Exploring biological shape analysis through topology, geometry and statistics

Ph. D. summer school: Biomedical image analysis, 2024/08/13

Jon Sporring,
Department of Computer Science

UNIVERSITY OF COPENHAGEN

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

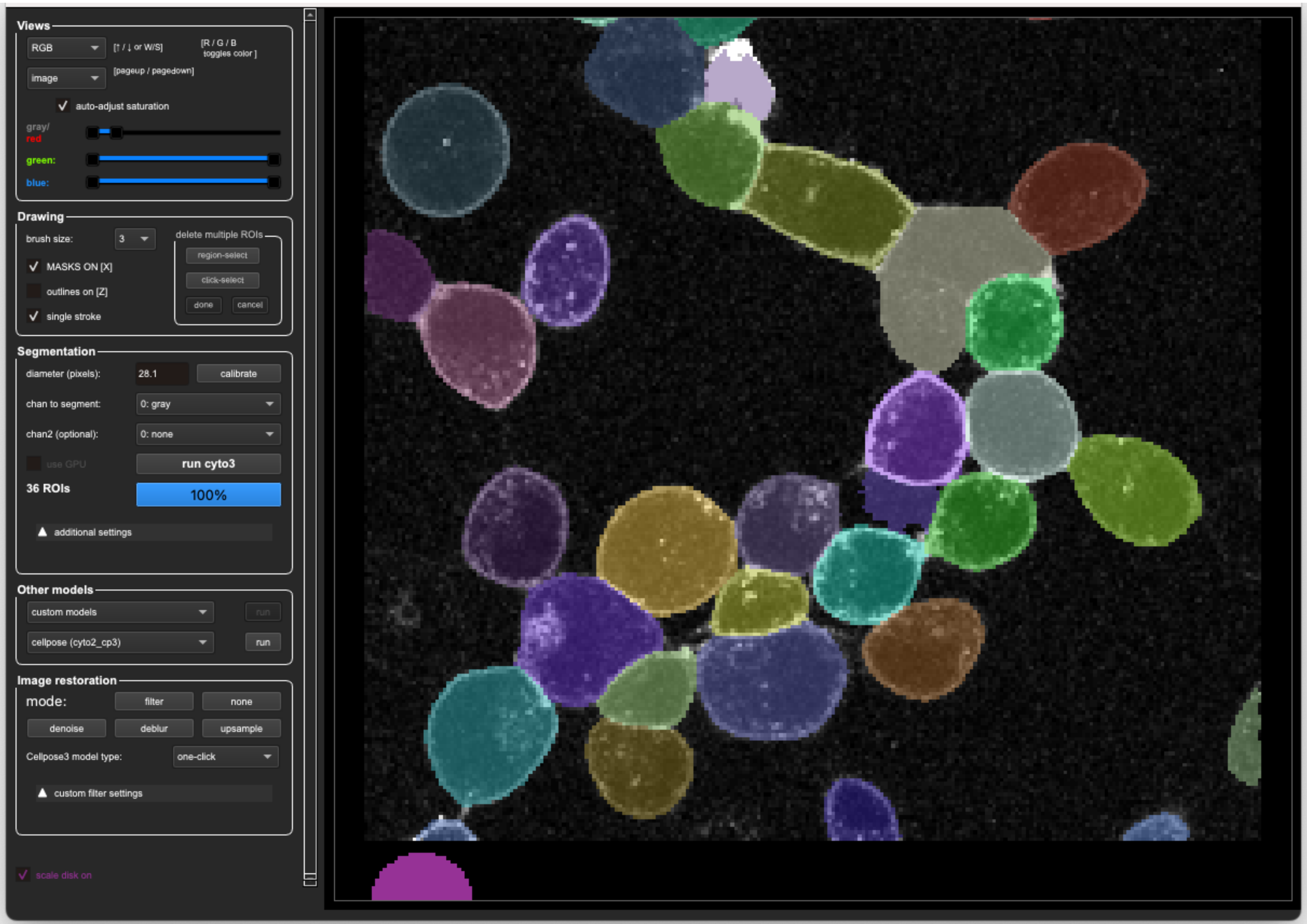


Image courtesy: Karen Martinez & Gabriella von Scheel von Rosing; AI: http://www.cellpose.org/

What to do next: Shape analysis

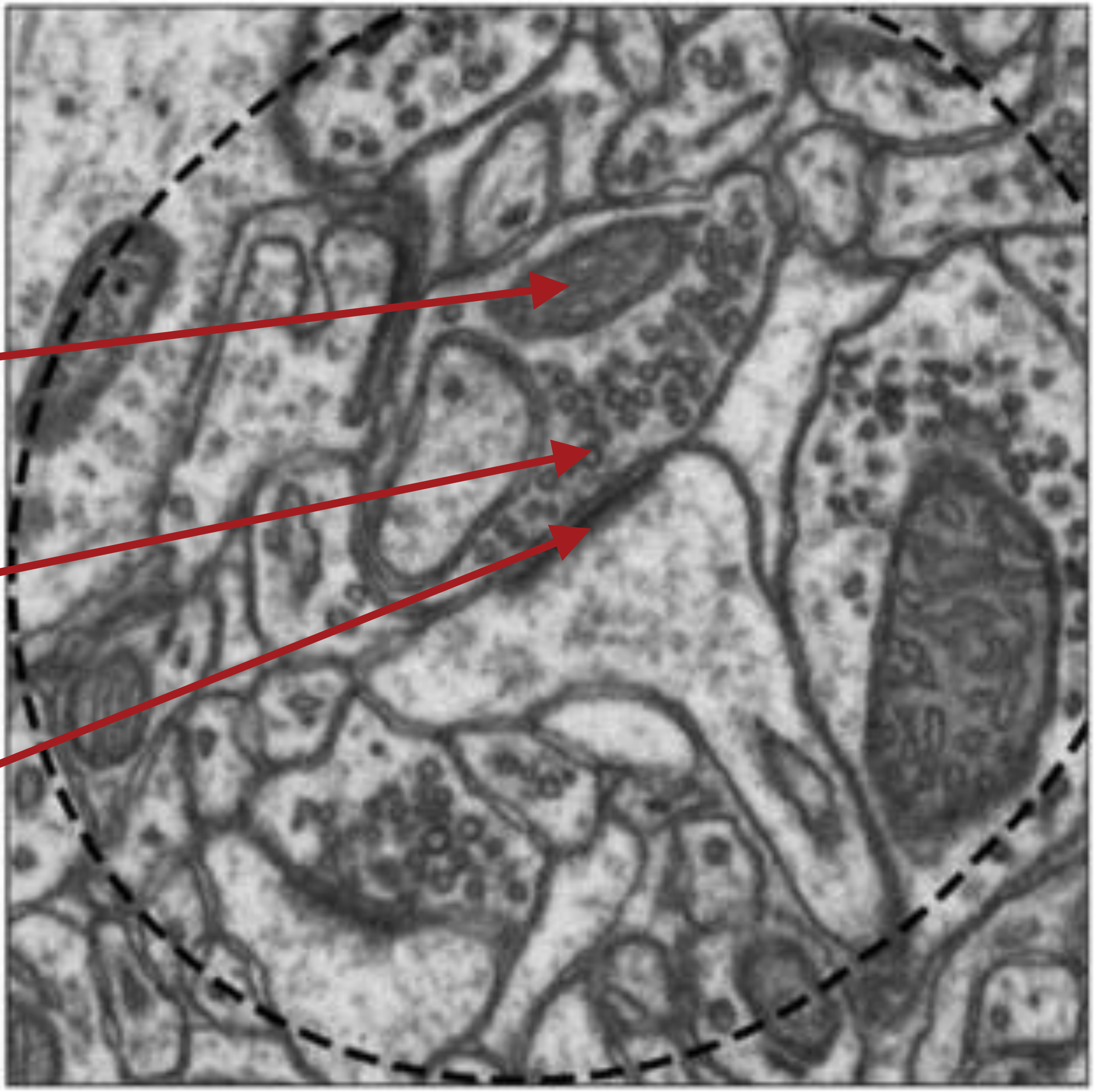
Focused ion-beam scanning electron microsopy (FIB-SEM)

Voxel size: (5 nm)^3

Mitochondria

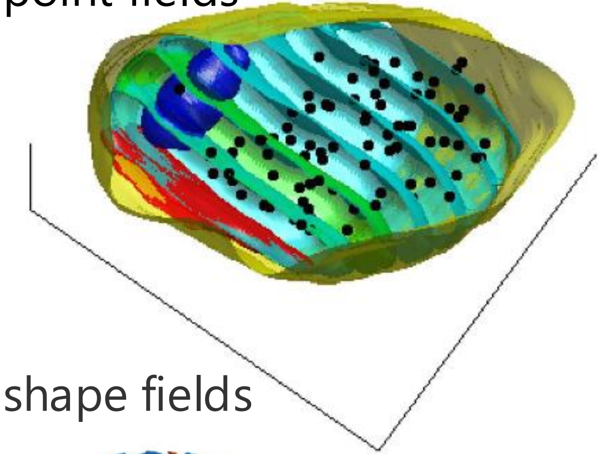
Vessicles

Active zone

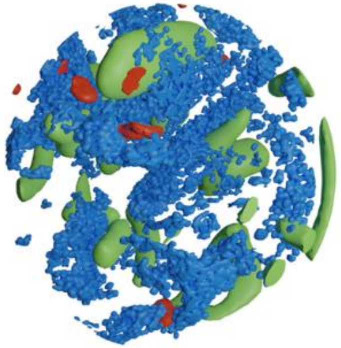


Graham Knott and Marco Cantoni. Electron microscopy dataset. https://cvlab.epfl.ch/data/ data-em/

