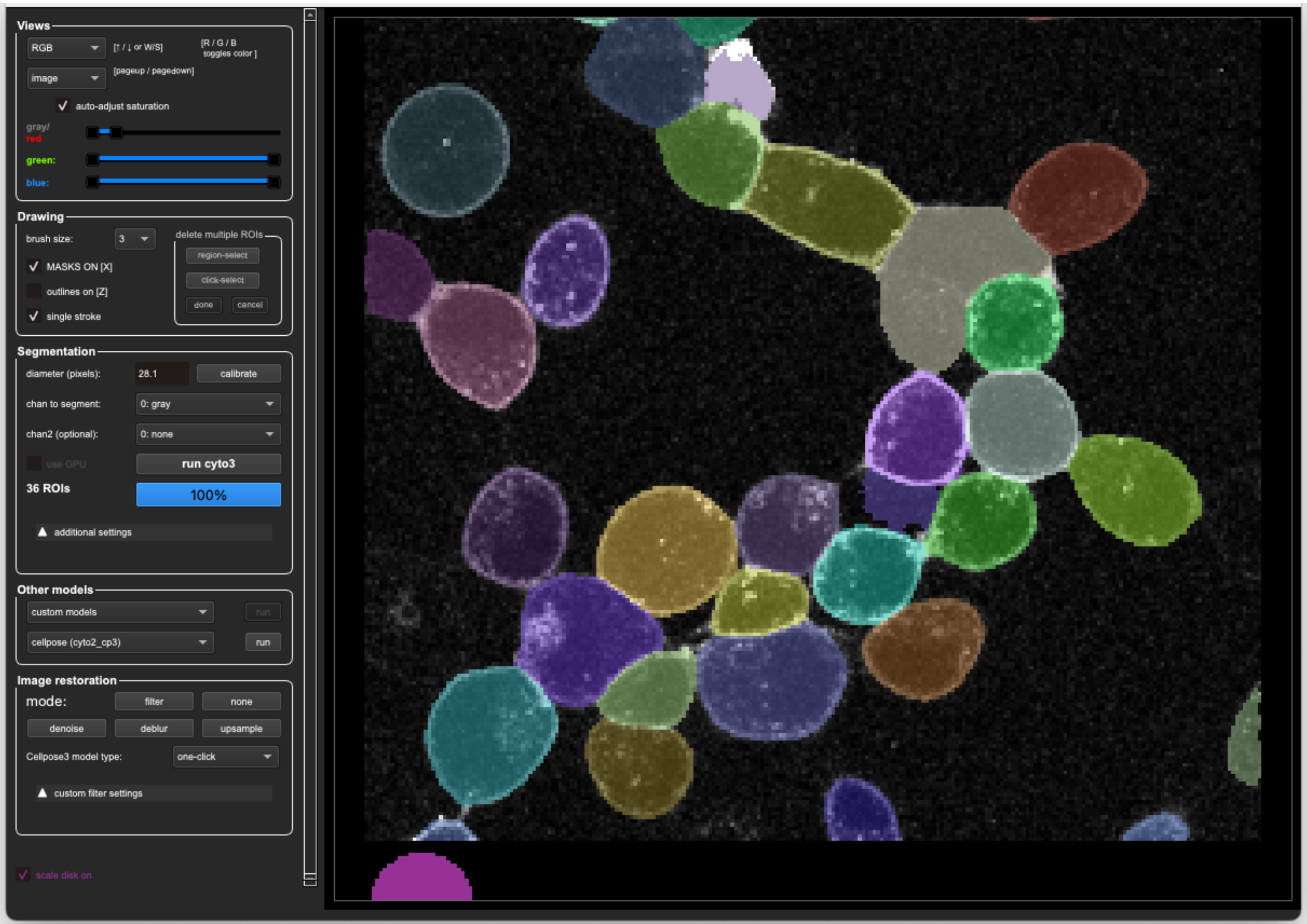



Image courtesy: Karen Martinez & Gabriella von Scheel von Rosing; AI: http://www.cellpose.org/

# What to do next: Shape analysis

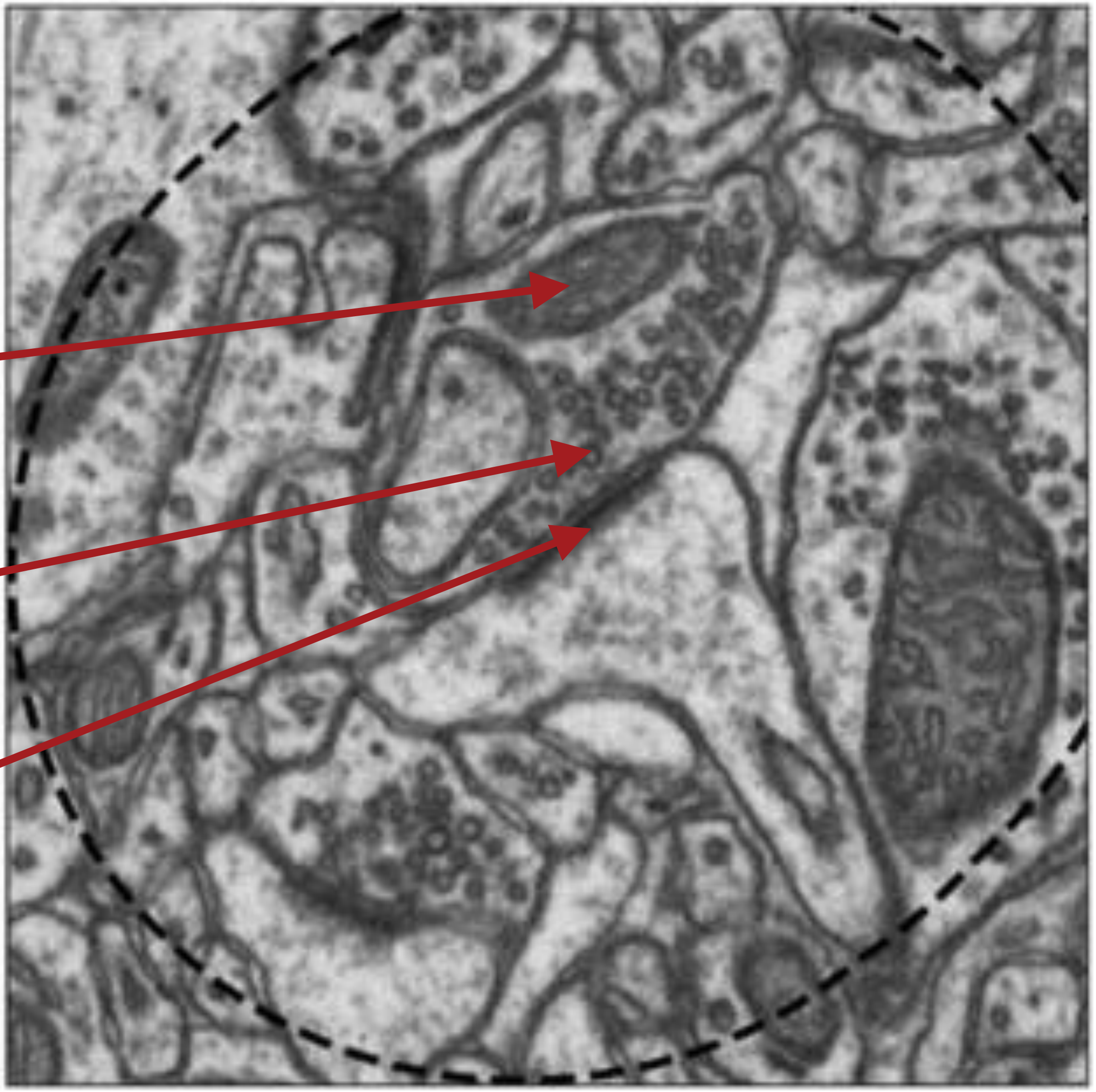
Focused ion-beam scanning electron microsopy (FIB-SEM)

Voxel size: (5 nm)^3

Mitochondria

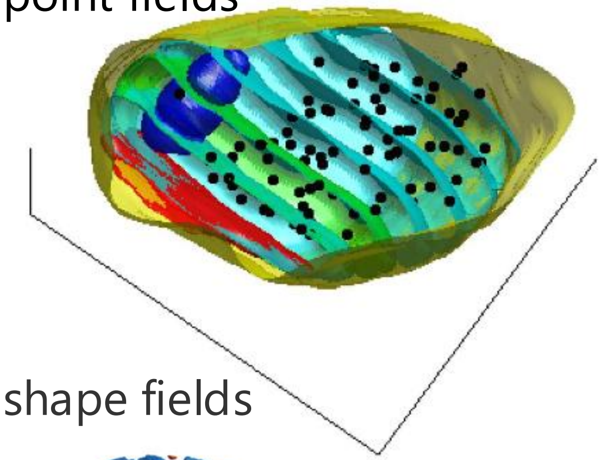
Vessicles

Active zone

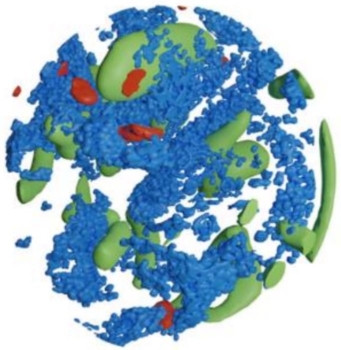


Graham Knott and Marco Cantoni. Electron microscopy dataset. https://cvlab.epfl.ch/data/ data-em/