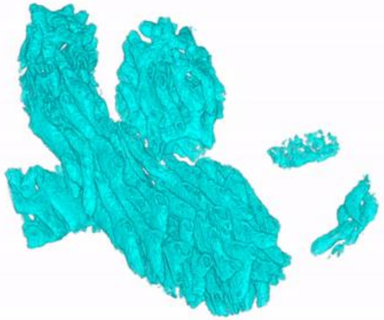
Spatial point fields



Spatial shape fields

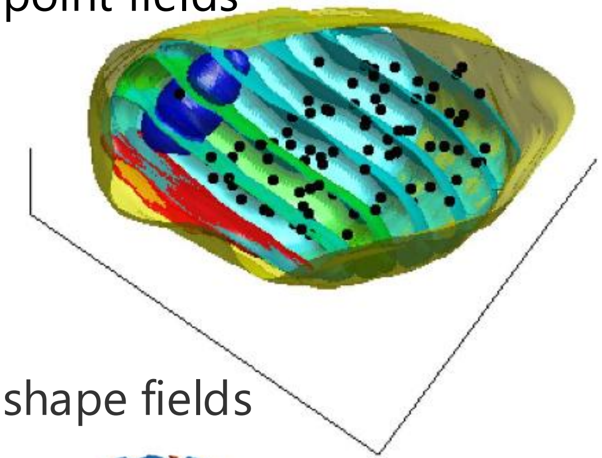


Topological data analysis

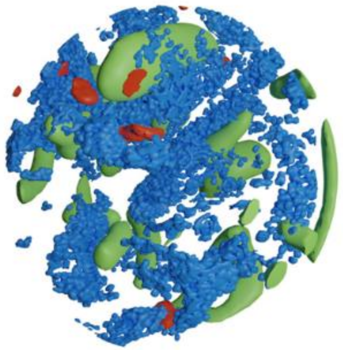


Literature

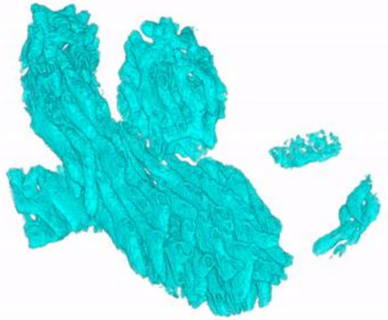
Spatial point fields



Spatial shape fields

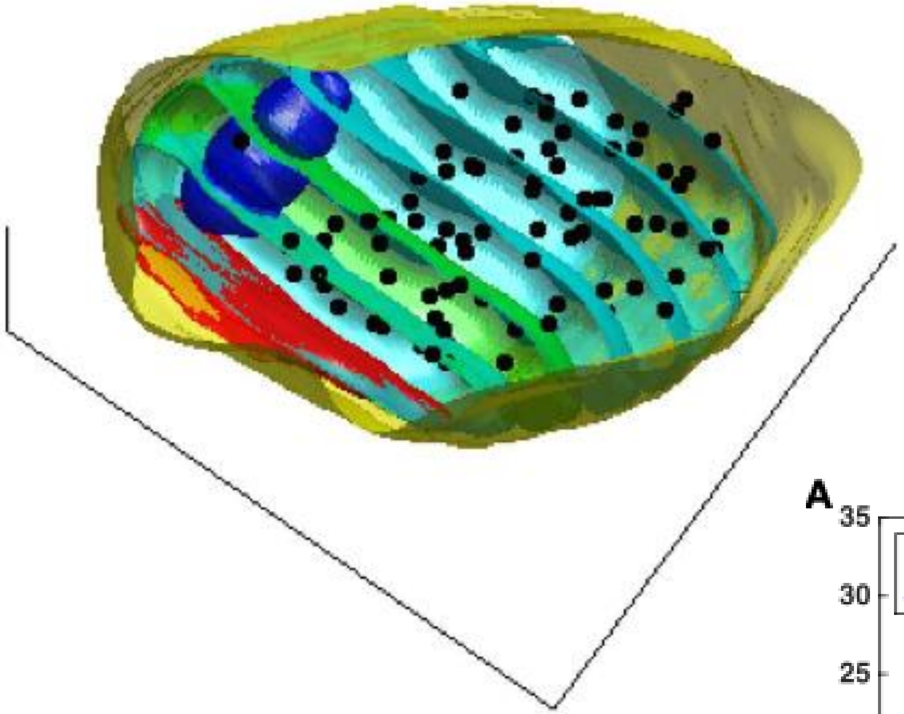


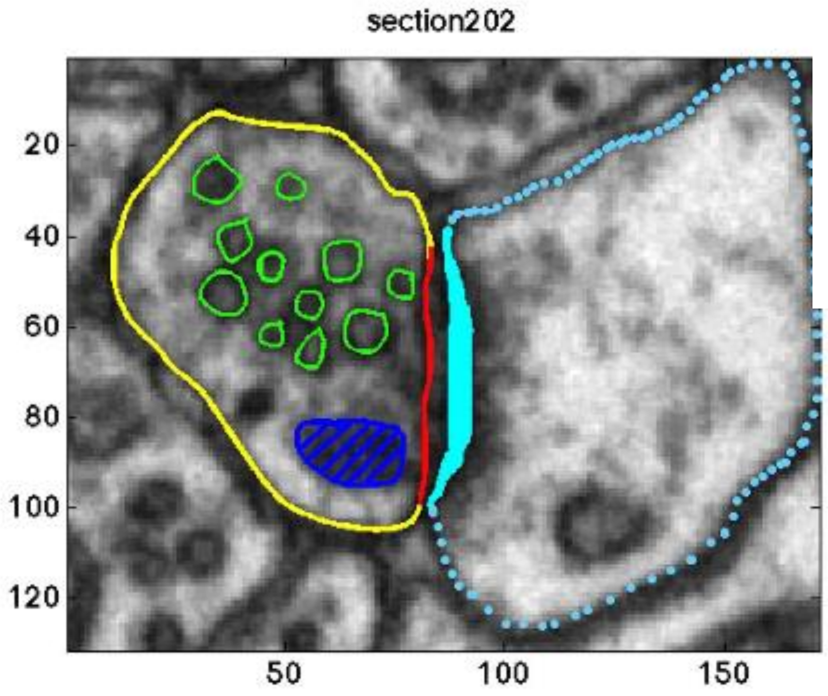
Topological data analysis

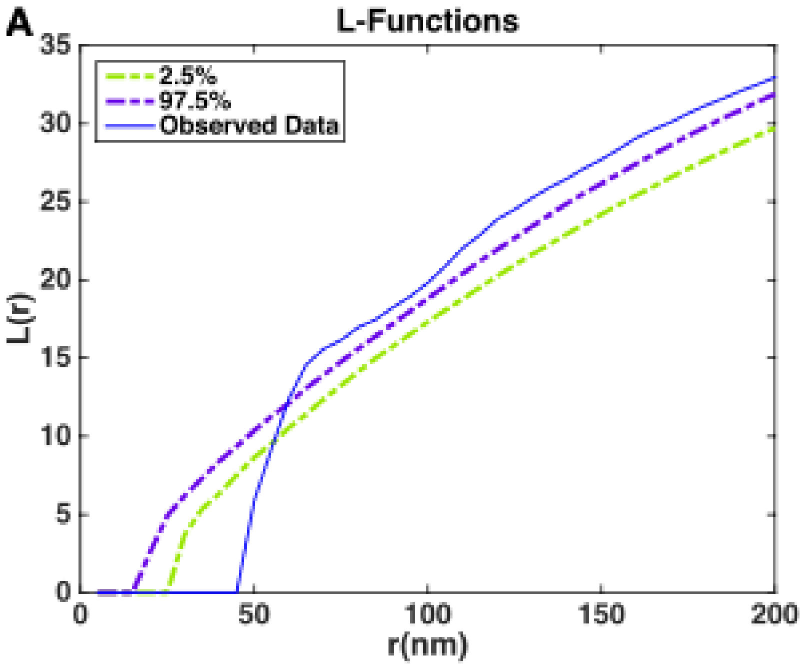


- Analysis of shape and spatial interaction of synaptic vesicles using data from focused ion beam scanning electron microscopy (FIB-SEM); M Khanmohammadi, RP Waagepetersen & J Sporring, Frontiers in Neuroanatomy, 2015
- Stoyan, D. (2006). Fundamentals of Point Process Statistics. In: Baddeley, A. et 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

1. Spatial point fields

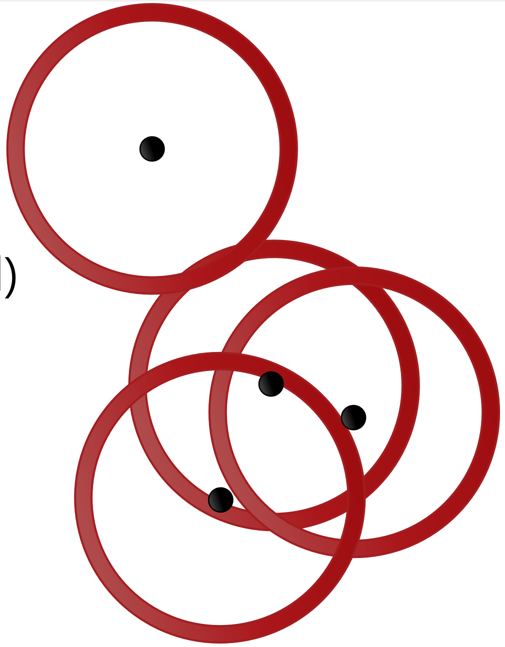






Analysis of shape and spatial interaction of synaptic vesicles using data from focused ion beam scanning electron microscopy (FIB-SEM); M Khanmohammadi, RP Waagepetersen & J Sporring, Frontiers in Neuroanatomy, 2015

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



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

$$L(r) = \sqrt{\frac{K(r)}{\pi}}$$

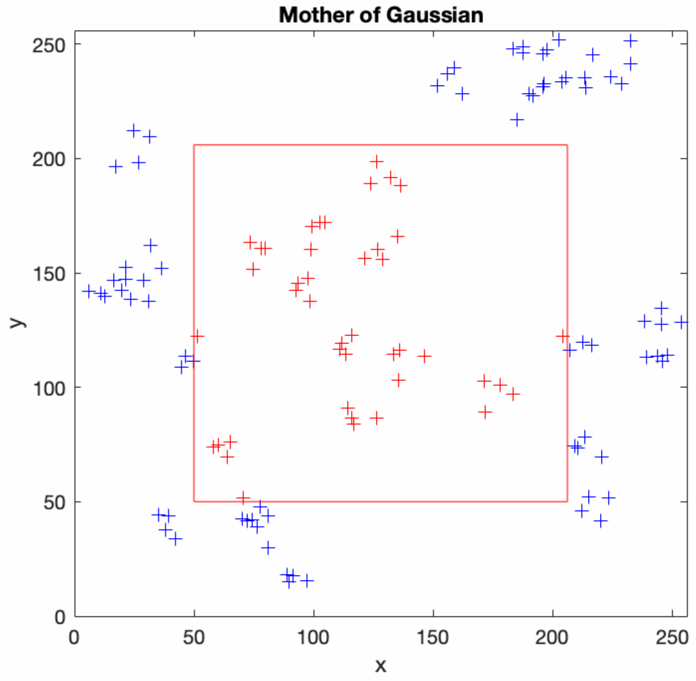
(homogeneous|stationary|uniform) Poisson [point] (process|field)

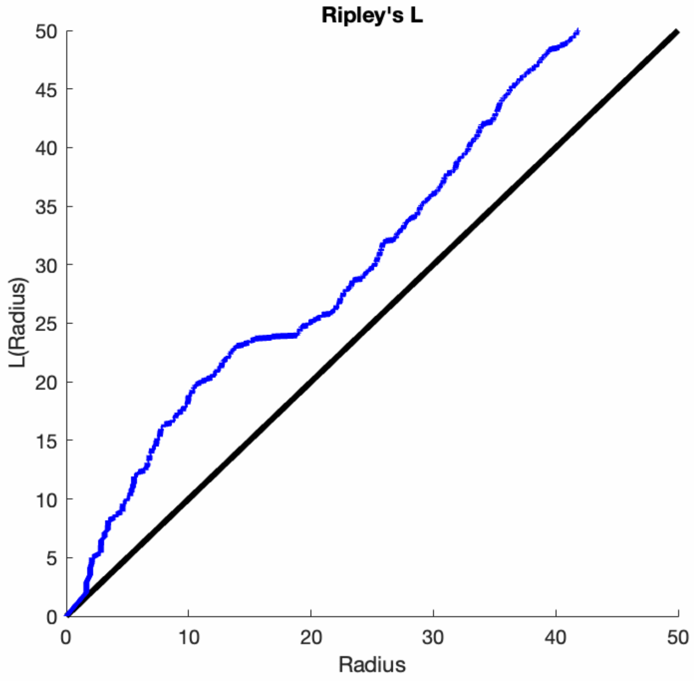
Euclidean d-space

$n \sim \text{Poisson}$

$x \sim \text{Uniform}$

2-space: $\lim_{n\to\infty} K(r) = \pi r^2$





R and rpy2 demo:
https://sporring.github.io/bia2024/talk.pdf
https://sporring.github.io/bia2024/spatstat_bia2024.zip

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

demoRpy2.py: Installation instructions for R, R-packages, and python packages:

```
# 1. Install R, which to my experience works best directly from  https://cran.r-project.org/
# then start R and install some packes:
#  install.packages("spatstat")
#  install.packages("lazyeval")
#  install.packages("GET")
…
```

GETDemo.r

```
library("GET")
library("spatstat.model")
library("ggplot2")
X <- spruces
print(X)
plot(X)
k <- Kest(X)
print(k)
plot(k)
env <- envelope(X, nsim=1999, savefuns=TRUE, simulate=expression(runifpoint(ex=X)), verbose=FALSE)
print(env)
plot(env)
res <- global_envelope_test(env)
print(res)
plot(res)
```

GETDemo.r

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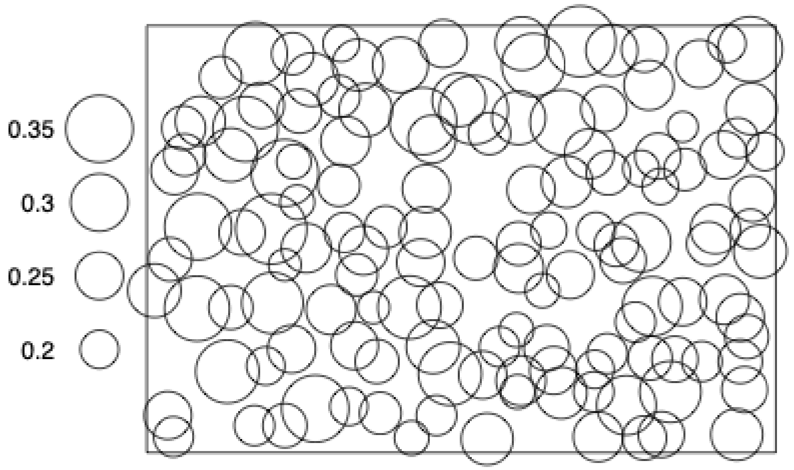
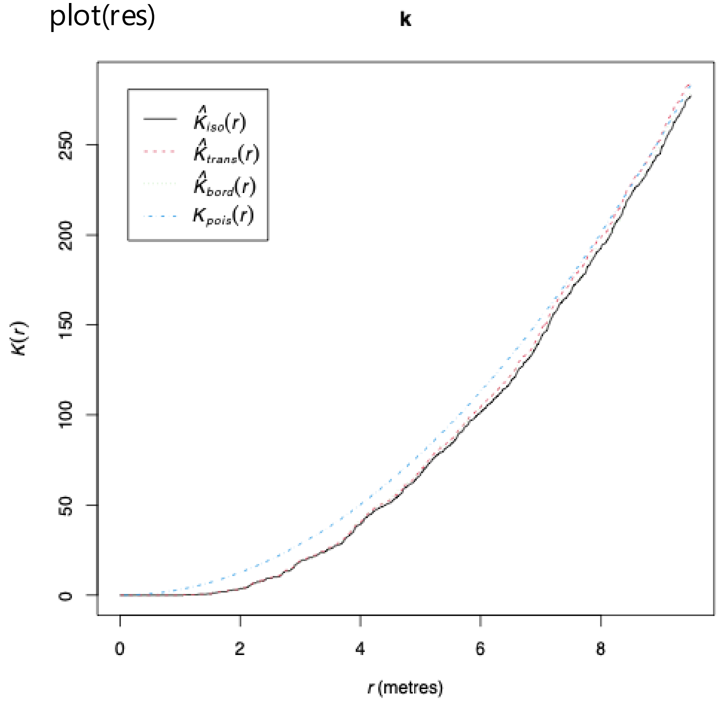
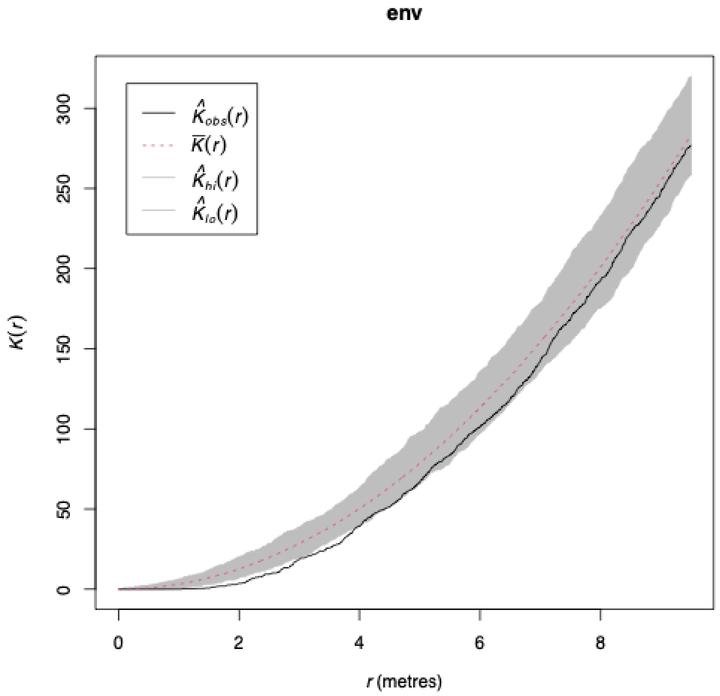
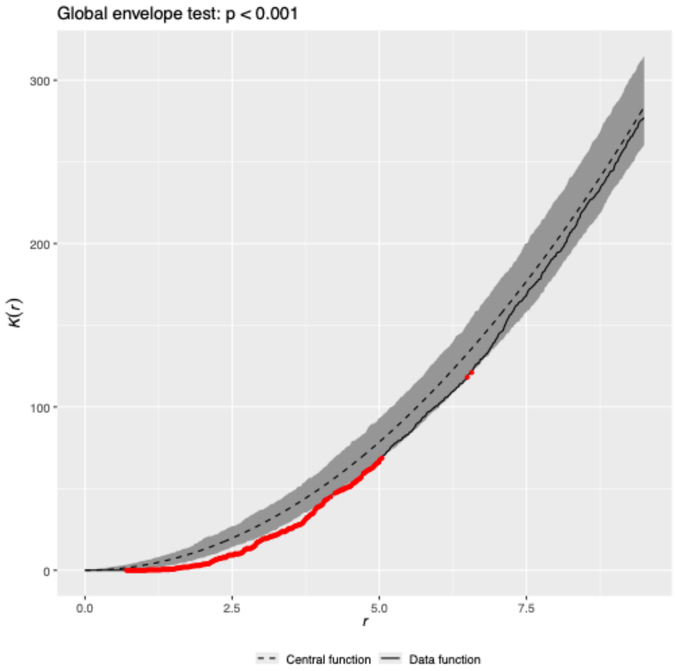






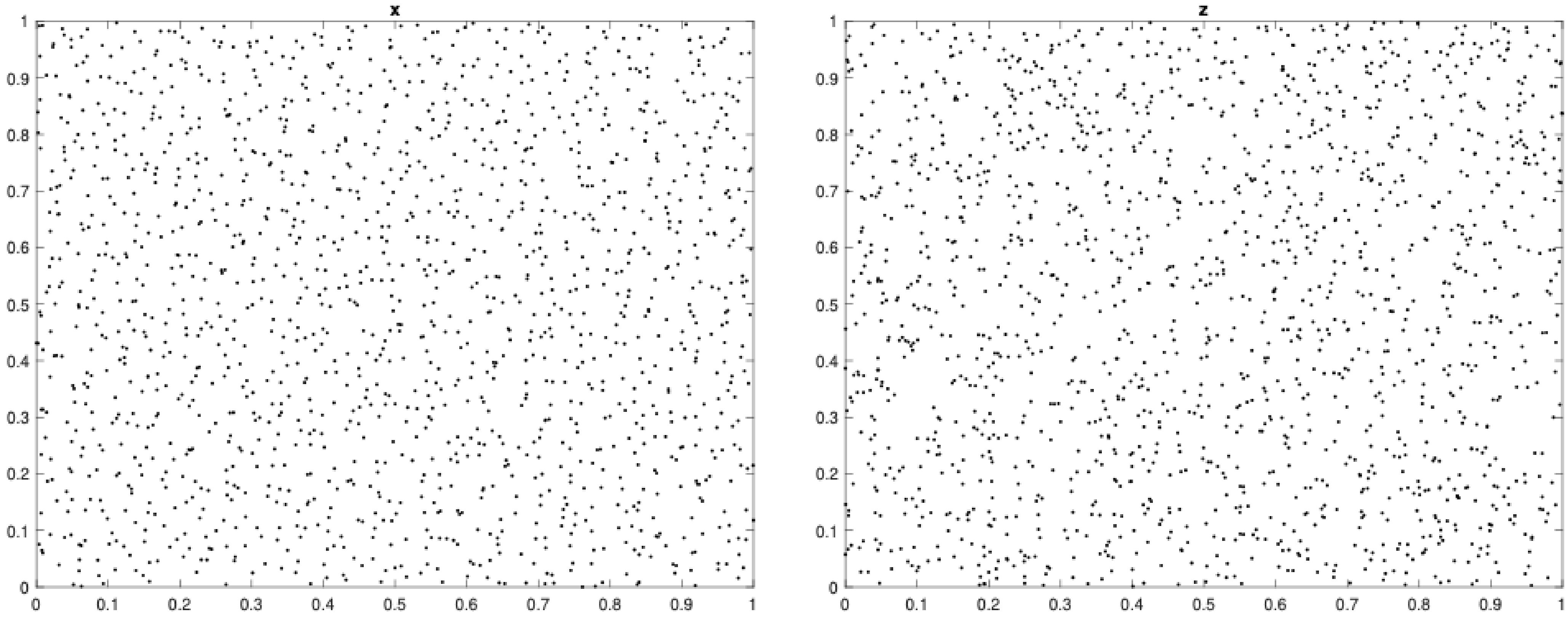


demoRpy2.py

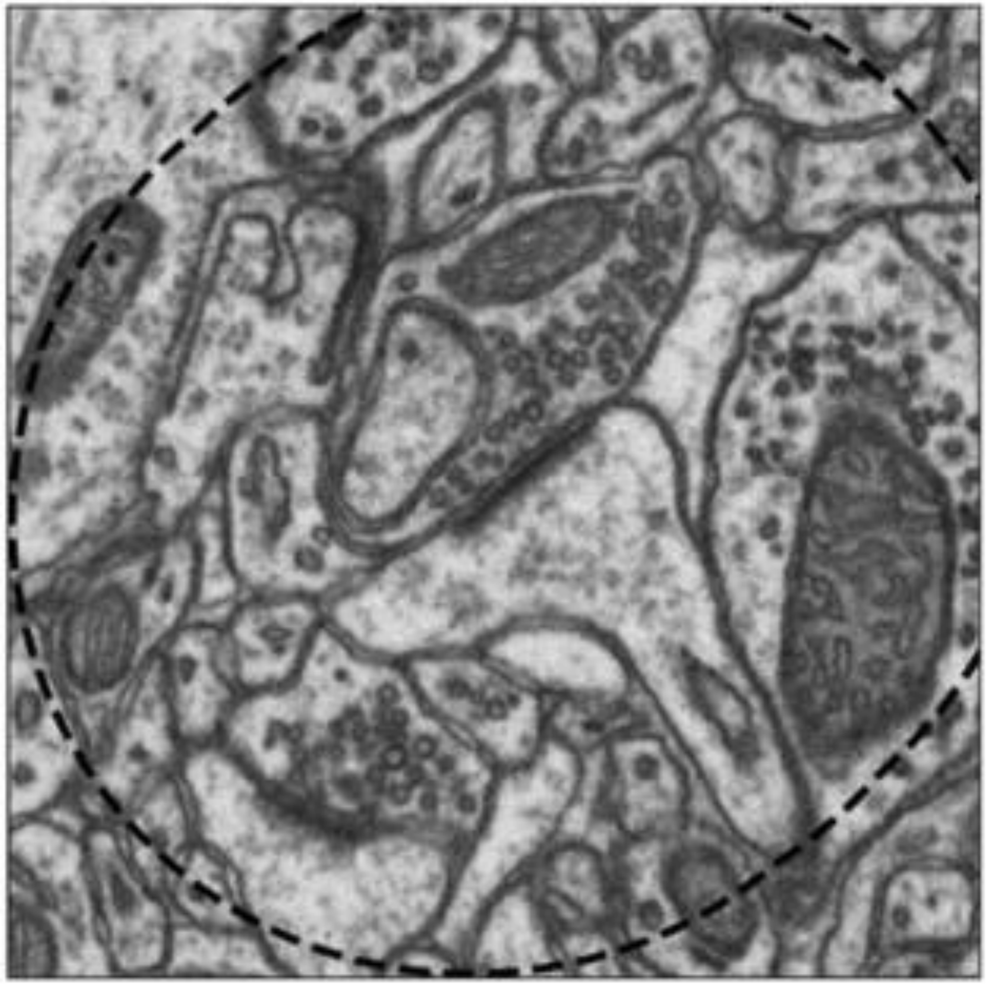
```python
# first we import a bunch of basic stuff and prepare working with rpy2
import rpy2
import rpy2.robjects as robjects
from rpy2.robjects.packages import importr
import matplotlib.pyplot as plt
import numpy as np
from rpy2.robjects import FloatVector
base = importr('base')
spatstat = importr('spatstat')
# shortcut
ro = robjects.r

# The following is an example of how to create a random 2-dimensional point pa
```

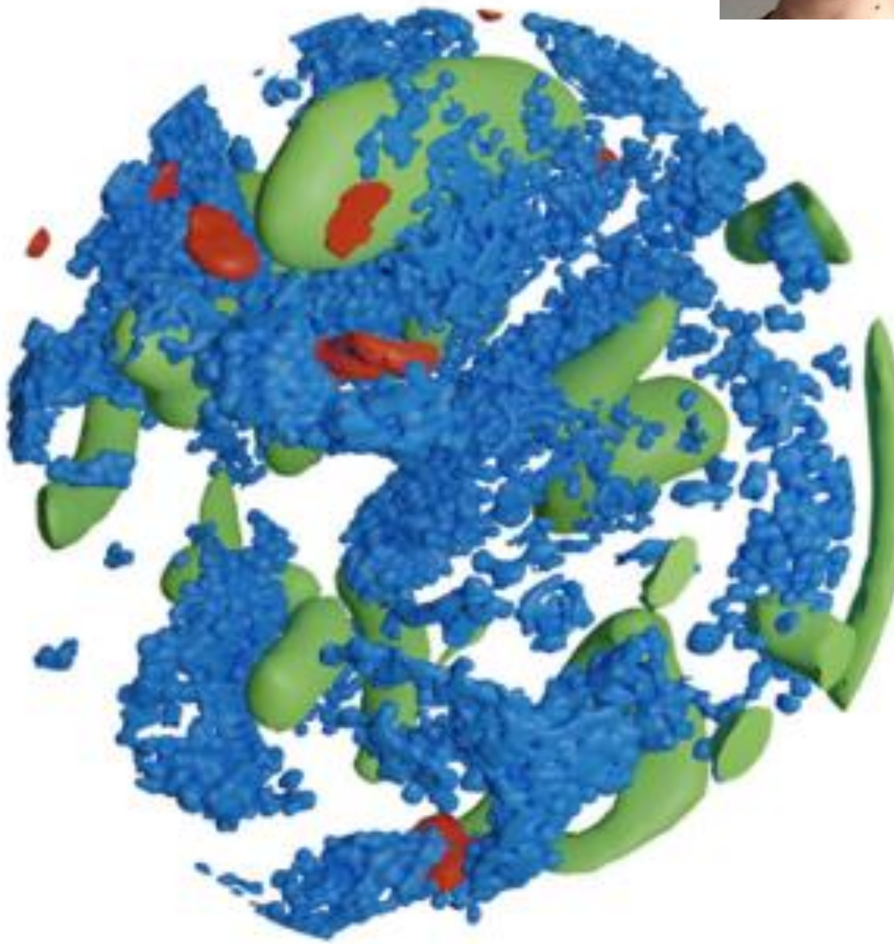
Exercise: Use GET's global_envelope_test to test whether x.csv and/or z.csv are likely to be random