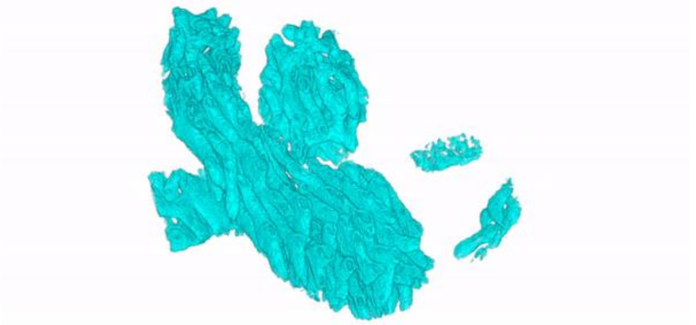
Spatial point fields



Spatial shape fields

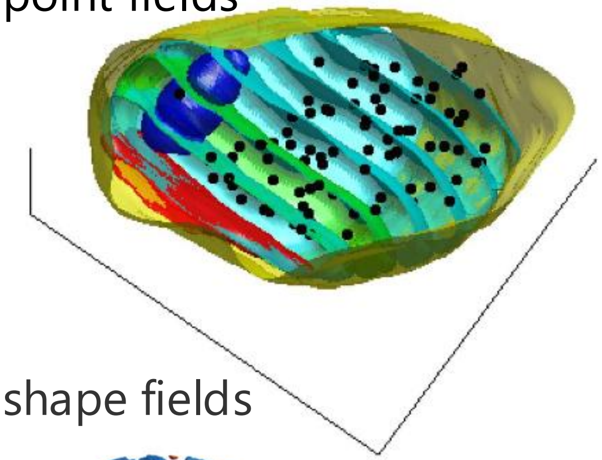


Topological data analysis

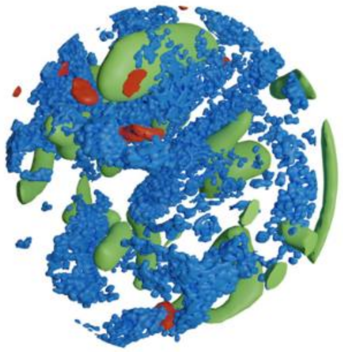


# Literature

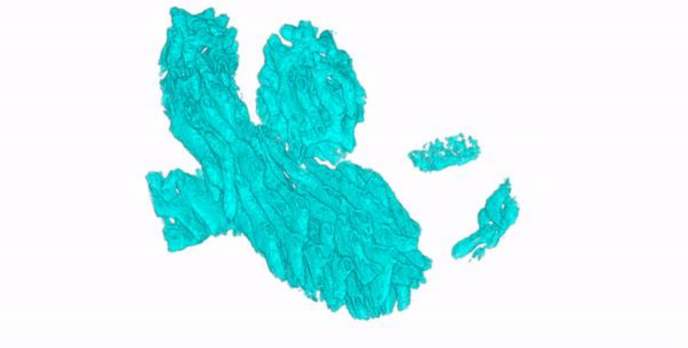
Spatial point fields



Spatial shape fields

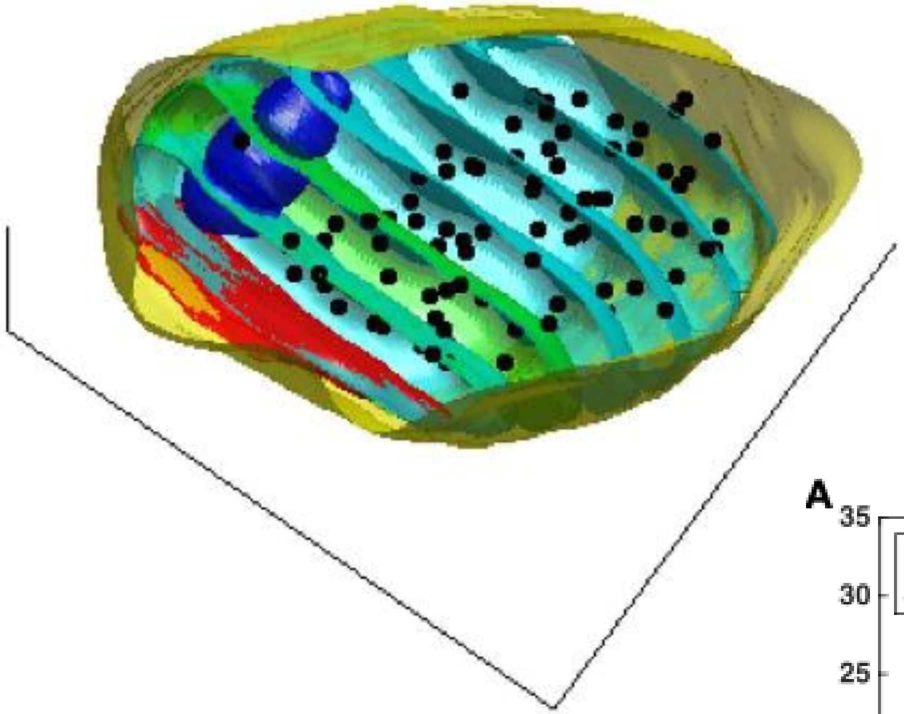


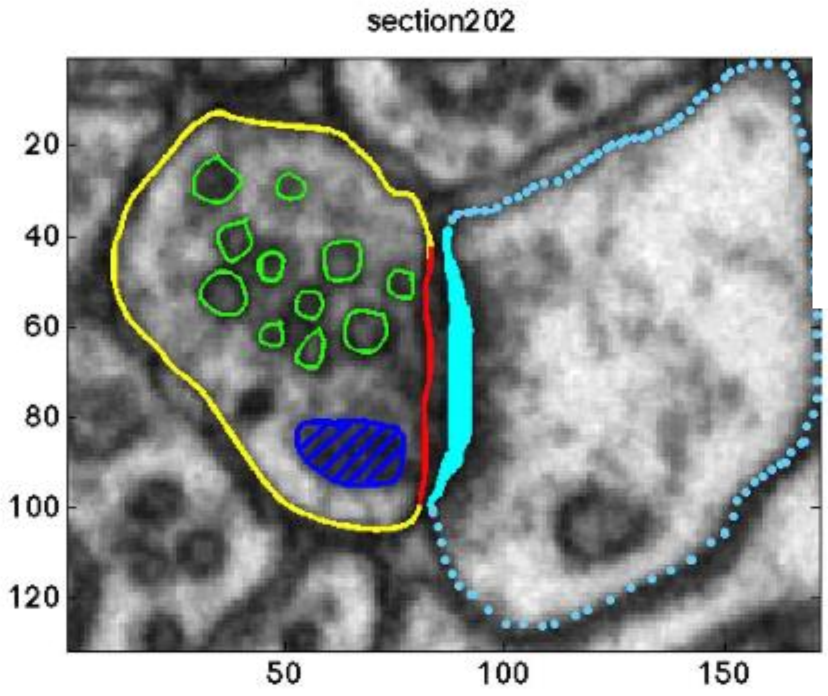
Topological data analysis

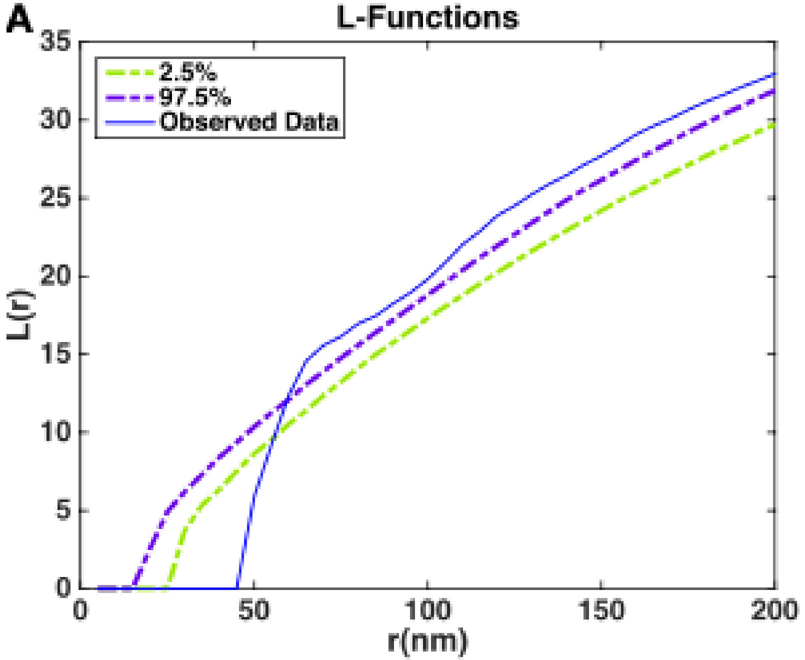



- Analysis of shape and spatial interaction of synaptic vesicles using data from focused ion beam scanning electron microscopy (FIB-SEM); M Khanmohammadi, RP Waagepetersen & J Sporring, Frontiers in Neuroanatomy, 2015
- Stoyan, D. (2006). Fundamentals of Point Process Statistics. In: Baddeley, A. et al. (eds) Case Studies in Spatial Point Process Modeling. Lecture Notes in Statistics, vol 185. Springer
- Mrkvička, Tomáš, et al. "A one-way ANOVA test for functional data with graphical interpretation." *Kybernetika* 56.3 (2020): 432-458.
- Stephensen, H.J.T., Svane, A.M., Villanueva, C.B. et al. Measuring Shape Relations Using r-Parallel Sets. J Math Imaging Vis, vol 63, 2021.
- Chazal F., Michel B., An Introduction to Topological Data Analysis: Fundamental and Practical Aspects for Data Scientists, In: Frontiers in Artificial Intelligence, vol 4, 2021

# Point models





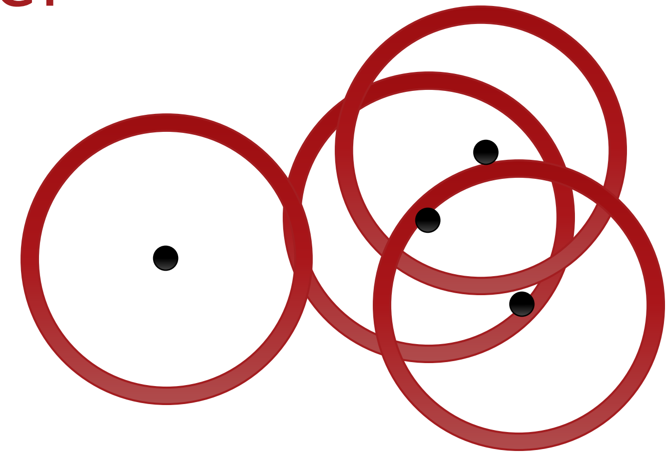



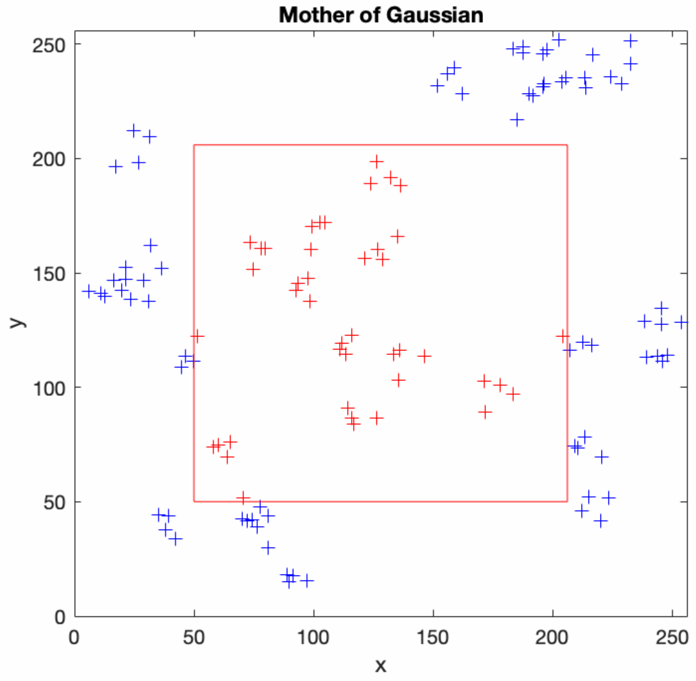

**Analysis of shape and spatial interaction of synaptic vesicles using data from focused ion beam scanning electron microscopy (FIB-SEM);** M Khanmohammadi, RP Waagepetersen & J Sporring, Frontiers in Neuroanatomy, 2015

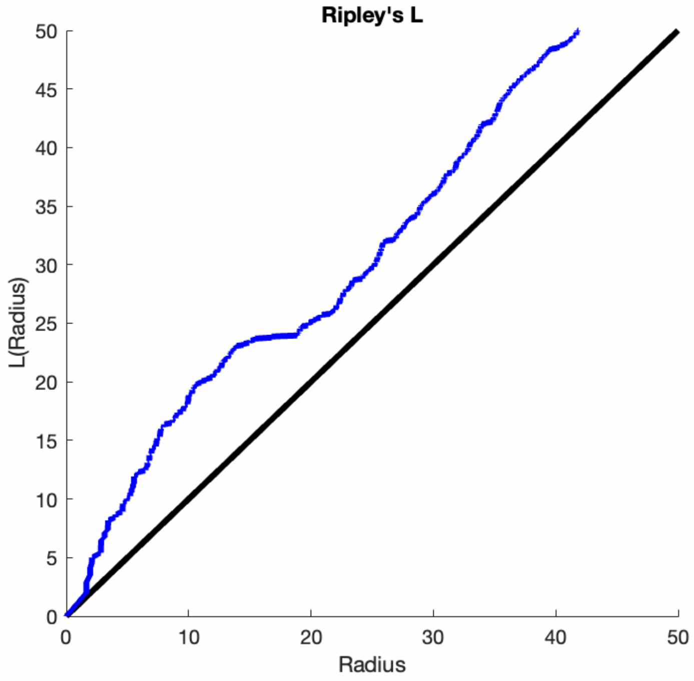
# Ripley’s K- and L-functions: expected number of neighboring points by radius

$$K(r) = \frac{1}{\lambda}\mathbb{E}\left[I\left(d_{ij} < r\right)\right]$$

$$L = \sqrt{\frac{K}{\pi}}$$





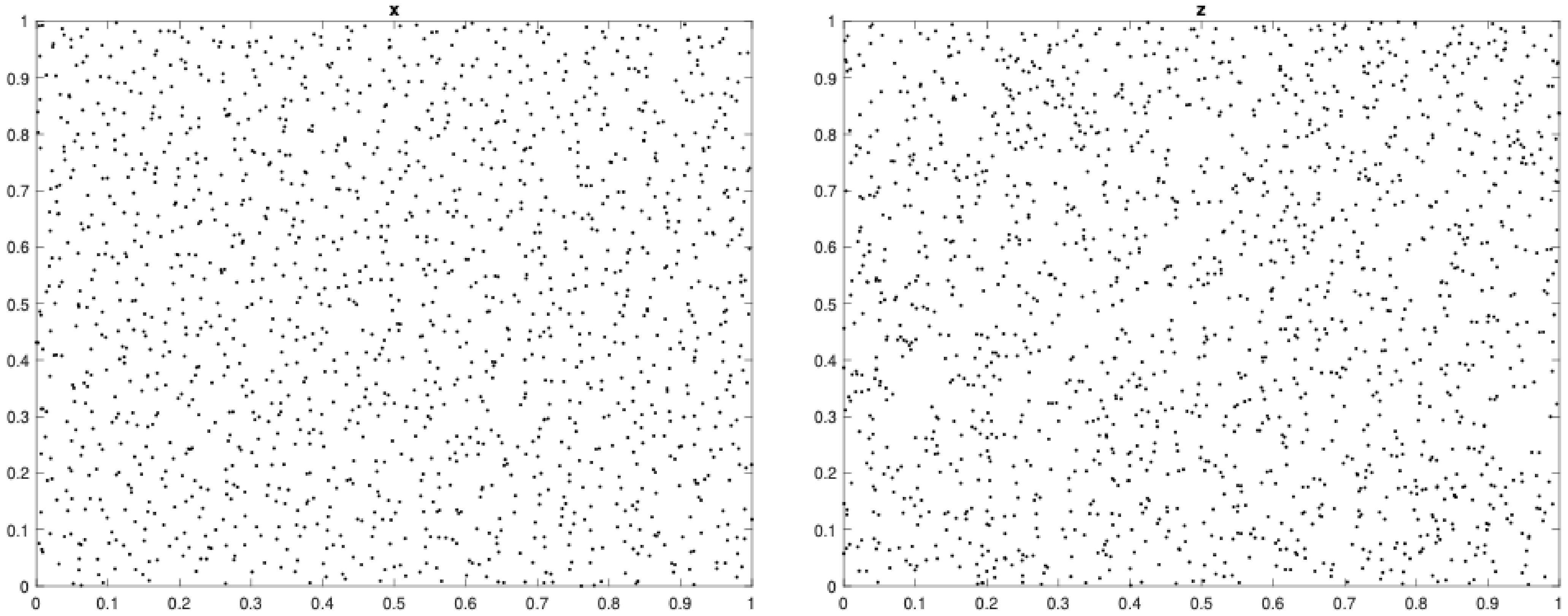



# R and rpy2 demo: https://sporring.github.io/bia2024/ demoRpy2.py

https://cran.r-project.org/

https://spatstat.org/

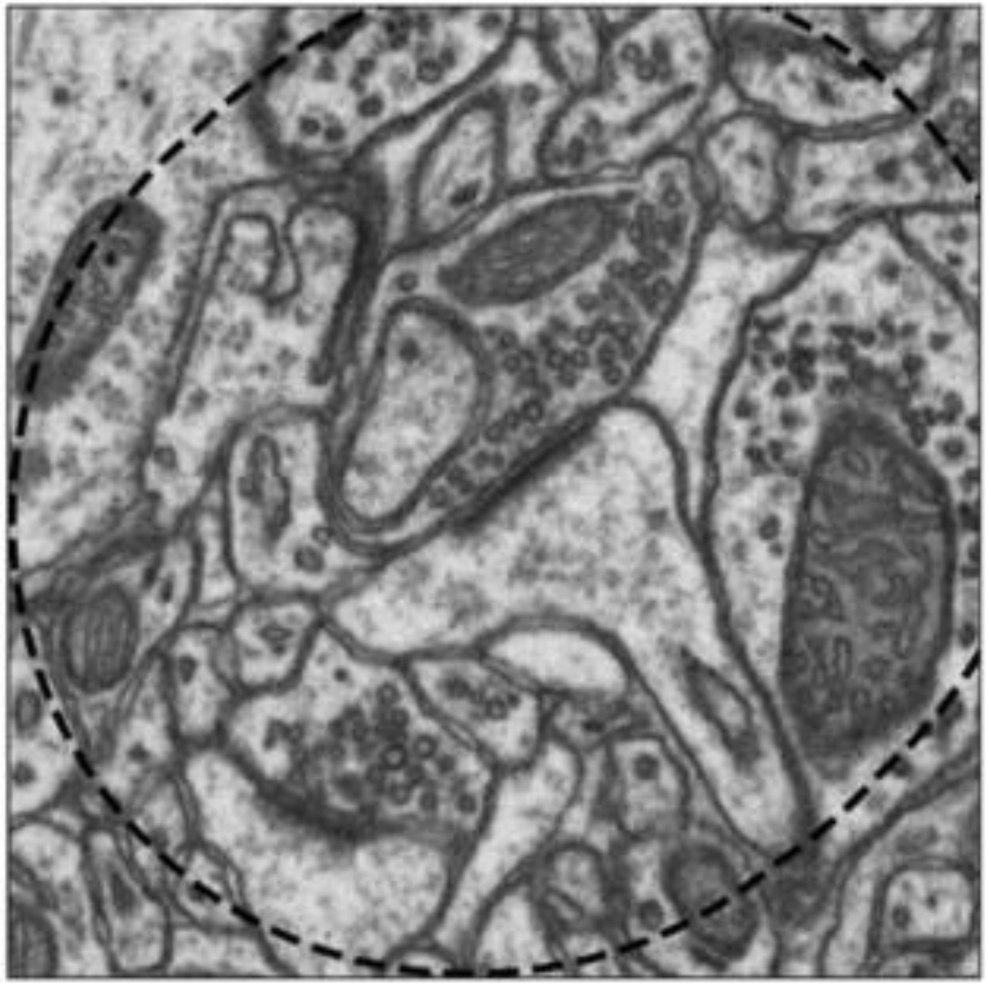
https://cran.r-project.org/web/packages/GET/vignettes/pointpatterns.pdf