2. Spatial shape fields: Real structures are not points, small structures are difficult to separate

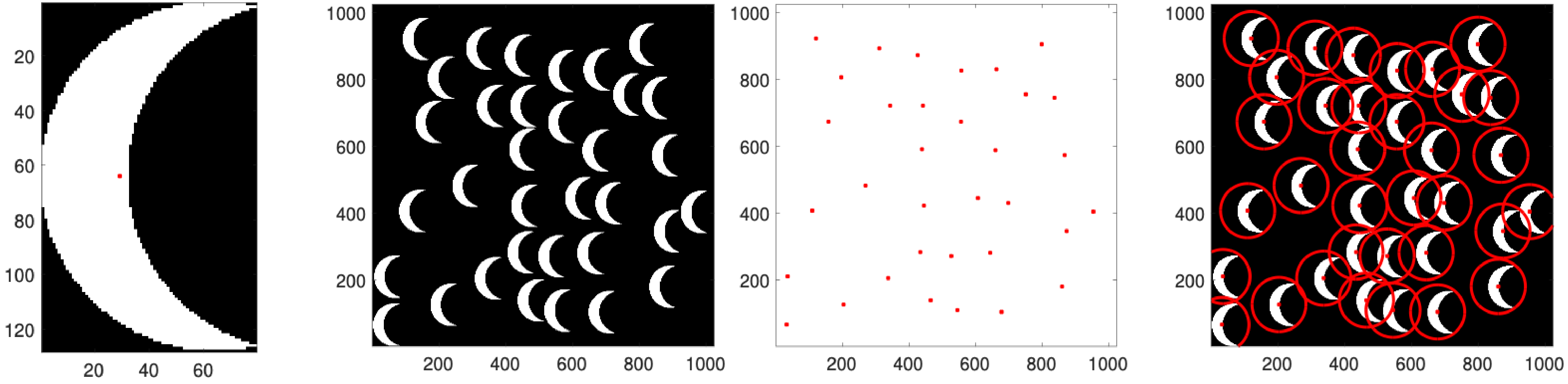


Deep Learning

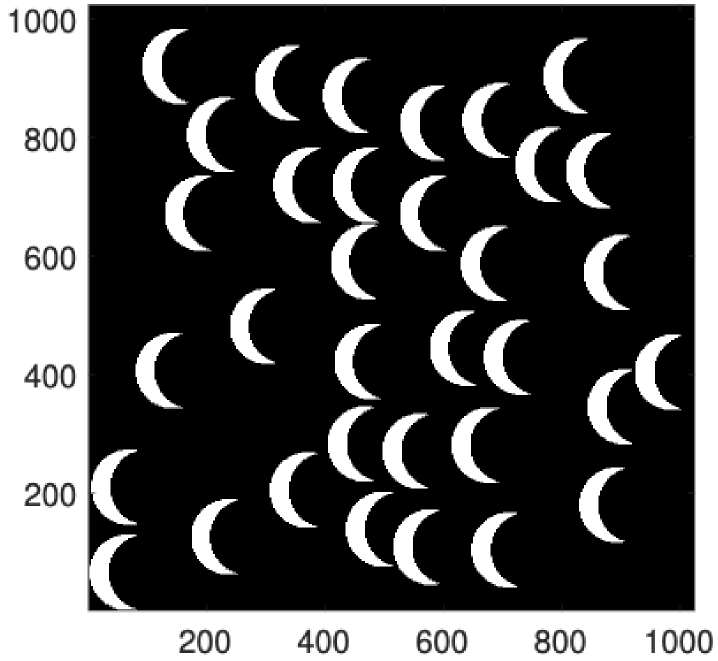


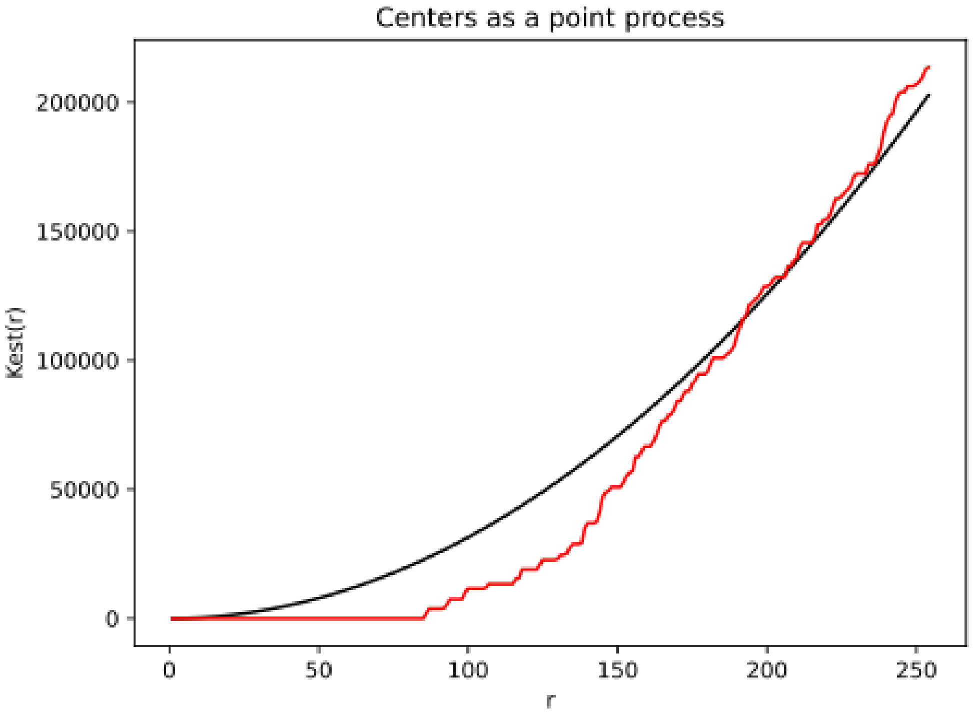
Measuring Shape Relations Using r-Parallel Sets; HJT Stephensen, AM Svane, CB Villanueva, SA Goldman, & J Sporring; Journal of mathematical imaging and vision, 2021

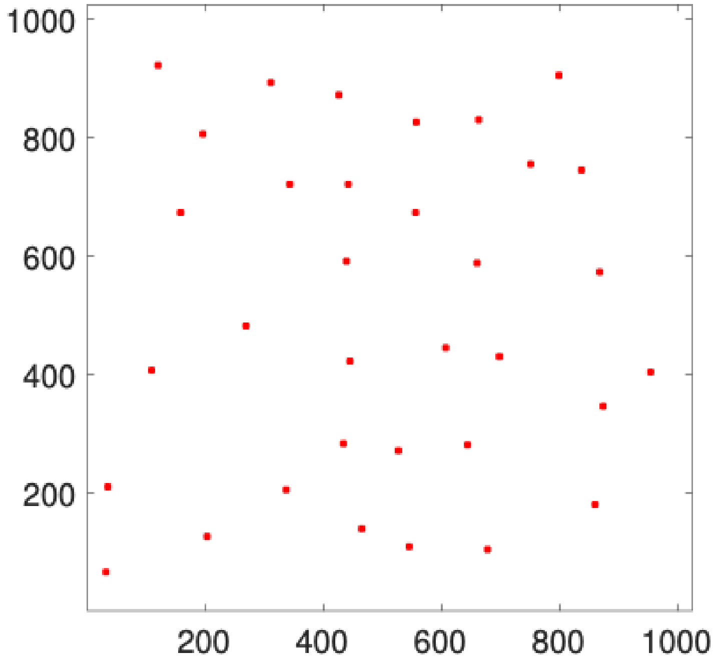
Not all shapes are well summarized as a reference point



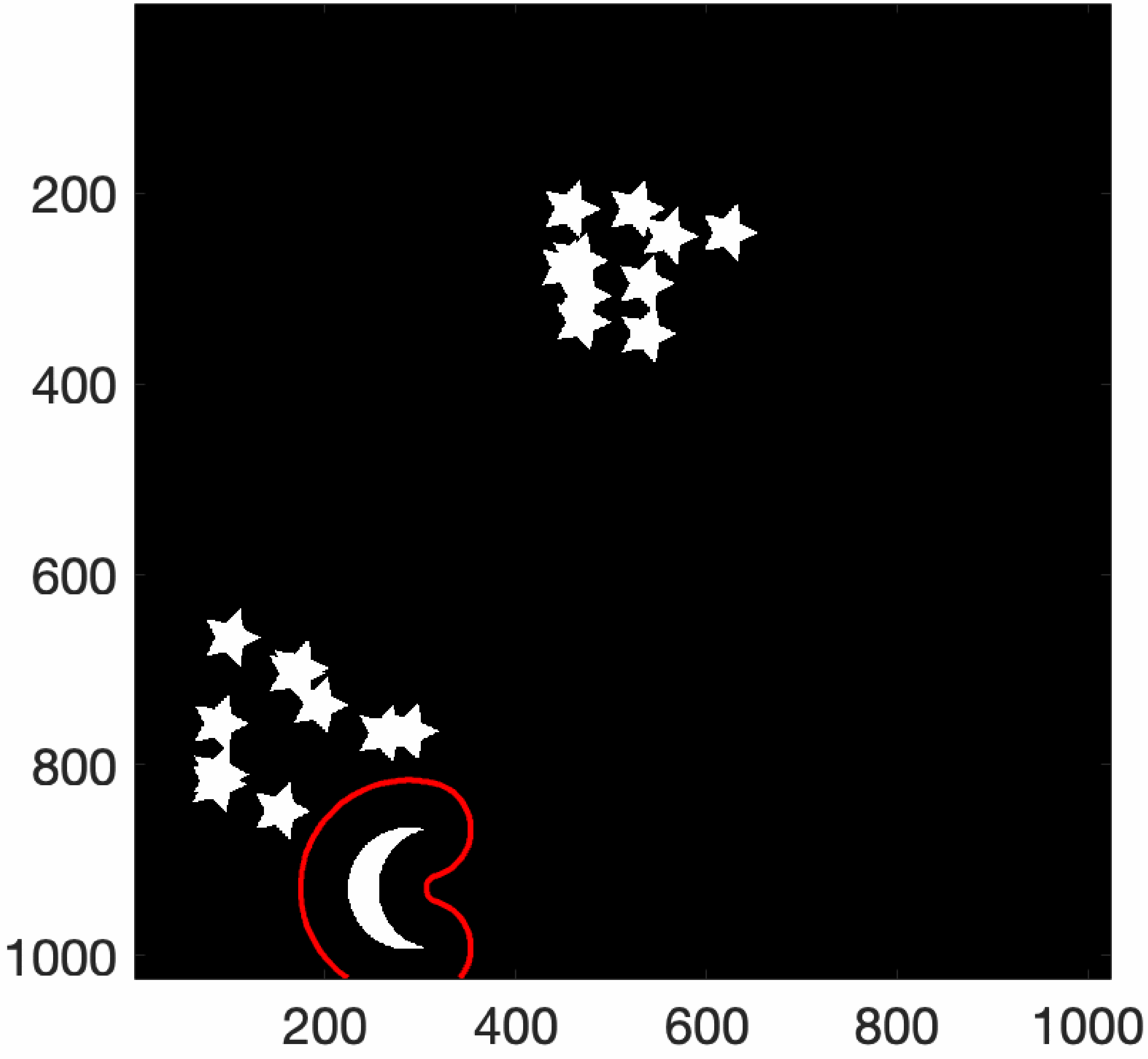
Ripley’s K-function indicates strong repulsion