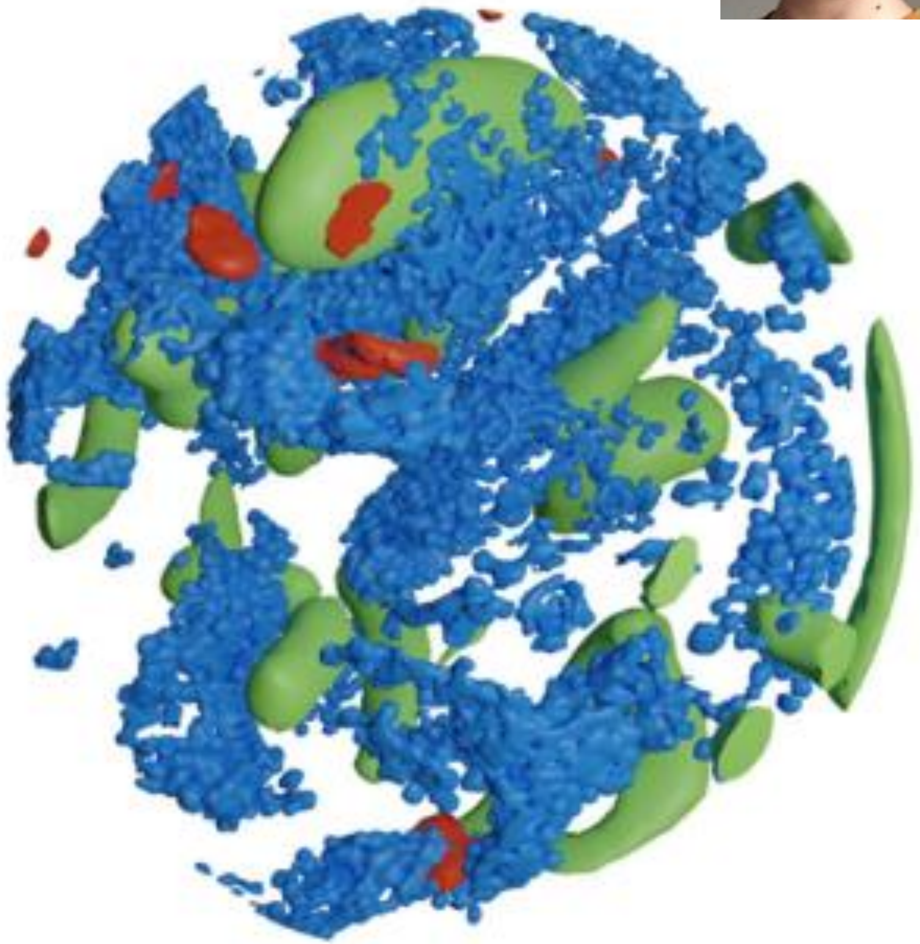

Exercise: Use GET’s global_envelope_test to test whether x and/or z are likely to be random

# Real structures are not points, small structures are difficult to separate

Graham Knott and Marco Cantoni. Electron microscopy dataset. https://cvlab.epfl.ch/data/ data-em/

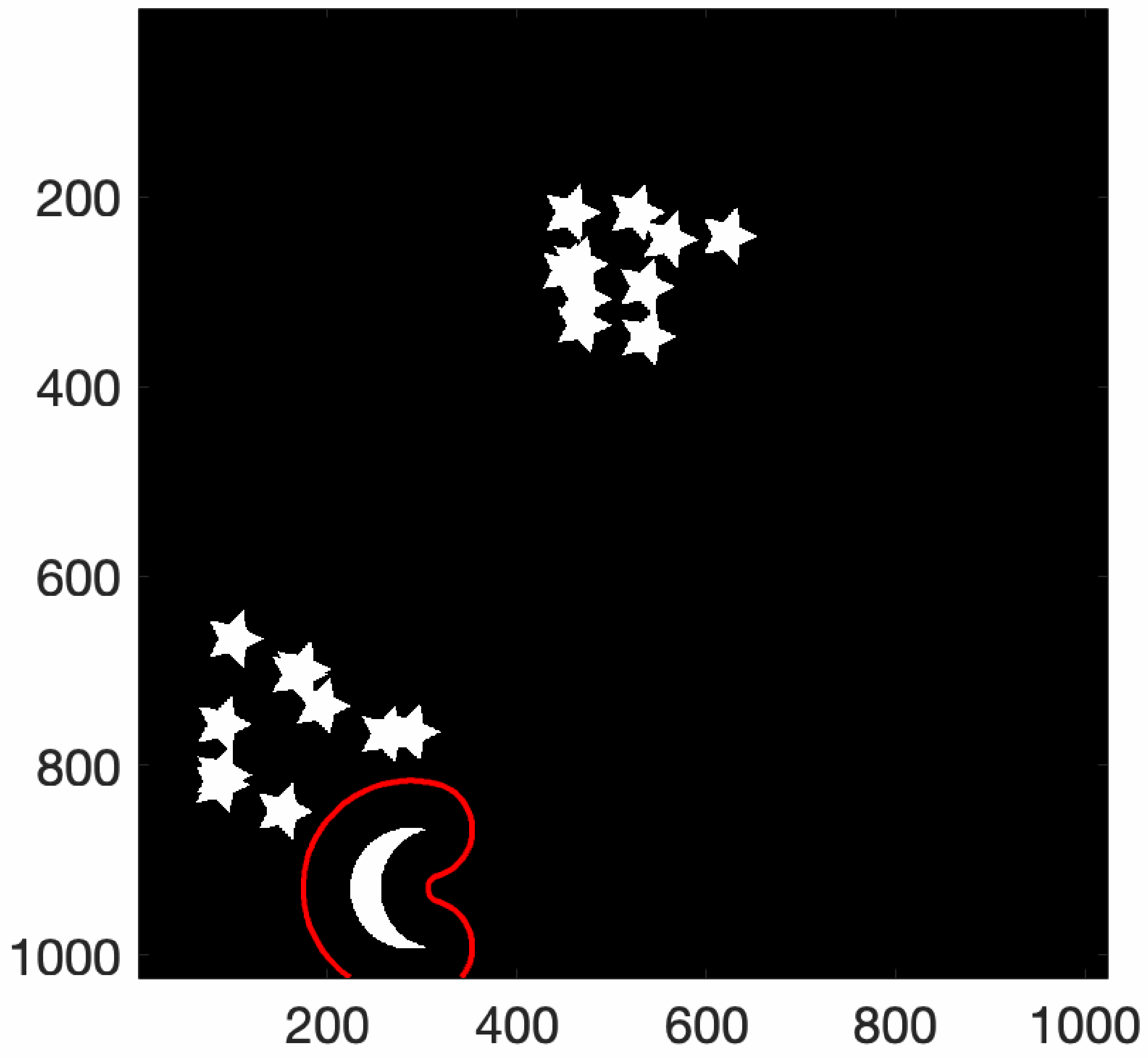


Deep Learning

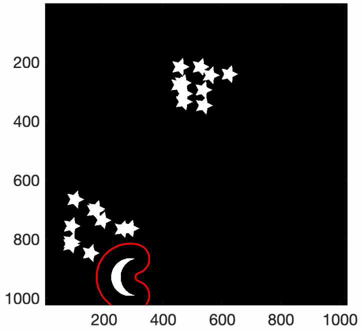


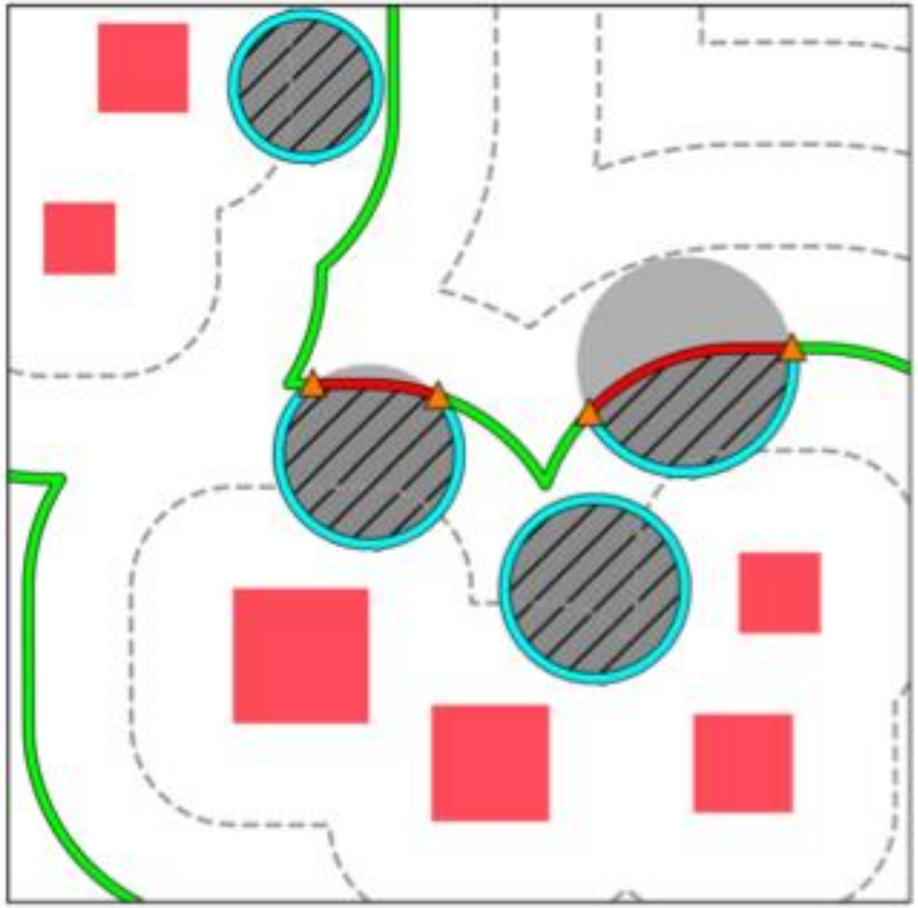
**Measuring Shape Relations Using r-Parallel Sets;** HJT Stephensen, AM Svane, CB Villanueva, SA Goldman, & J Sporring; Journal of mathematical imaging and vision, 2021

# Shape relation measures: K-functions for objects



# Shape relation measures: K-functions for objects



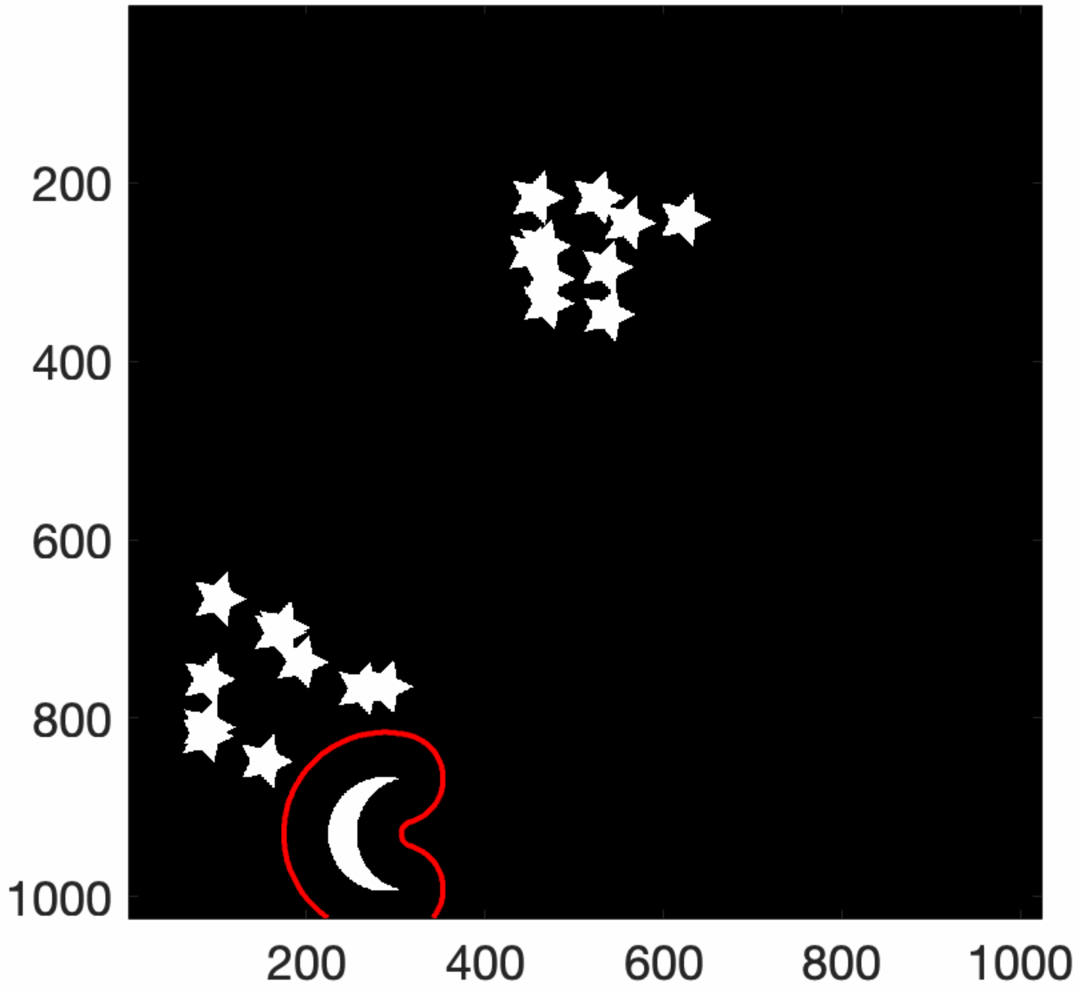
$$Y^r = \{\alpha \in \mathbb{R}^d \mid \inf_{y \in Y} d(\alpha, y) \le r\} \quad (1)$$

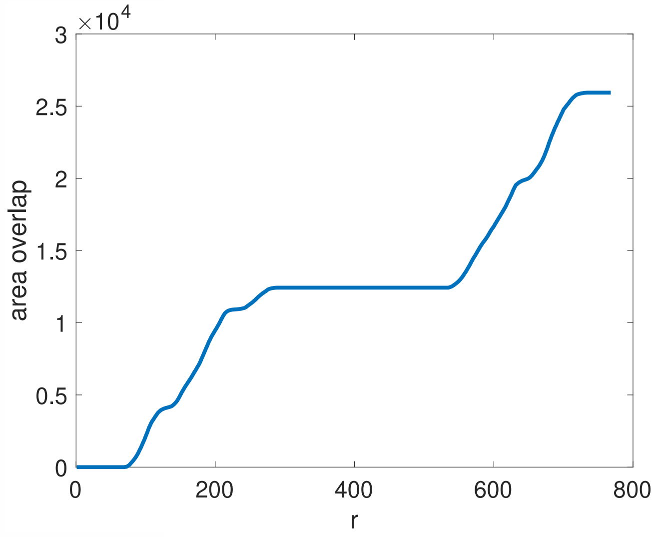
$$\mu_{\varepsilon,\varepsilon'}(X, Y^r) = \mathcal{H}^{d-\varepsilon-\varepsilon'}(\partial^{\varepsilon} X \cap \partial^{\varepsilon'} Y^r) \ . \quad (2)$$

| $d = 2$ | $(\varepsilon, \varepsilon')$ | $\mathcal{H}^{d-\varepsilon-\varepsilon'}$ | $\partial^{\varepsilon} X \cap \partial^{\varepsilon'} Y^r$ | Interpretation of $\mu_{\varepsilon,\varepsilon'}(X, Y^r)$ |
|---|---|---|---|---|
| | $(0, 0)$ | Area | $X \cap Y^r$ | Area of intersection |
| | $(0, 1)$ | Curve length | $X \cap \partial Y^r$ | Boundary length of intersection inside interior of $X$ |
| | $(1, 0)$ | Curve length | $\partial X \cap Y^r$ | Boundary length of intersection inside boundary of $X$ |
| | $(1, 1)$ | Point counts | $\partial X \cap \partial Y^r$ | Number of points in intersection of boundaries |
| $d = 3$ | $(\varepsilon, \varepsilon')$ | $\mathcal{H}^{d-\varepsilon-\varepsilon'}$ | $\partial^{\varepsilon} X \cap \partial^{\varepsilon'} Y^r$ | Interpretation of $\mu_{\varepsilon,\varepsilon'}(X, Y^r)$ |
| | $(0, 0)$ | Volume | $X \cap Y^r$ | Volume of intersection |
| | $(0, 1)$ | Surface area | $X \cap \partial Y^r$ | Surface area of intersection inside interior of $X$ |
| | $(1, 0)$ | Surface area | $\partial X \cap Y^r$ | Surface area of intersection inside boundary of $X$ |
| | $(1, 1)$ | Curve length | $\partial X \cap \partial Y^r$ | Length of intersection of boundaries |

https://lab.compute.dtu.dk/QIM/tools/relationalshapemeasure

# Shape relation measures: K-functions for objects

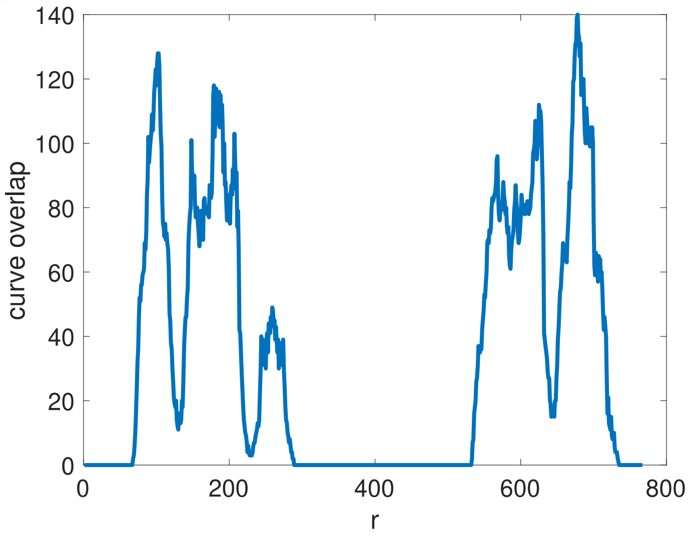


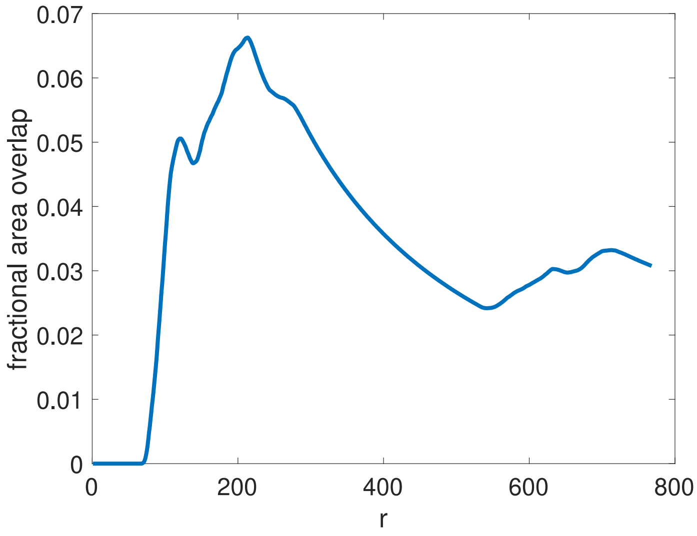




$$\mu_{00}(r) = \mathcal{H}(X \cap Y^r)$$

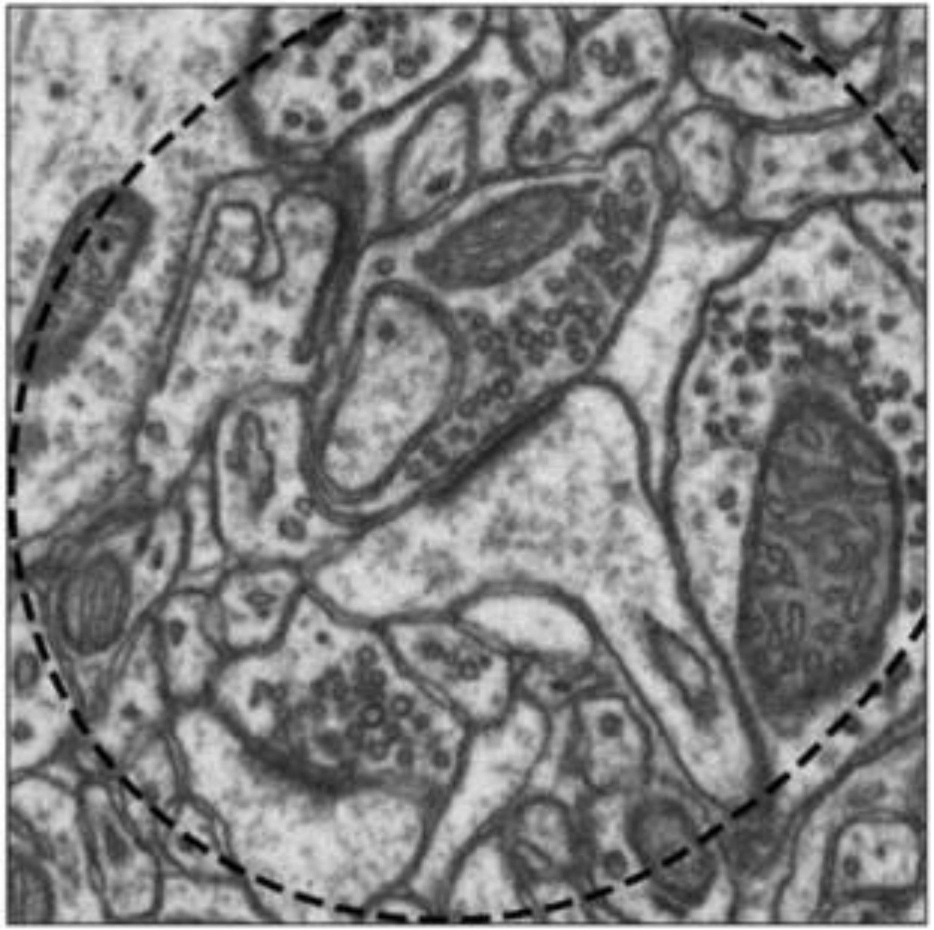
$$g_{00}(r) = \frac{d\mu_{00}(r)}{dr}$$

$$f_{00}(r) = \frac{\mu_{00}(r)}{\mathcal{H}(Y^r)}$$

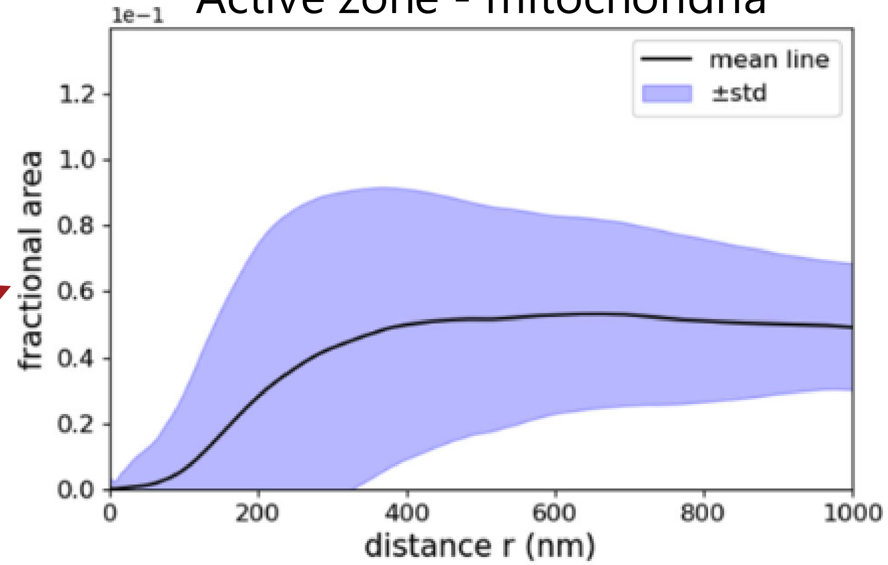


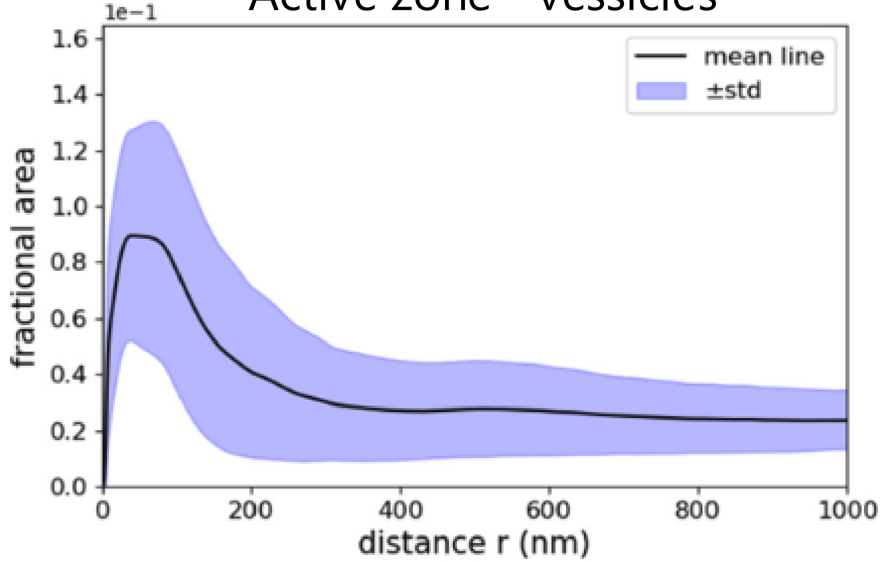
# Shape relations for statistical summary of families of shapes and their relations



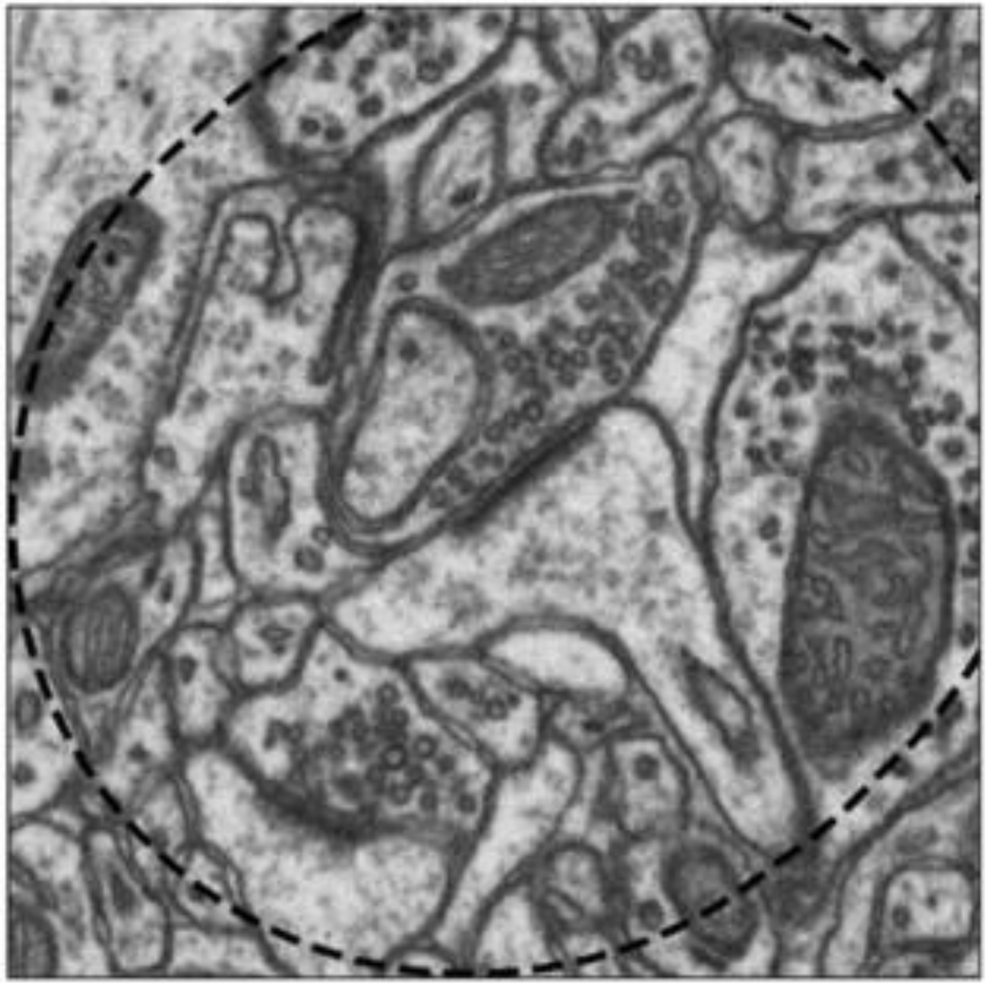
Active zone - mitochondria



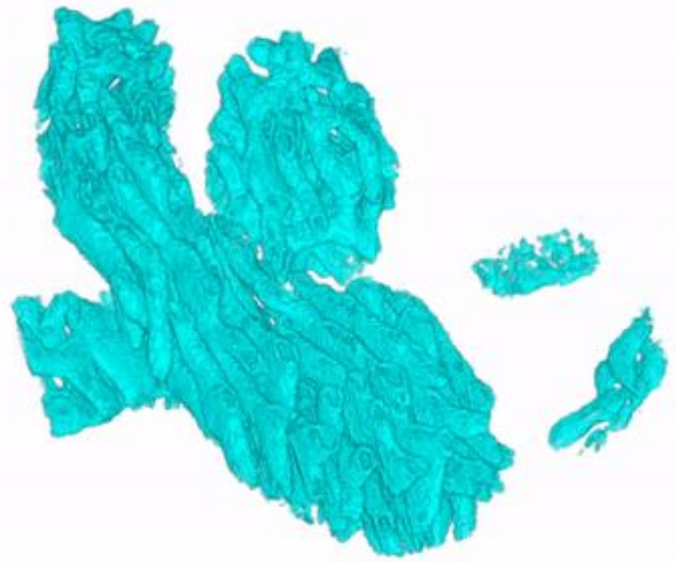

Active zone - vessicles



# Analyzing cristae membranes in Mitochondria

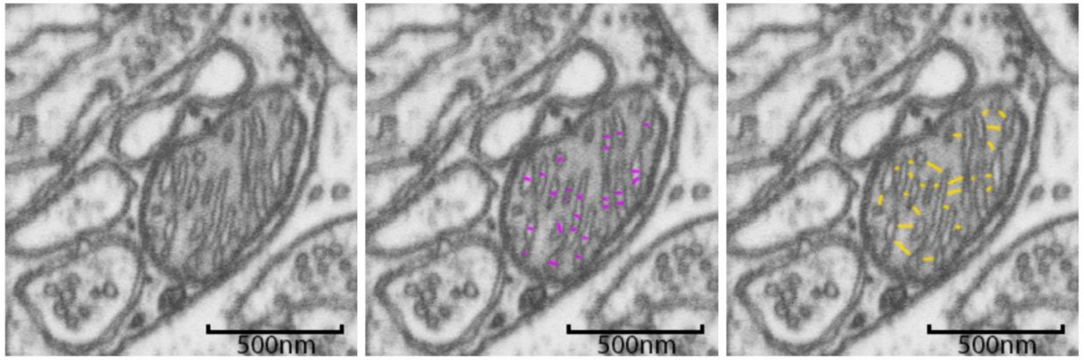


Deep Learning →

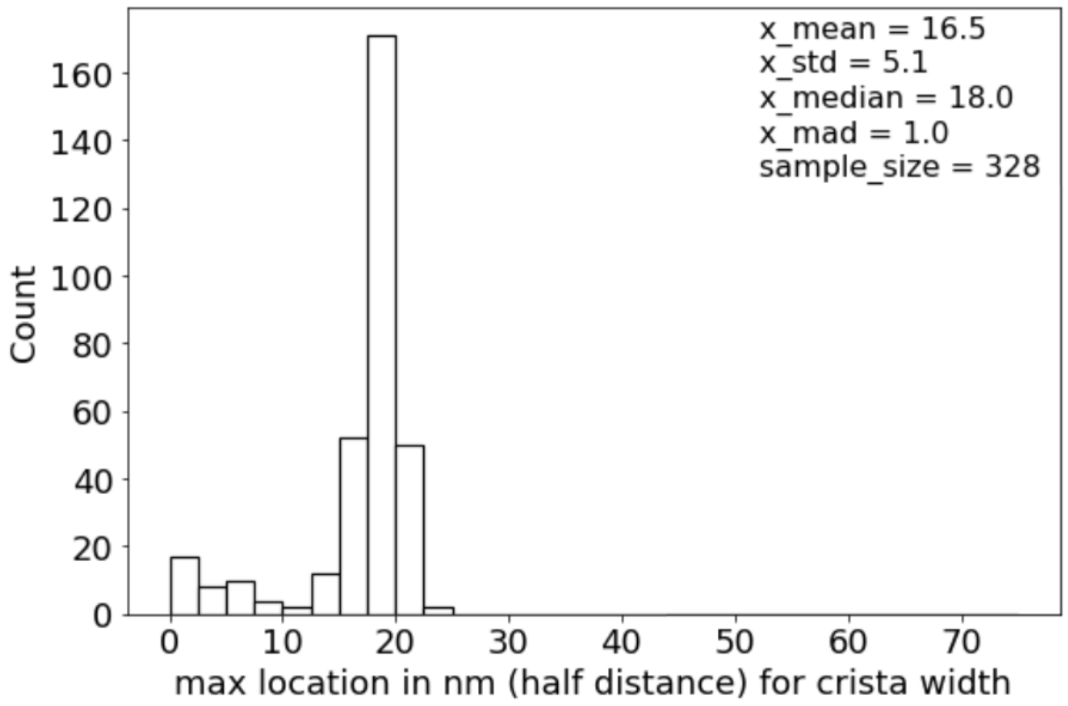


**Extracting Mitochondrial Cristae Characteristics from 3D Focused Ion Beam Scanning Electron Microscopy Data**, C Wang, L Østergaard, S Hasselholt, & J Sporring, to appear in Communications Biology, 2024