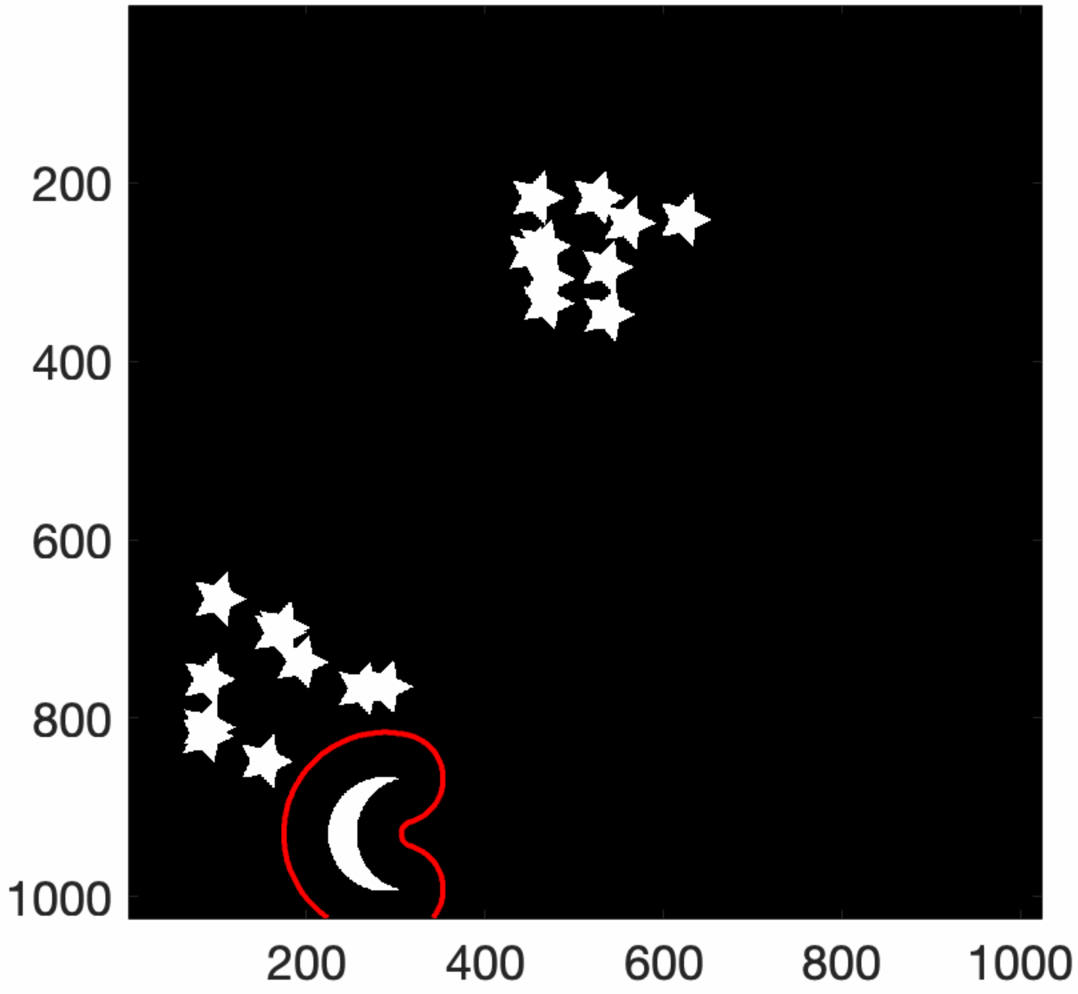


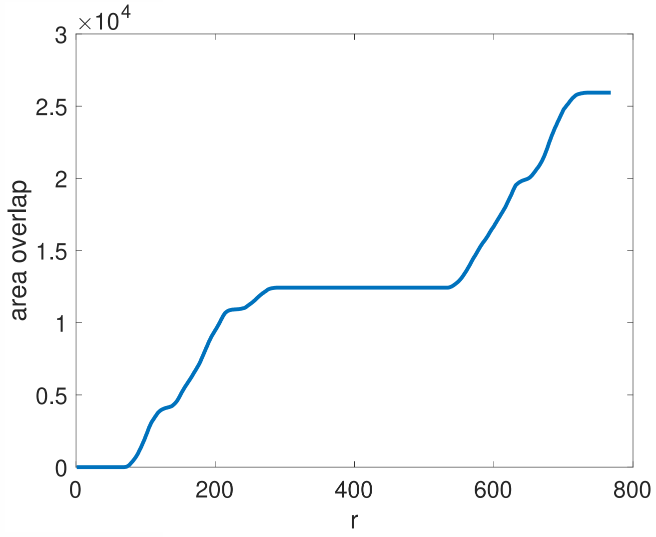


Shape relation measures = Interaction with distance fields



Shape relation measures: Some characteristic functions

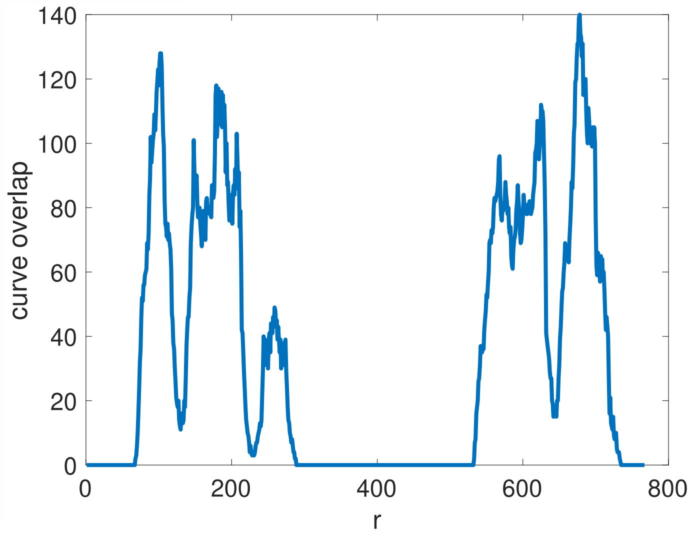


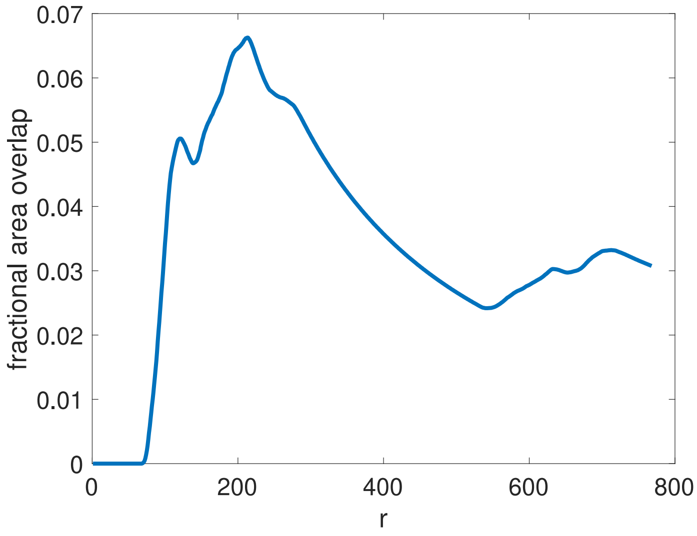


$$\mu_{00}(r) = \mathcal{H}(X \cap Y^r)$$

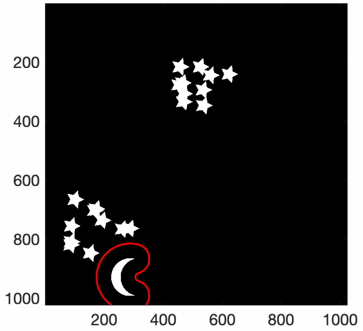
$$g_{00}(r) = \frac{d\mu_{00}(r)}{dr} = \mu_{01}(r)$$

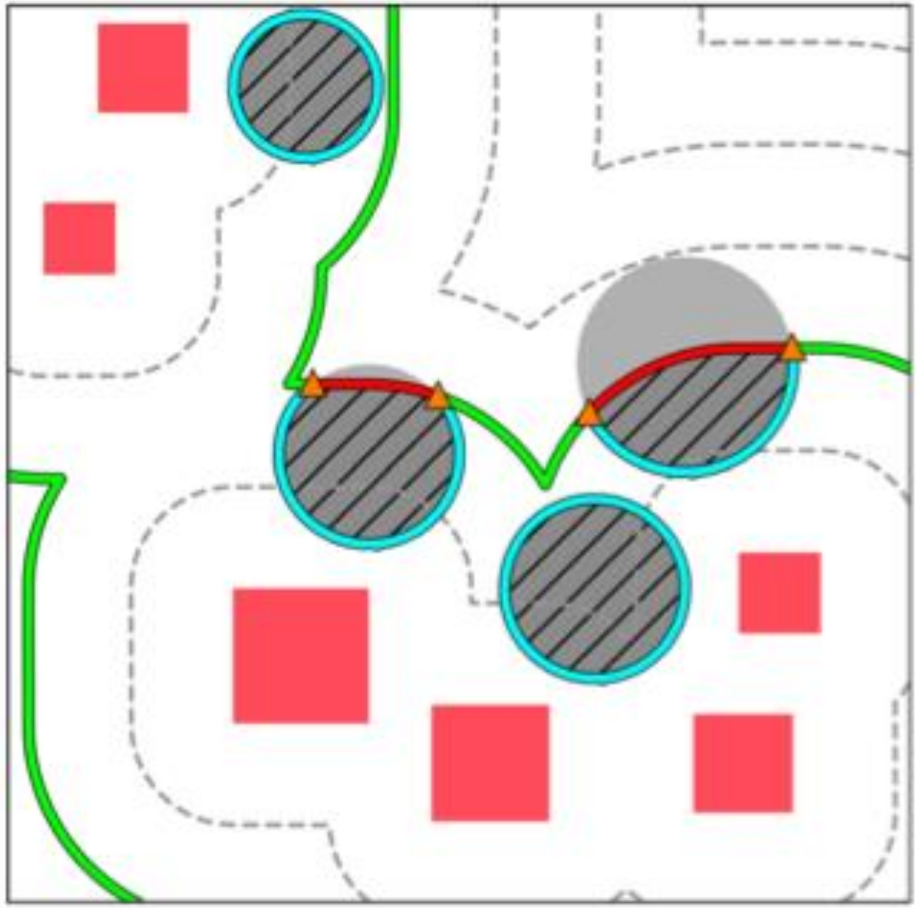
$$f_{00}(r) = \frac{\mu_{00}(r)}{\mathcal{H}(Y^r)}$$





There can be only 4





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

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

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

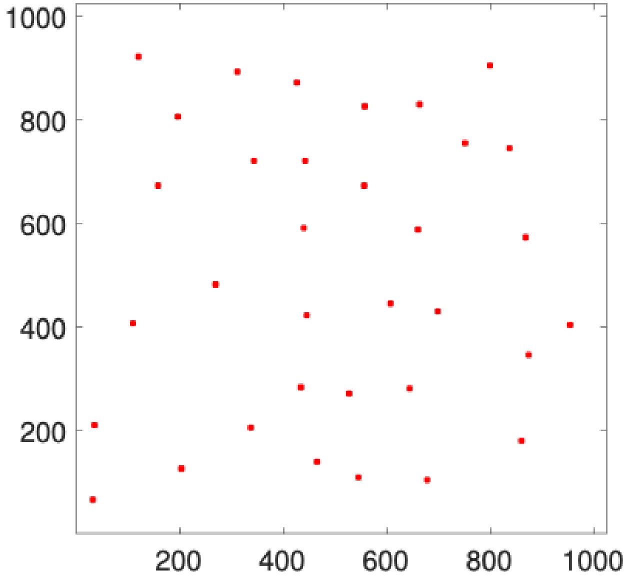
https://lab.compute.dtu.dk/QIM/tools/relationalshapemeasure

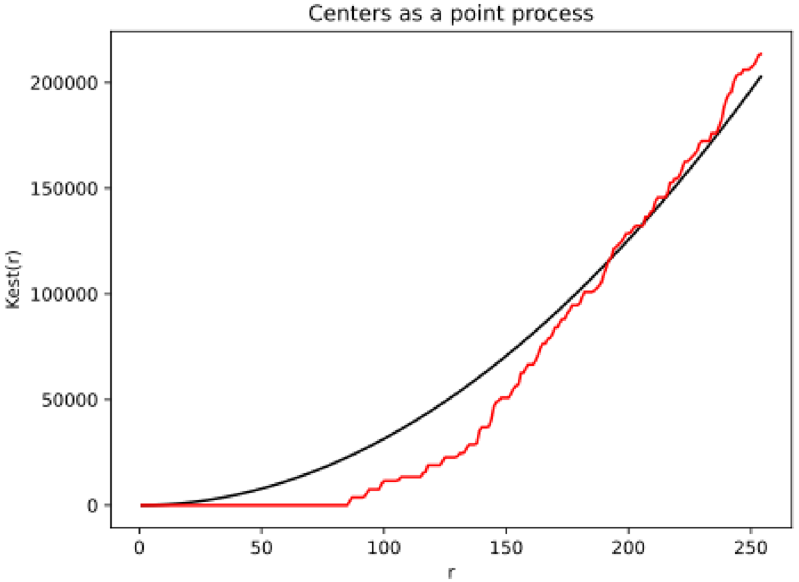
Spatial point fields vs. shape fields: shapeRelation.py

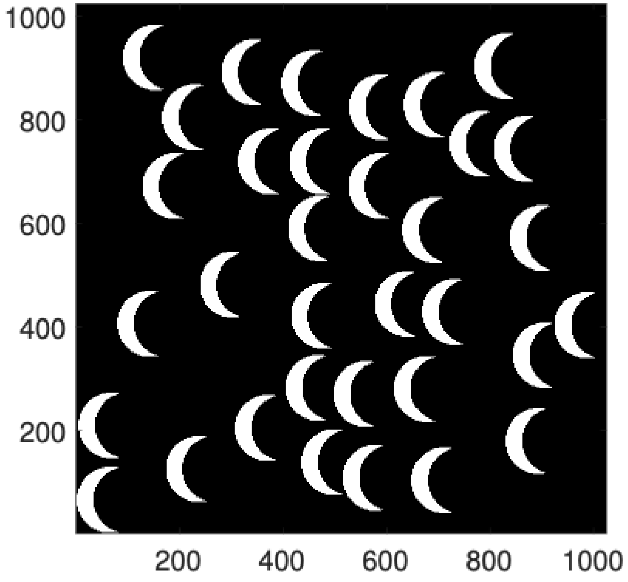
$$\mu_{00}(r) = \mathcal{H}(X \cap Y^r)$$

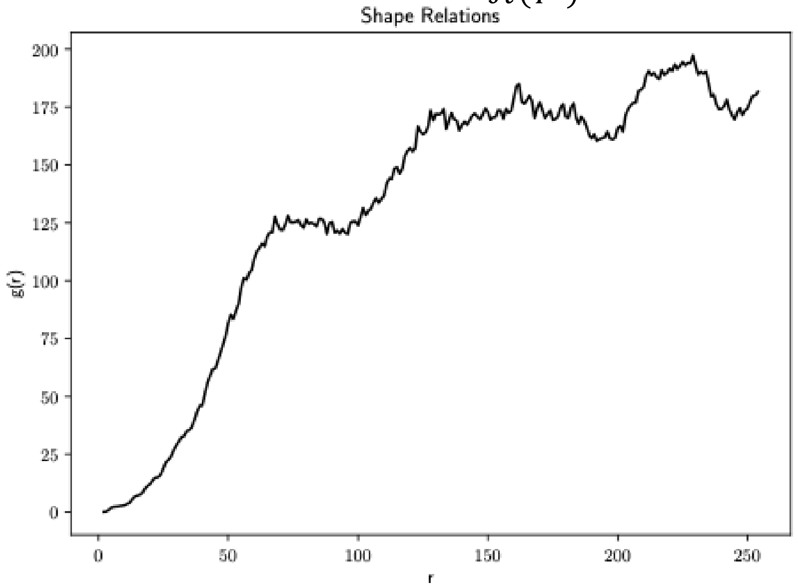
$$g_{00}(r) = \frac{d\mu_{00}(r)}{dr} = \mu_{01}(r)$$

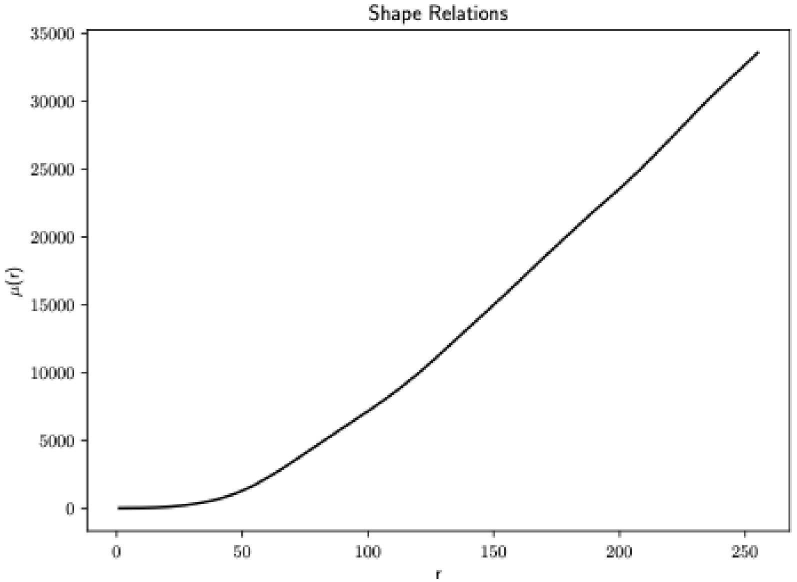
$$f_{00}(r) = \frac{\mu_{00}(r)}{\mathcal{H}(Y^r)}$$