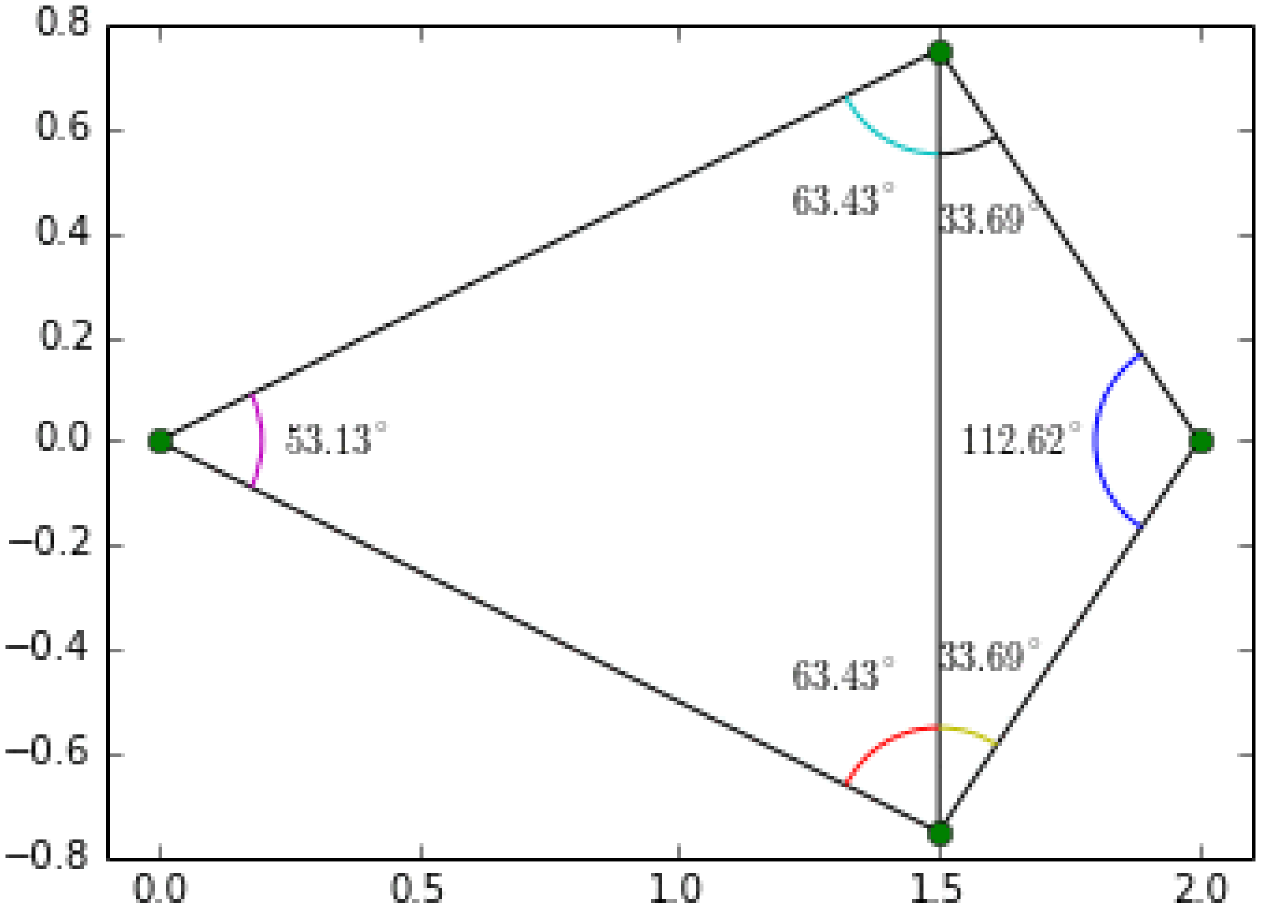
# Persistent homology: Statistical measures on H_0




(a) (b) (c)

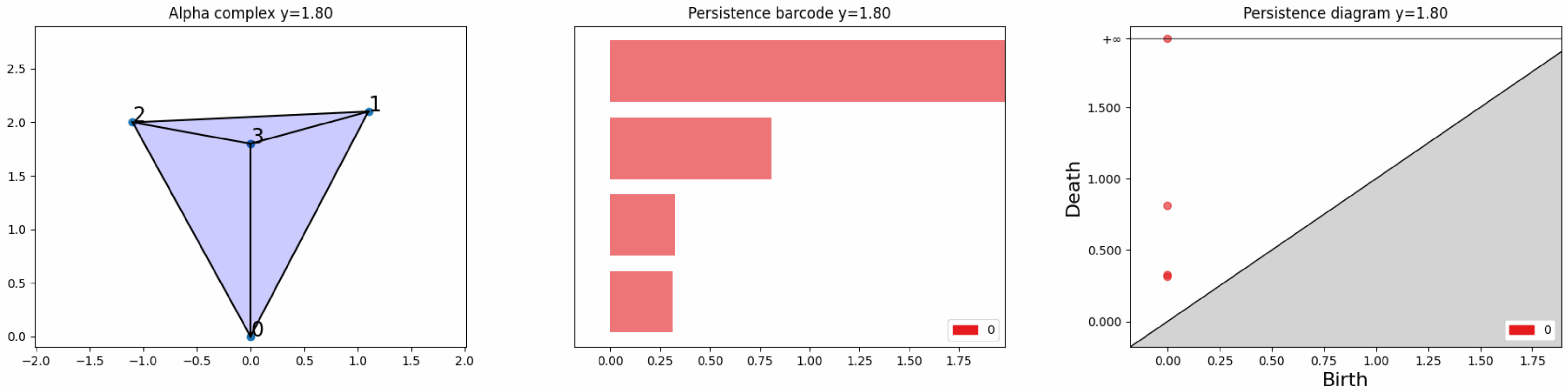


# Alpha complexes = Delaunay triangulation + Vietoris-Rips

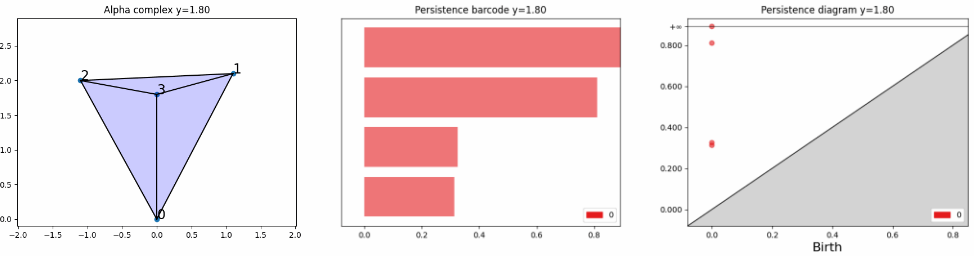


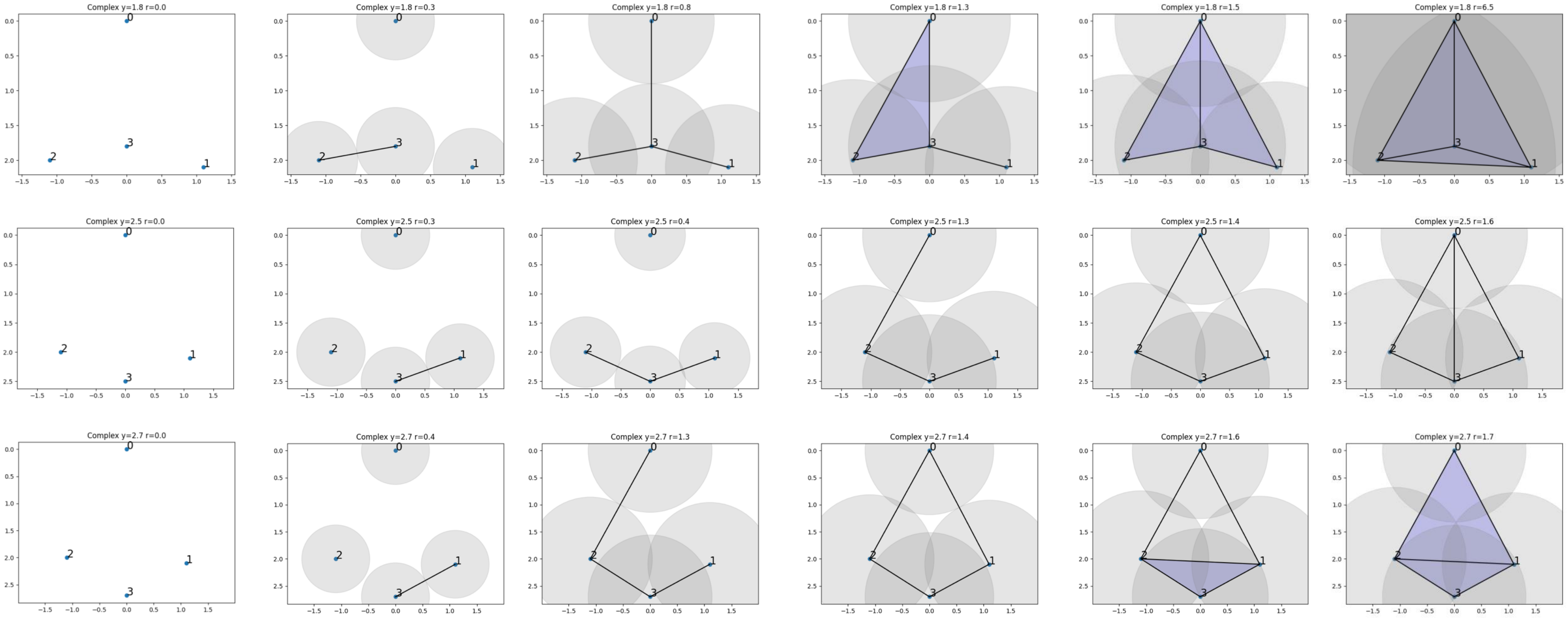

https://en.wikipedia.org/wiki/Delaunay_triangulation#/media/File:Delaunay_triangulation_does_not_minimize_edge_length.gif

# Observations on alpha complexes of 1-parameter family of 4-gons



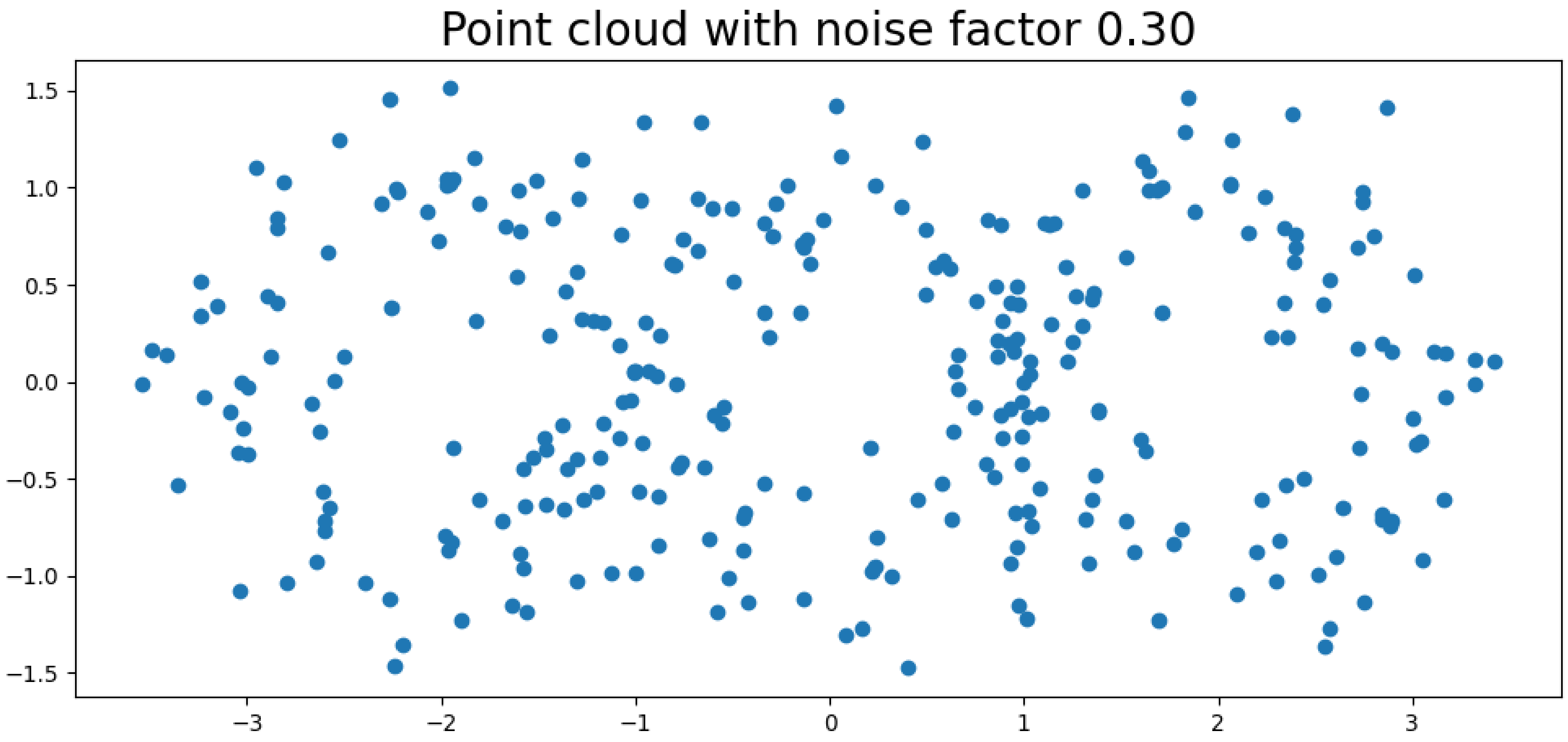
# Generic cases



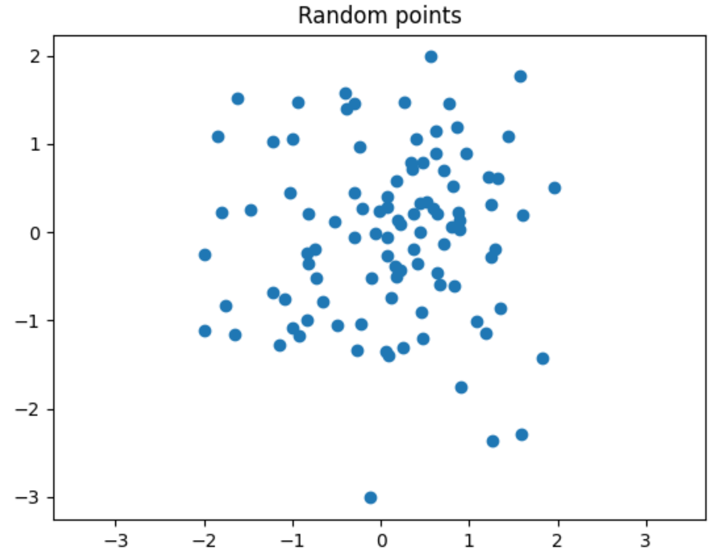

Observations: $H_0$ is continuous in $y$ but non-smooth. $H_1$ is same + birth and death events.

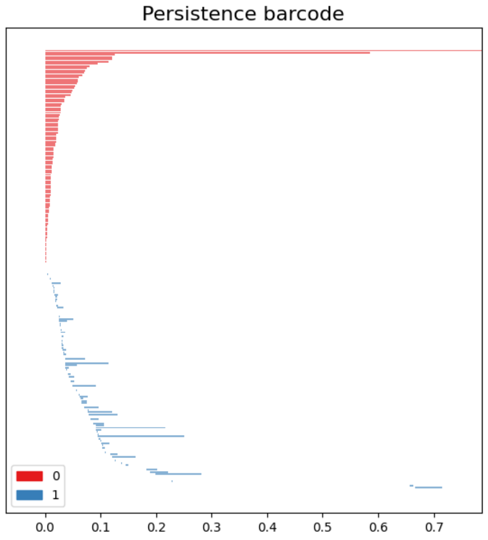
# Persistence under noise: $\mathrm{dgm} = \mathrm{dgm}^{\mathrm{Signal}} \cup \mathrm{dgm}^{\mathrm{Noise}}$

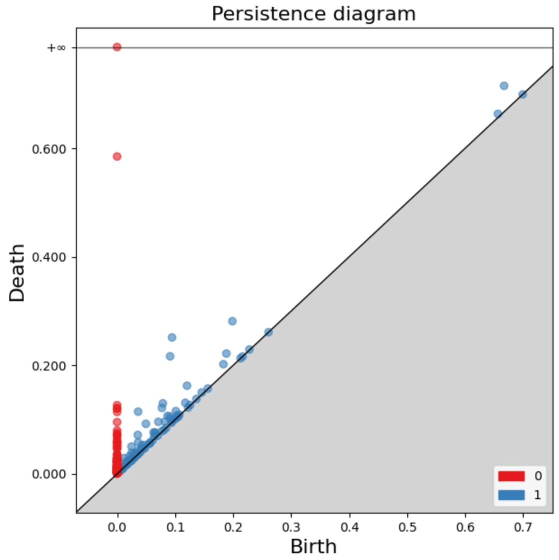


# Pure noise

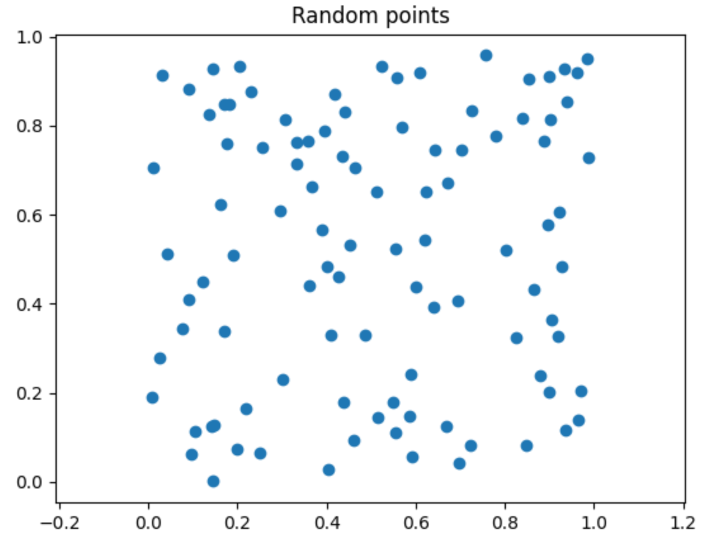
Normal

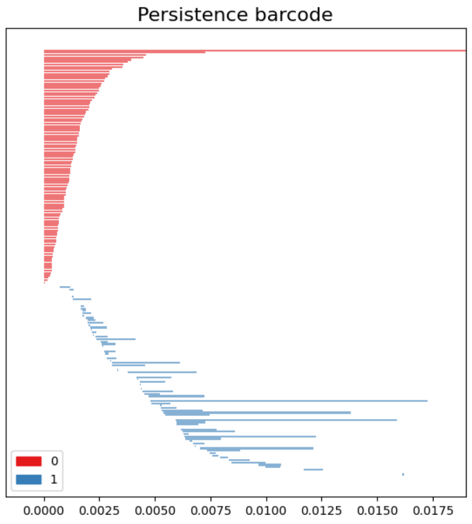


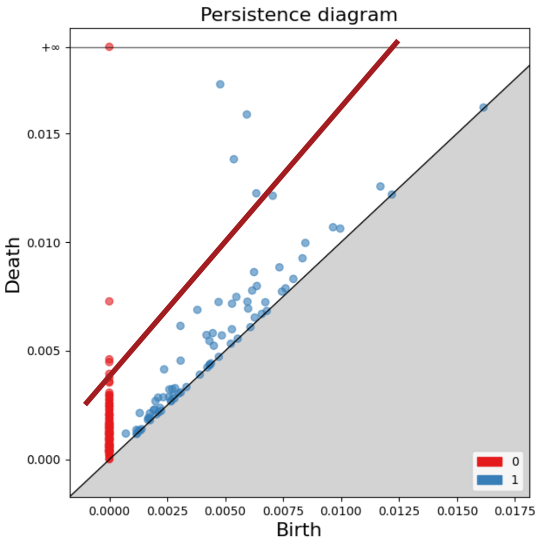




Uniform



# Bobrowski & Skraba, “A universal null-distribution for topological data analysis”, Nature/Scientific Reports, 2023

Random points:

$$x \in S(d), \qquad x \sim f, \qquad p = (r_{\text{birth}}, r_{\text{death}})$$

Left-skewed Gumbel distribution:

$$F(x) = 1 - e^{-e^x}, \qquad f(x) = e^{x-e^x}, \qquad \mu = -\gamma = -0.57721, \qquad \sigma^2 = \frac{\pi^2}{6}$$

Transformation:

$$\rho = \ln\ln\frac{r_{\text{death}}}{r_{\text{birth}}}$$

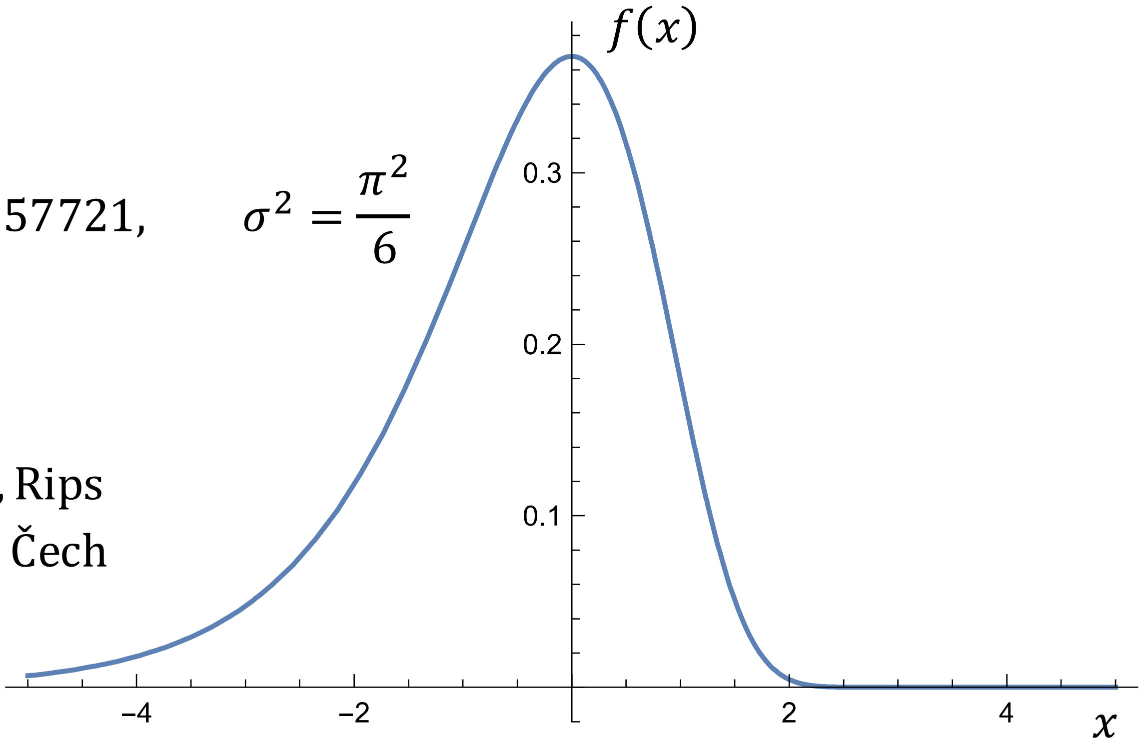
$$\mathrm{x} = \frac{(\rho - \bar{\rho})}{\beta} - \gamma, \qquad \bar{\rho} = \frac{1}{|\mathrm{dgm}_k|}\sum_{p \in \mathrm{dgm}_k} \rho\,, \qquad \beta = \begin{cases} 1, \text{Rips} \\ 2, \text{Čech} \end{cases}$$

Bonferroni testing (family-wise error rate $< \alpha$):

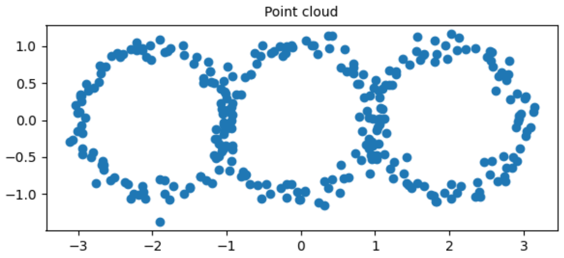
$$P(x \geq x_0 | x \text{ is noise}) = 1 - F(x) = e^{-e^{x_0}}$$

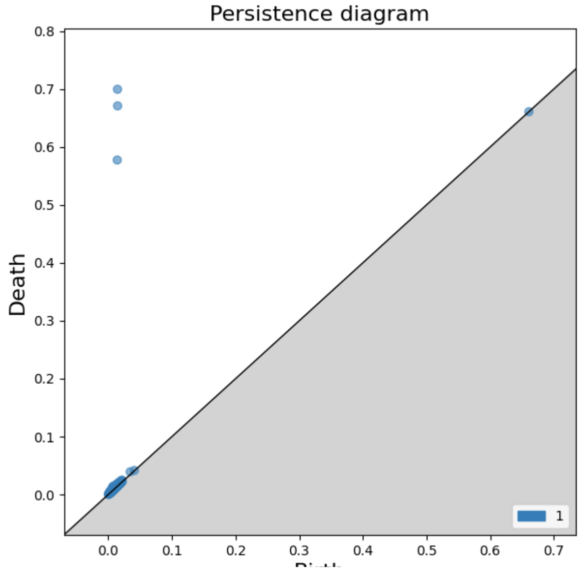
$$\mathrm{dgm}_k^{\text{Signal}}(\alpha) = \left\{ p \in \mathrm{dgm}_k\colon e^{-e^x} < \frac{\alpha}{|\mathrm{dgm}_k|} \right\}$$

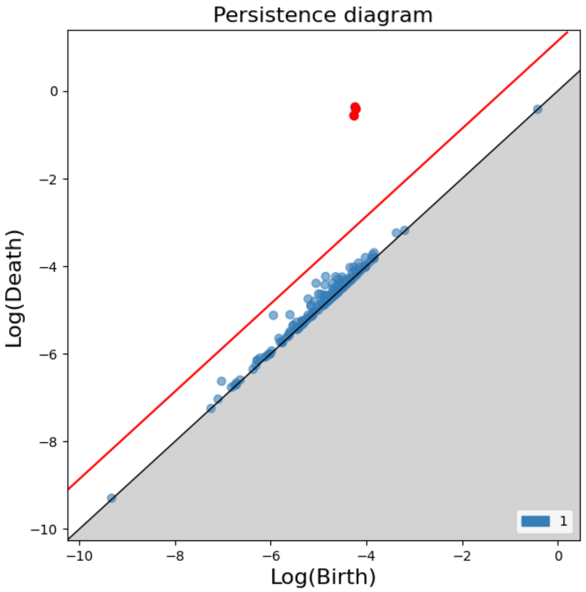
$$e^{\rho} = \ln\frac{r_{\text{death}}}{r_{\text{birth}}} = (-1)^{\beta} e^{\beta\gamma + \bar{\rho}} \left( \ln\frac{\alpha}{|\mathrm{dgm}_k|} \right)^{\beta}$$