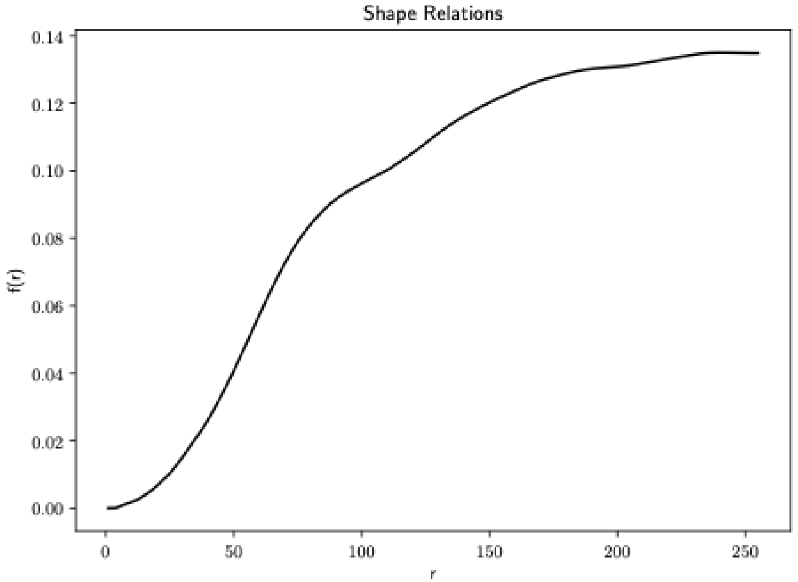




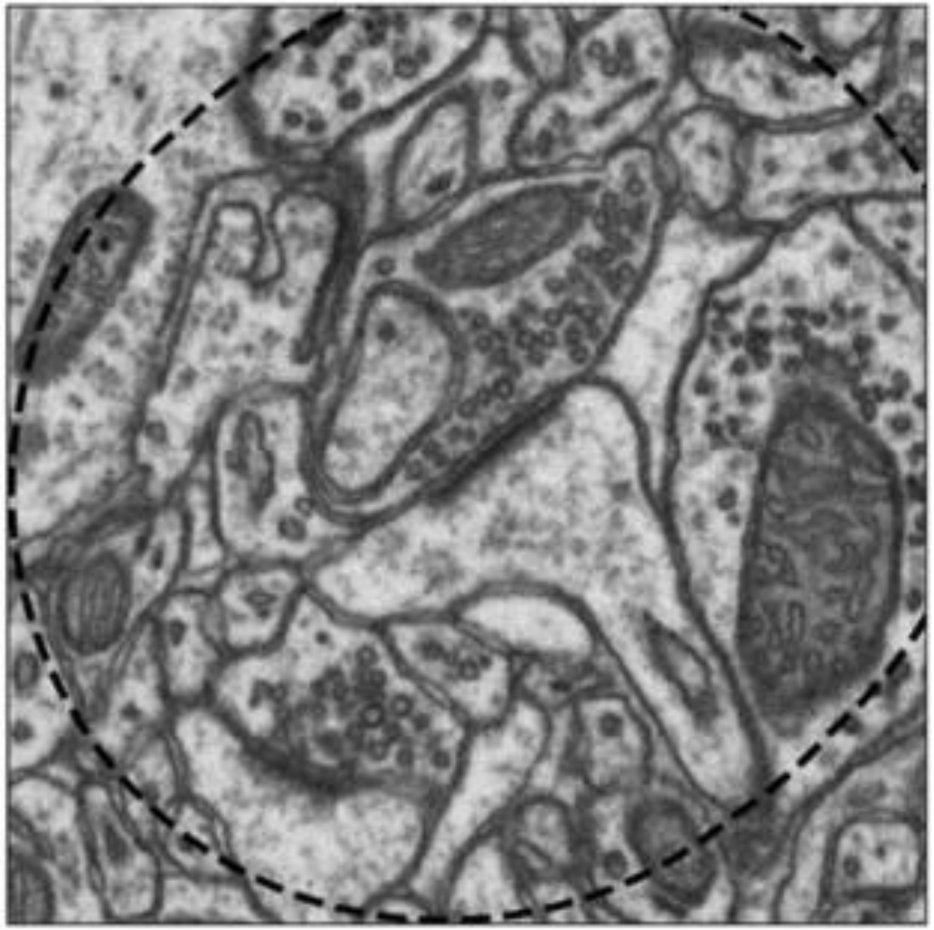


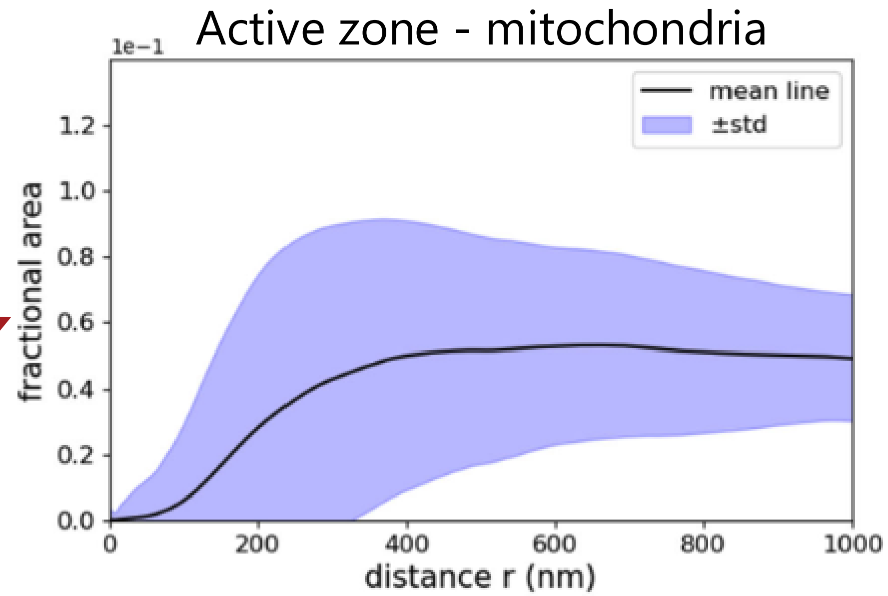


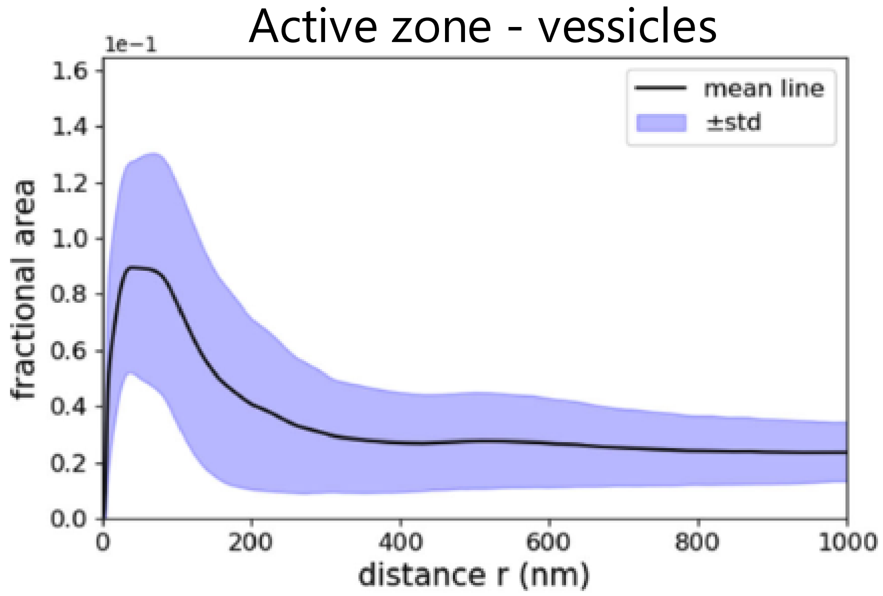




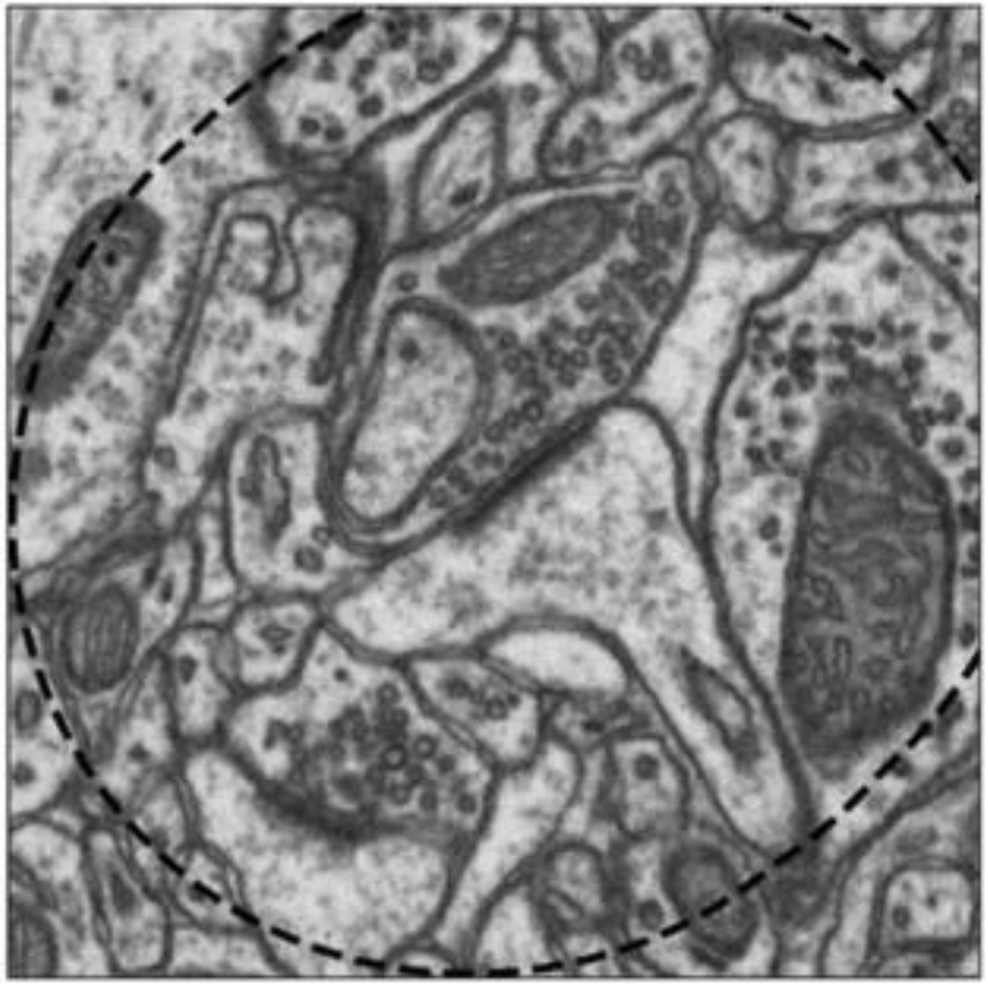
Shape relations for statistical summary of families of shapes and their relations