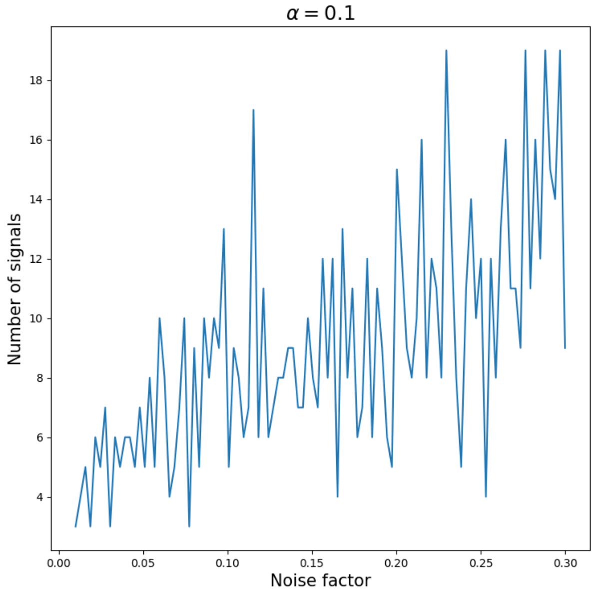


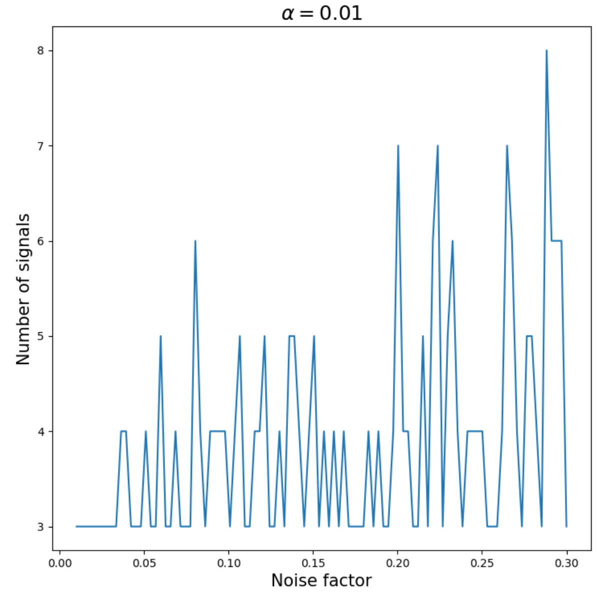
# Family-wise error rate

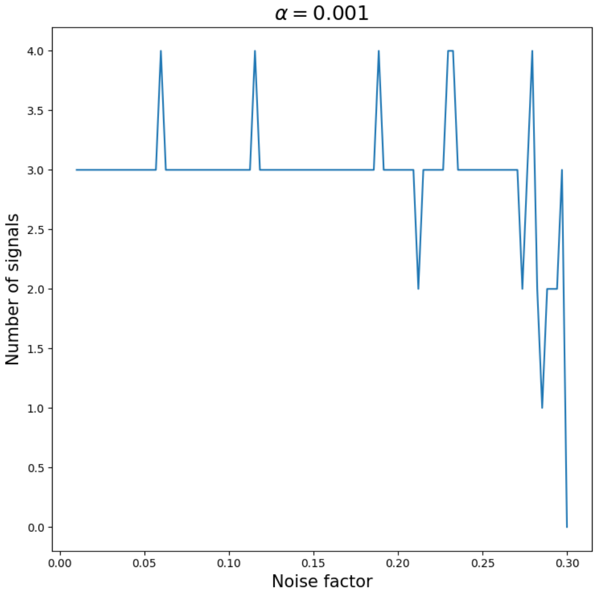


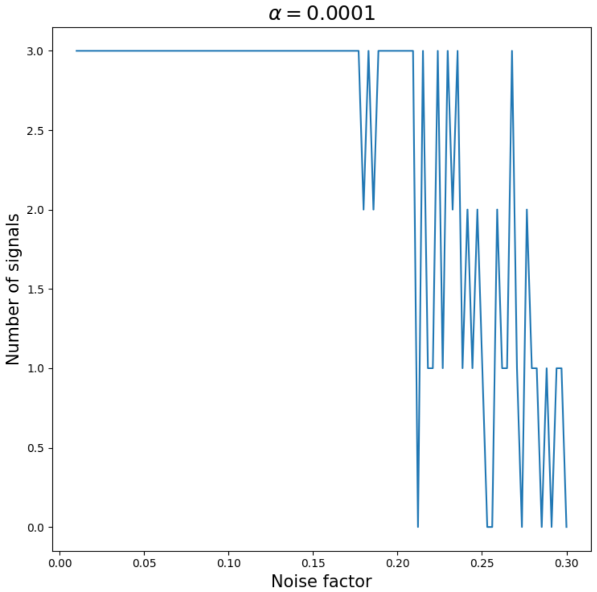



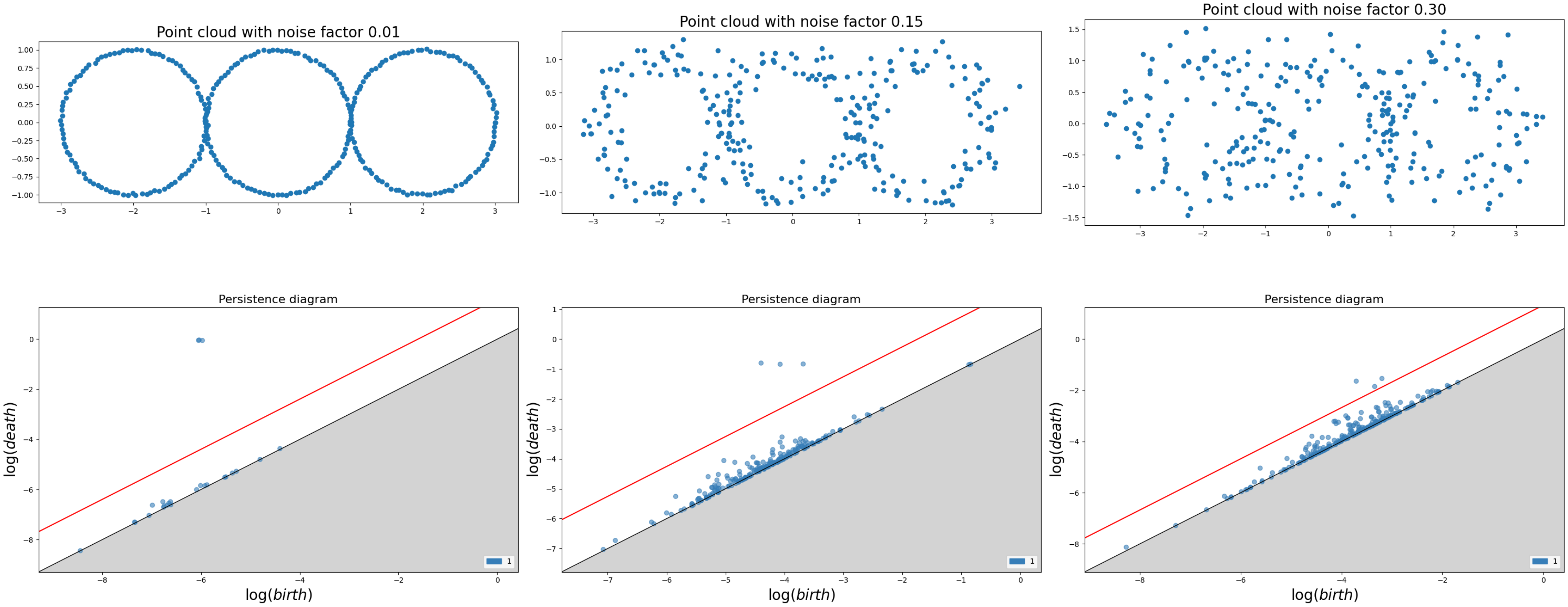



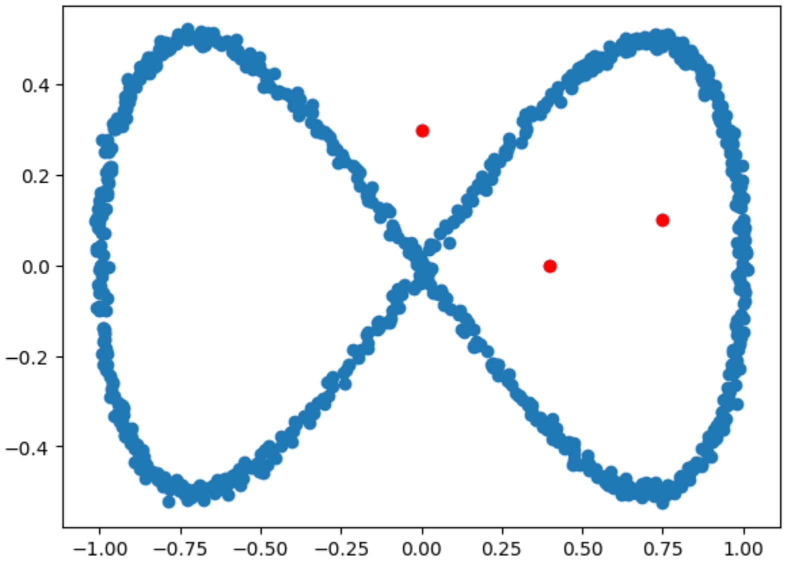



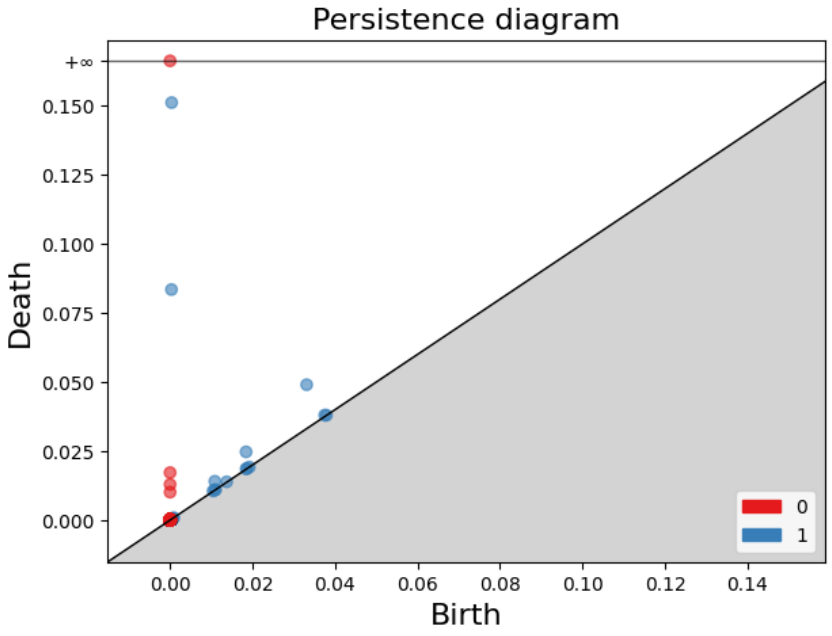



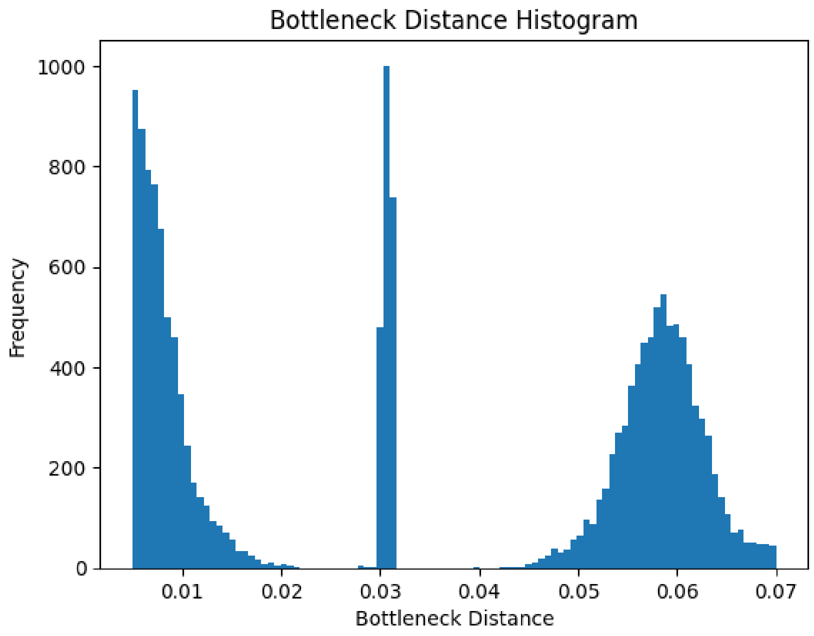
# The universal distribution can separate very noisy cases

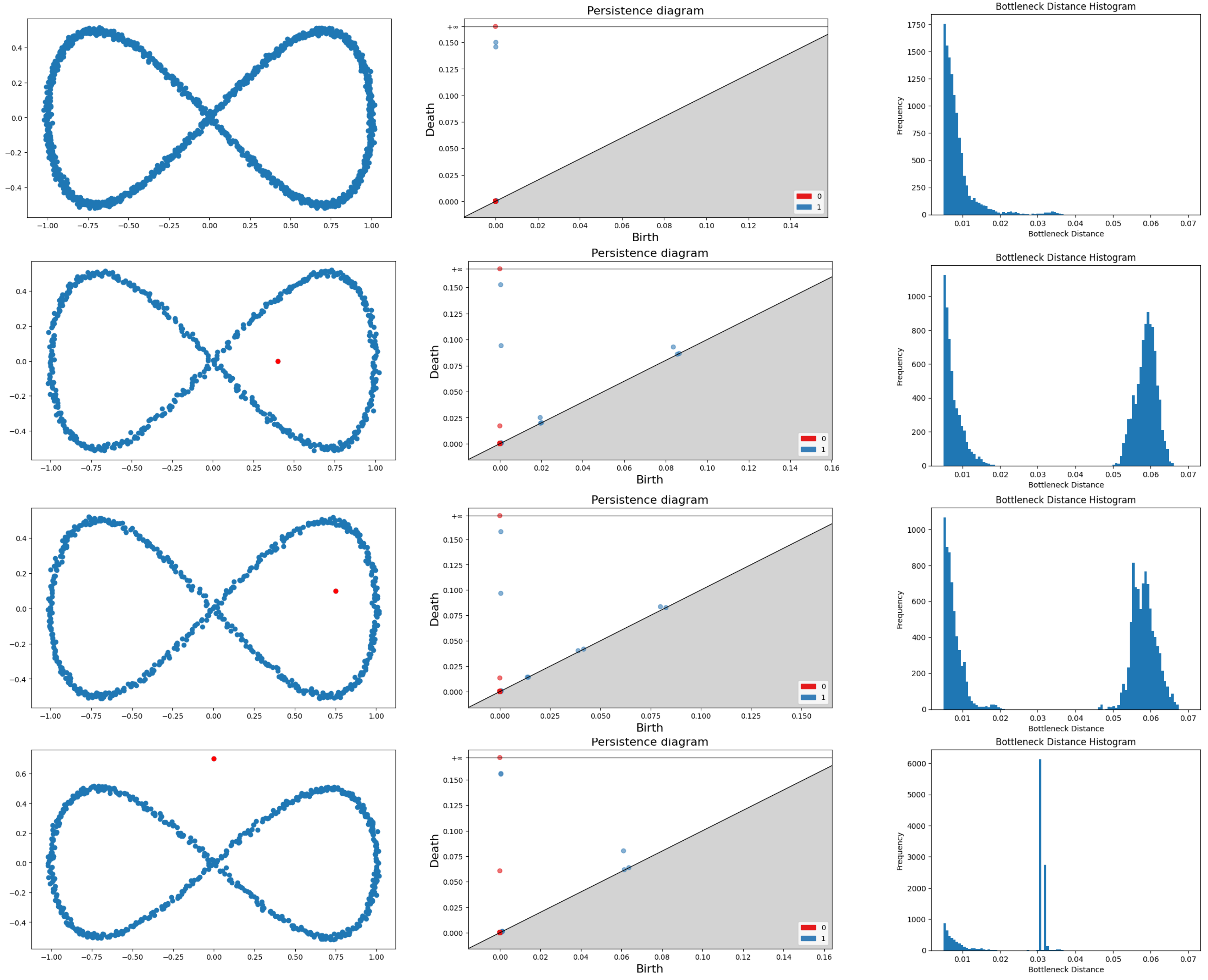


# Random sampling and outlier detection



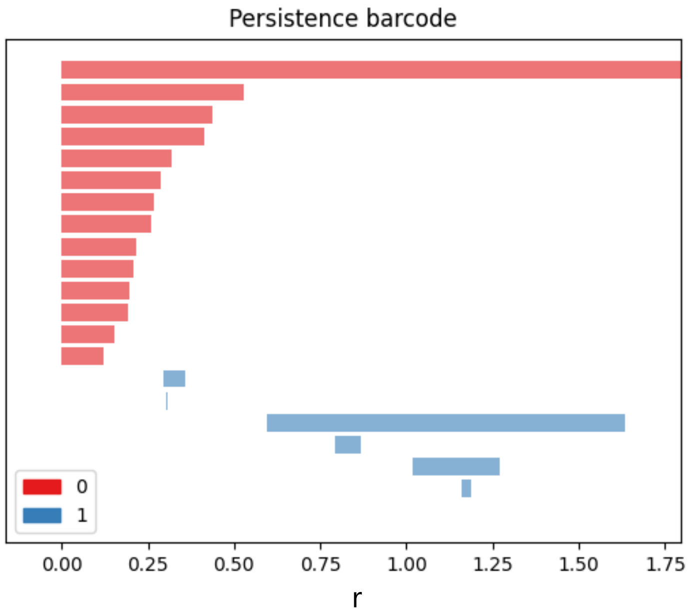



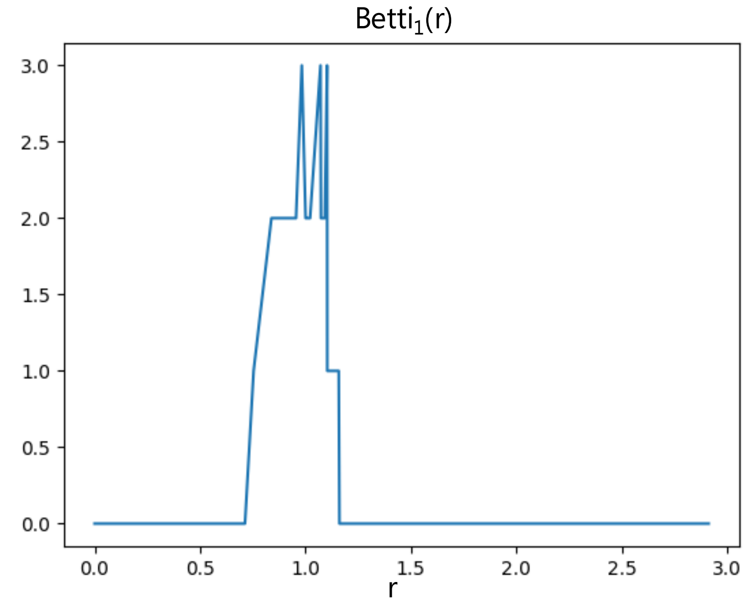

Persistence diagram
Death
Birth
+∞
0
1
Bottleneck Distance Histogram
Frequency
Bottleneck Distance