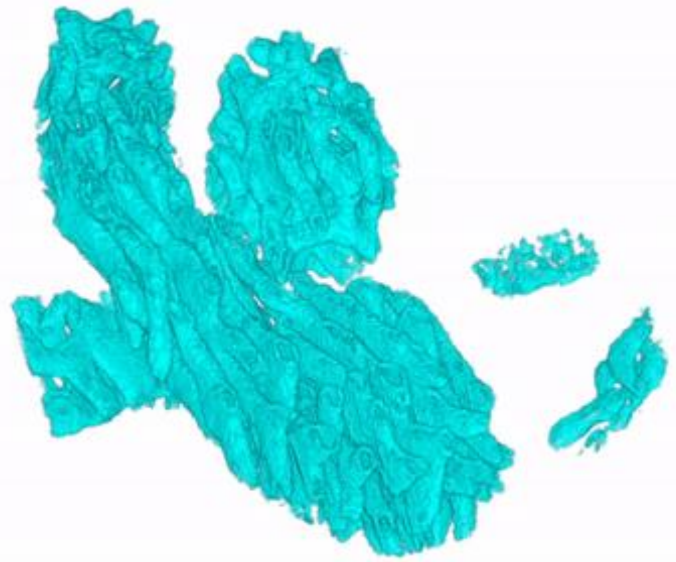




3. With a little help from topology: Cristae membranes in Mitochondria

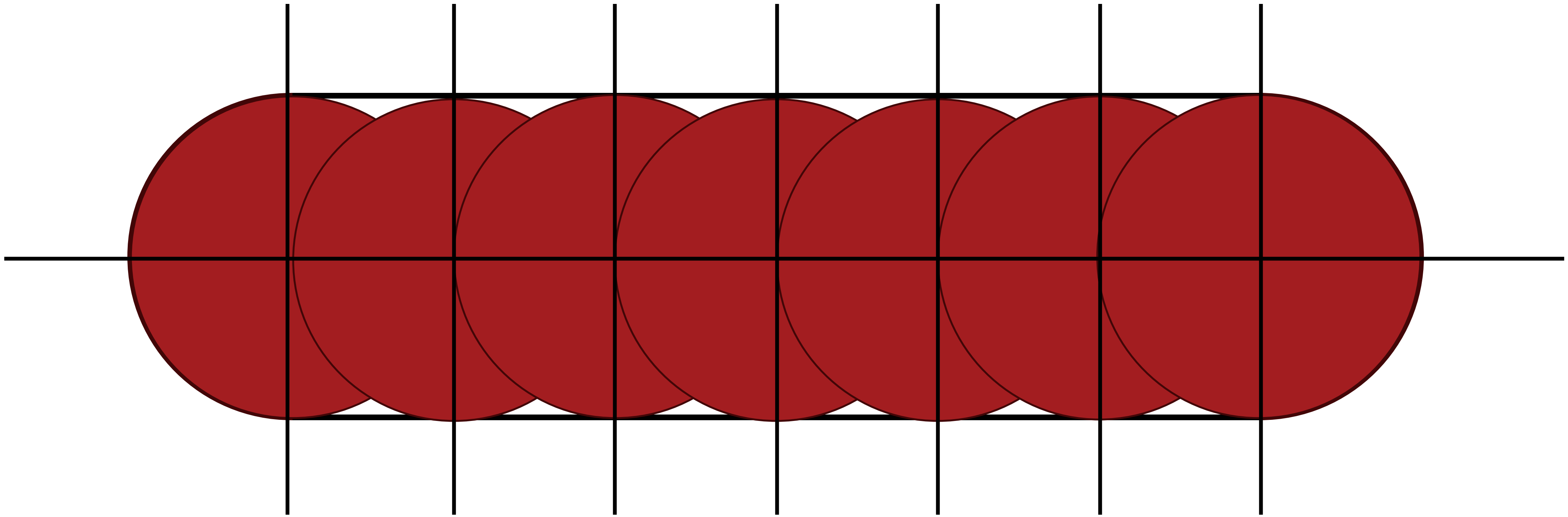


Deep Learning

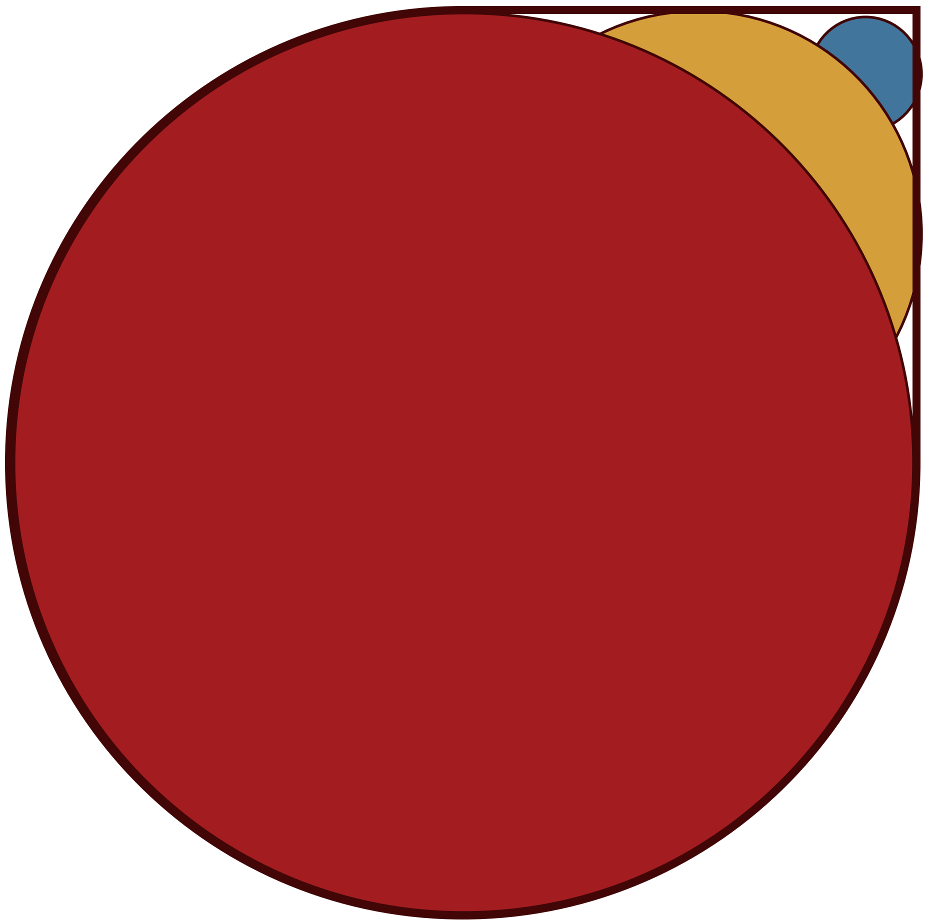


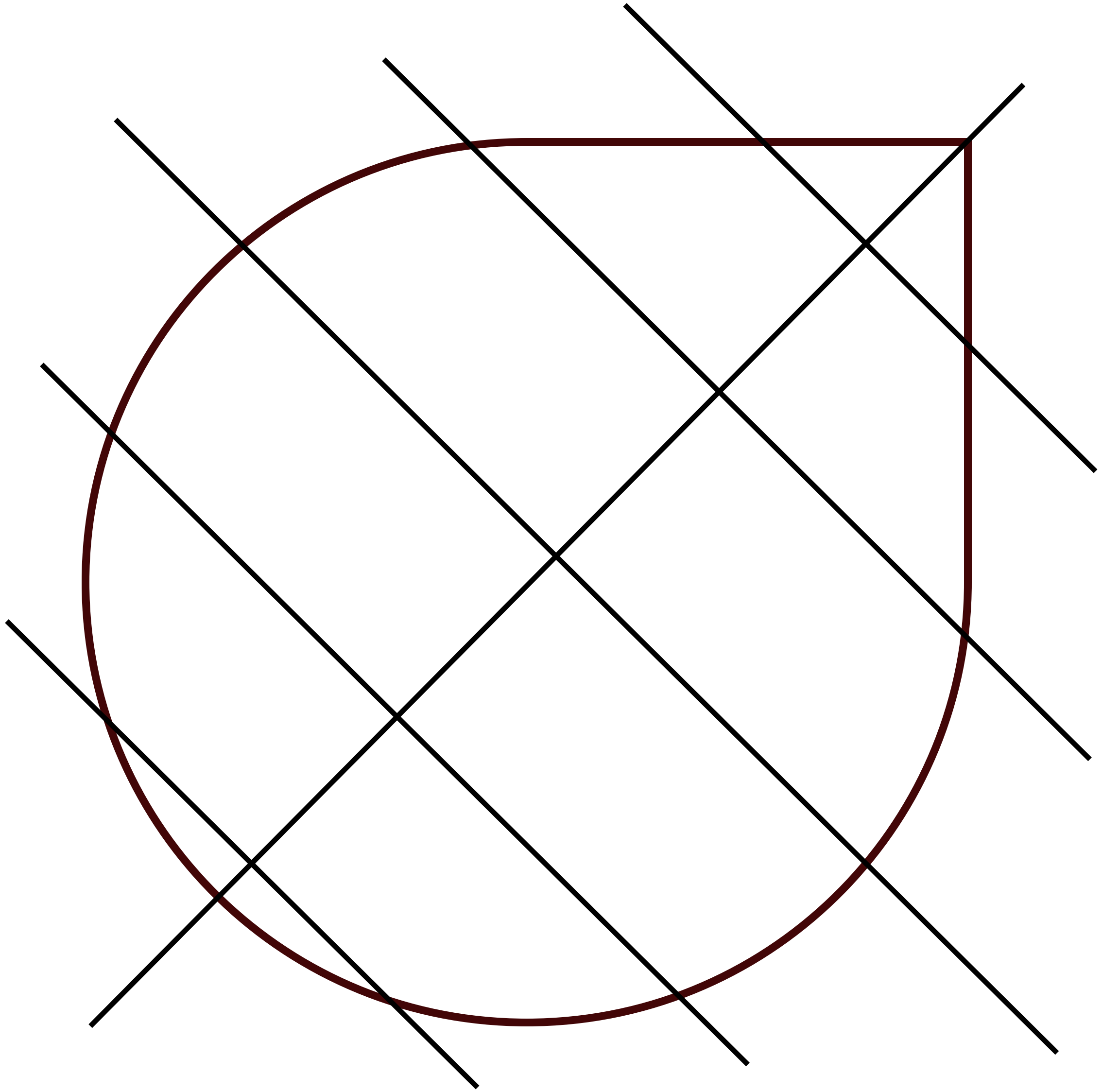
Extracting Mitochondrial Cristae Characteristics from 3D Focused Ion Beam Scanning Electron Microscopy Data, C Wang, L Østergaard, S Hasselholt, & J Sporring, to appear in Communications Biology, 2024

Local thickness is biased, but what is the definition of thickness?



Local thickness is biased, but what is the definition of thickness?





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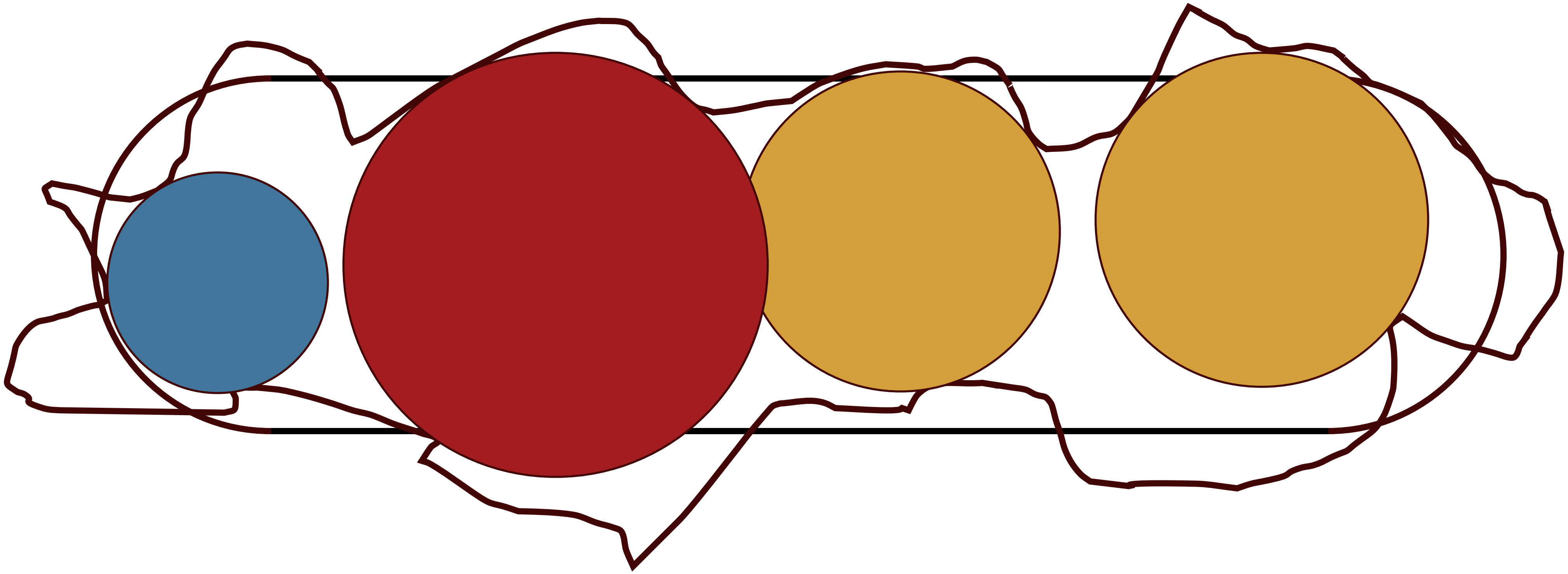
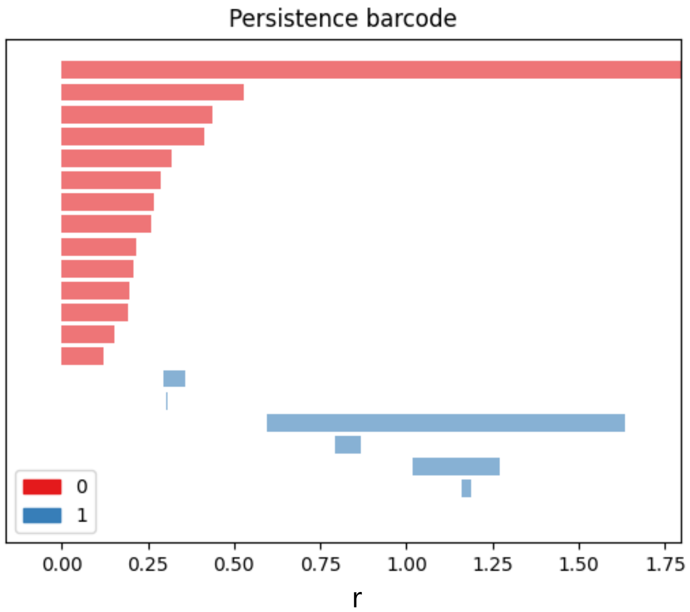
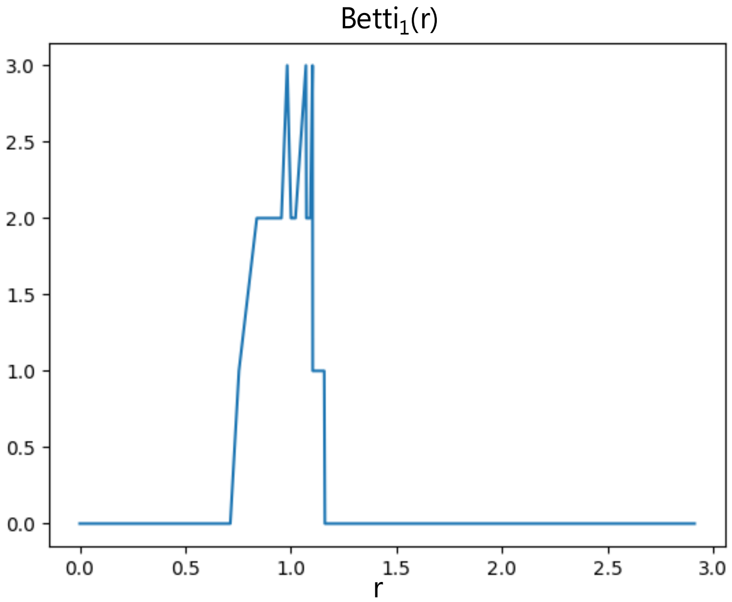