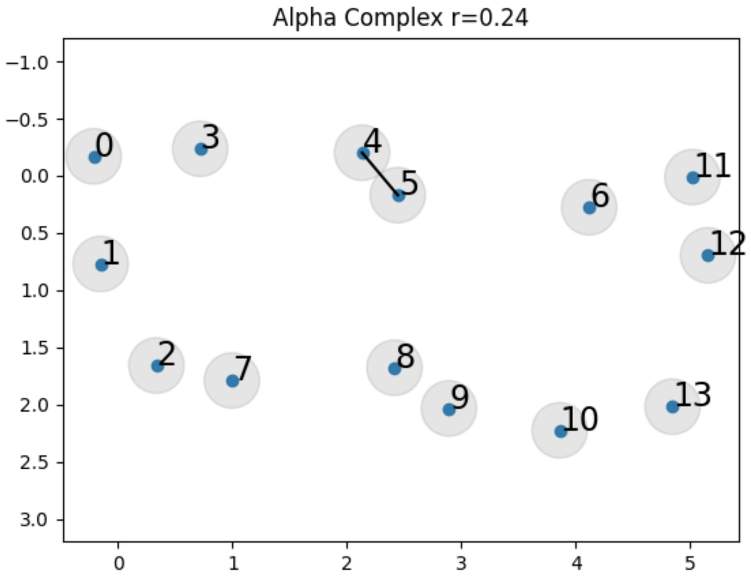
# Persistent homology and bar codes

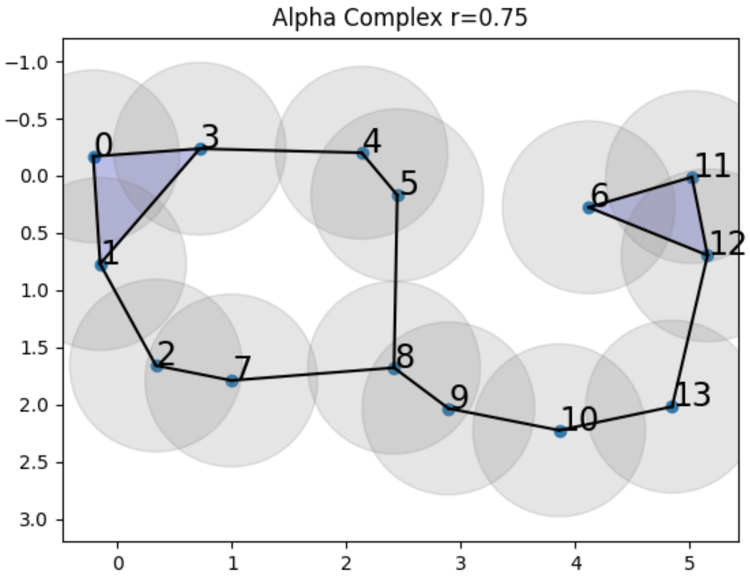
Simplex $\sigma = [x_0, x_1, \ldots x_k]$ is in the alpha complex if

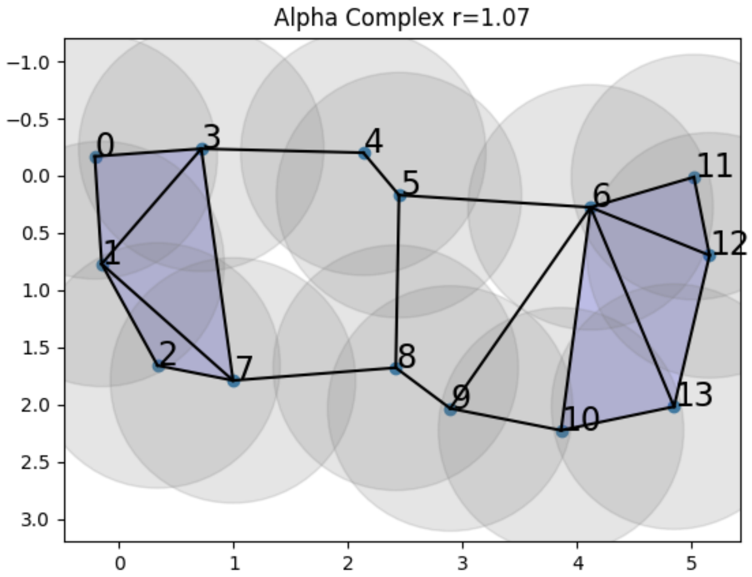
$$\bigcap_{x_i \in \sigma} B(x_i, r) \neq \emptyset$$



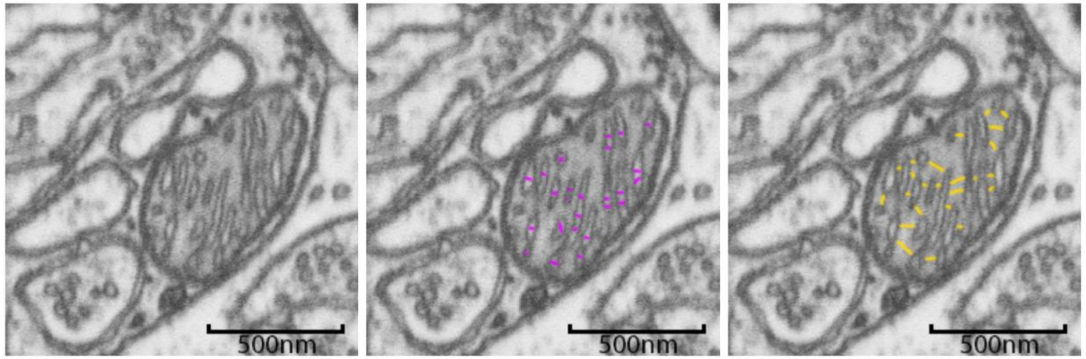



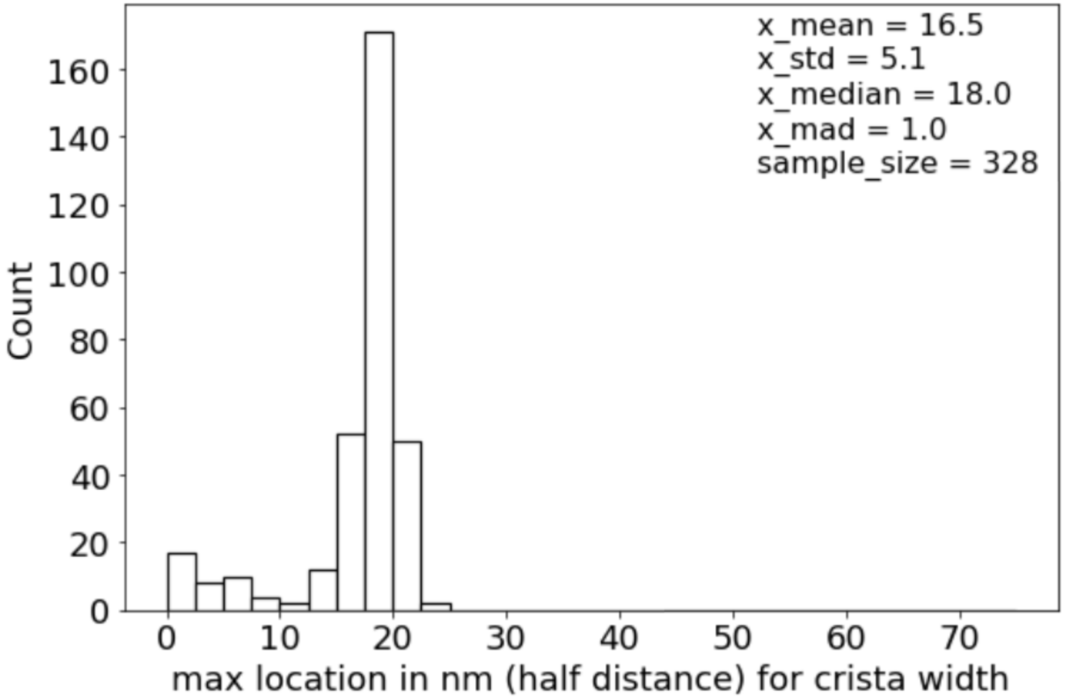



# Persistent homology: Statistical measures on H_0

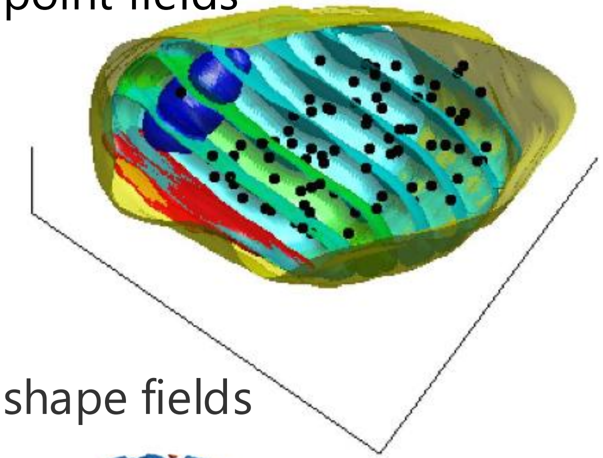



(a) (b) (c)



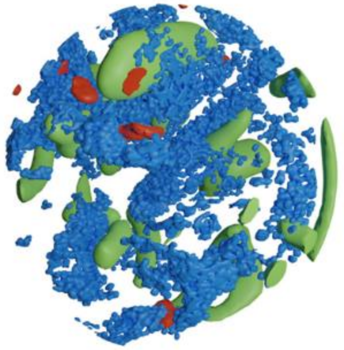
# Statistical summary of object collections

## Spatial point fields



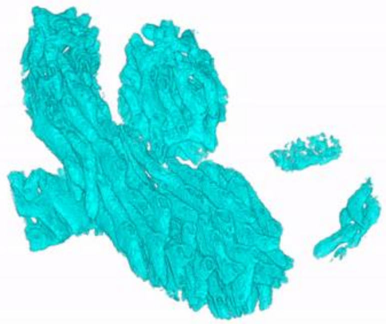
Pair correlation and Ripley's K functions summarizes 1st order point relations – e.g., do the vessicles cluster?

## Spatial shape fields

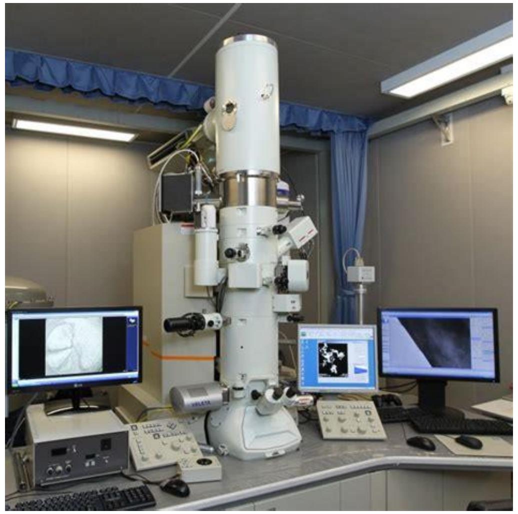


Hausdorf measures on overlaping sets extends notion of points to shapes – e.g., are mitochondria seen close to the synapse?

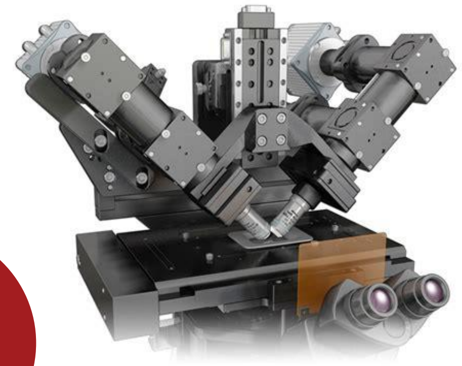
## Topological data analysis

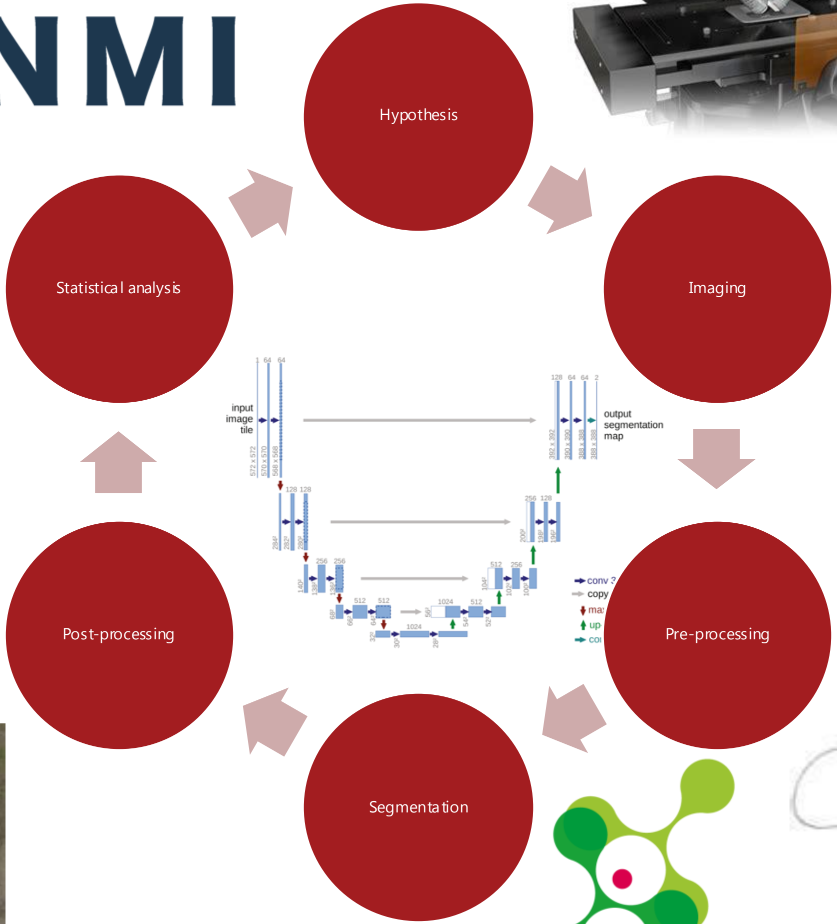


Filtrations brings topological concepts to measurements - e.g., what is the average tubular radius of complicated objects



BNMI



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