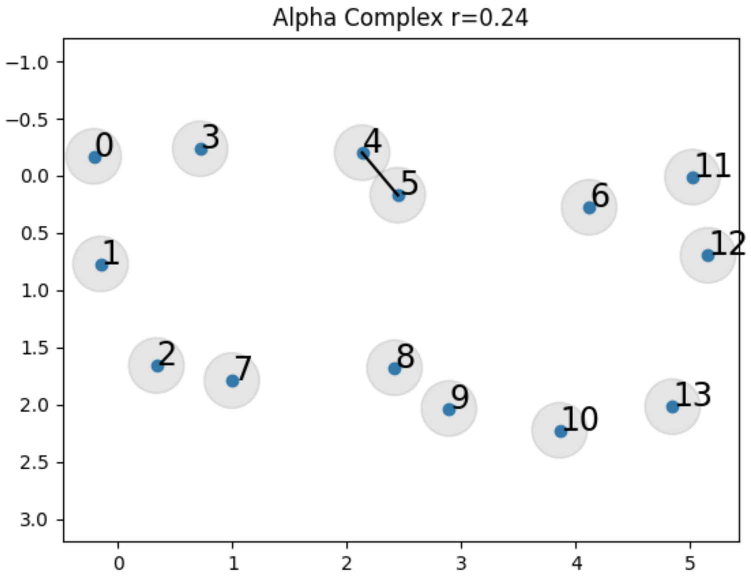
Persistent homology and friends: https://gudhi.inria.fr/

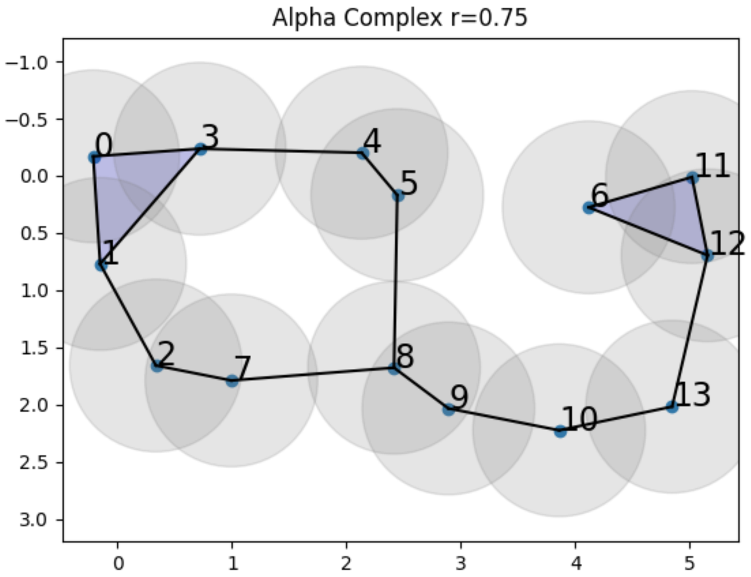
Simplex $\sigma = [x_0, x_1, \ldots x_k]$ is in the alpha complex if

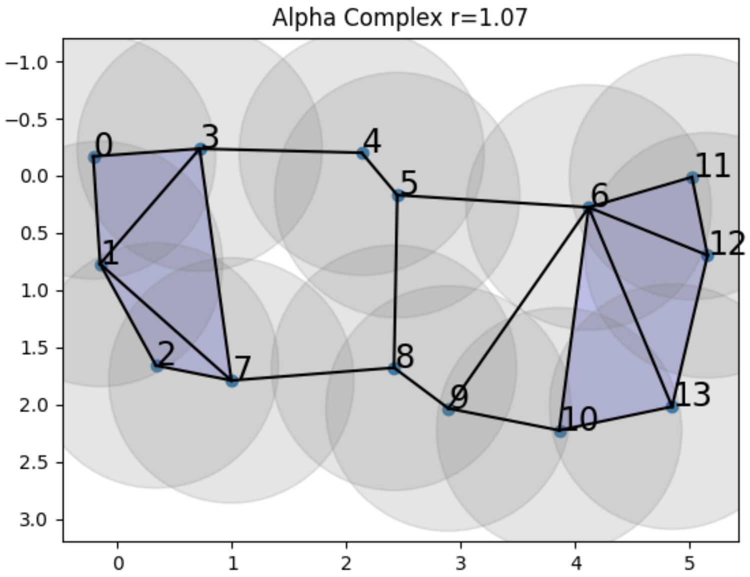
$$\bigcap_{x_i \in \sigma} B(x_i, r) \neq \emptyset$$



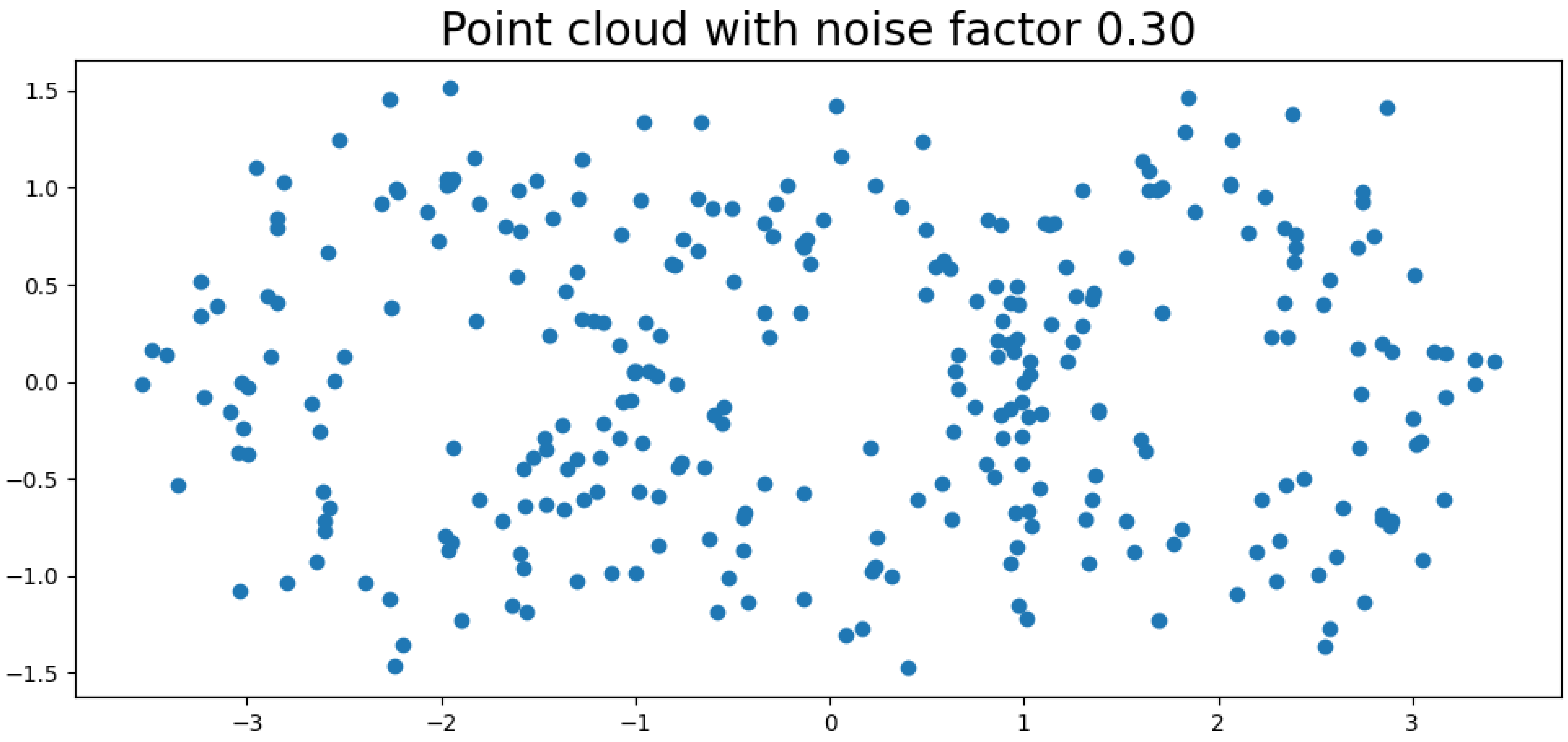






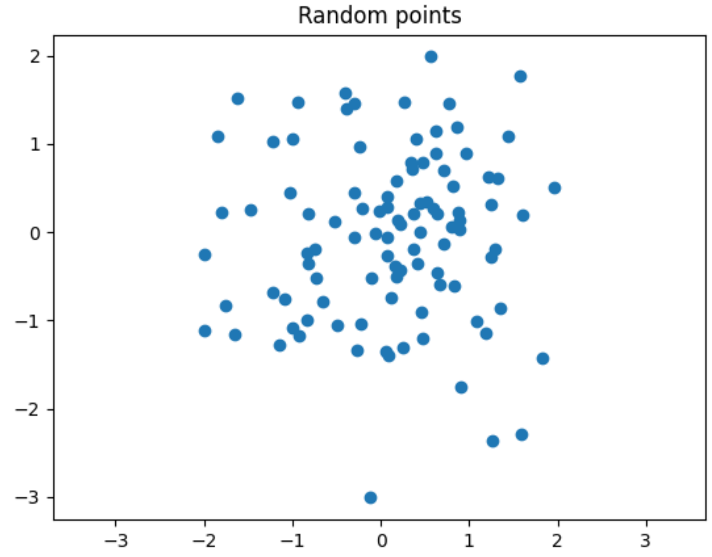


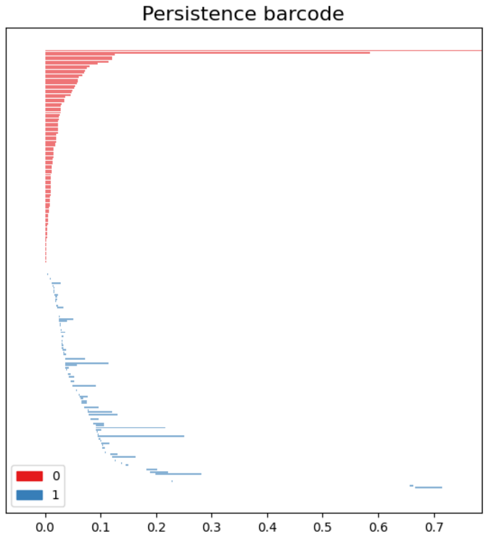
Persistence under noise: $\mathrm{dgm} = \mathrm{dgm}^{\mathrm{Signal}} \cup \mathrm{dgm}^{\mathrm{Noise}}$

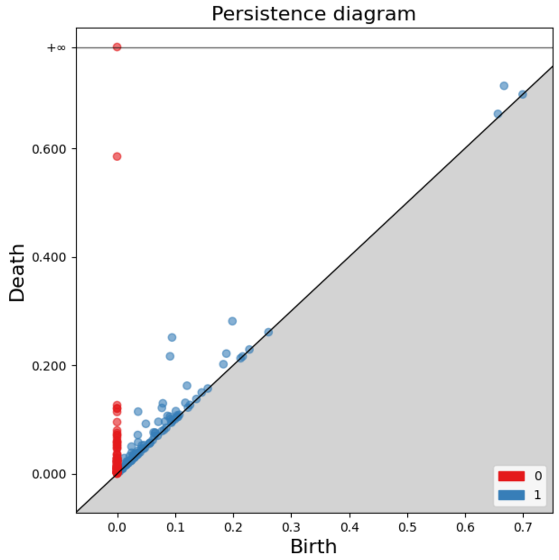


Pure noise

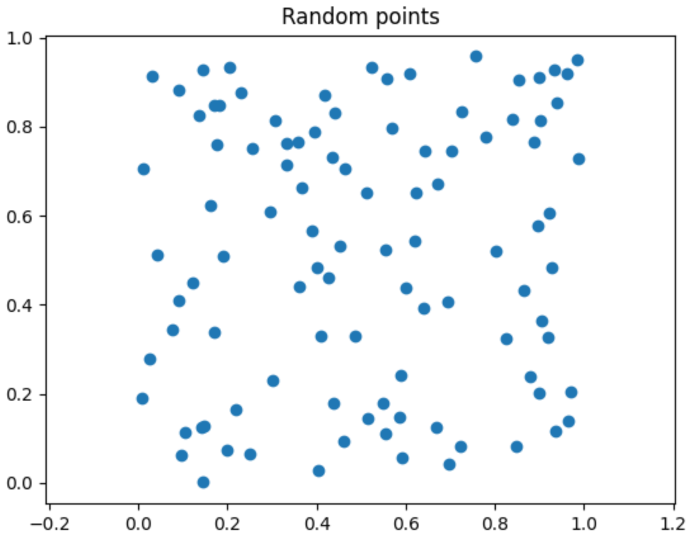
Normal

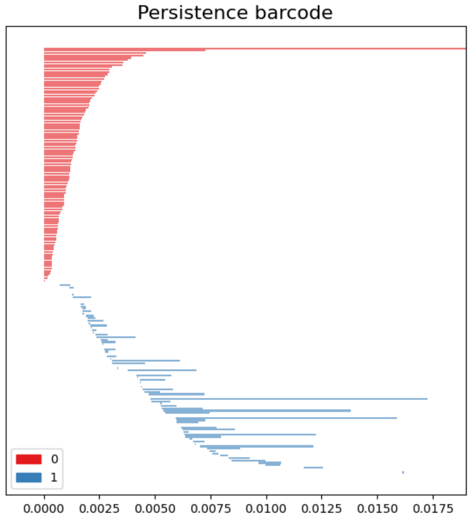


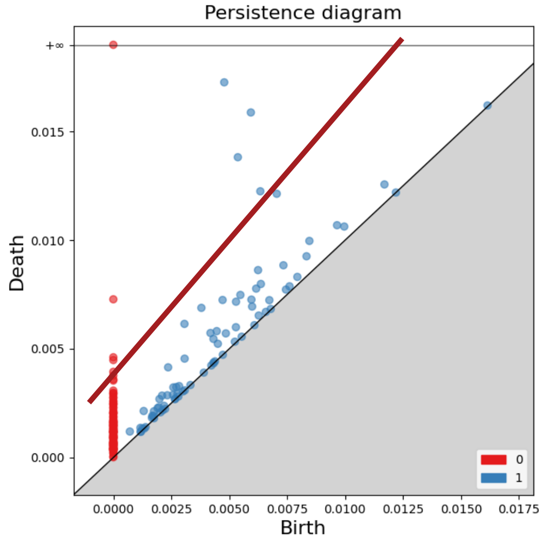




Uniform







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:

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

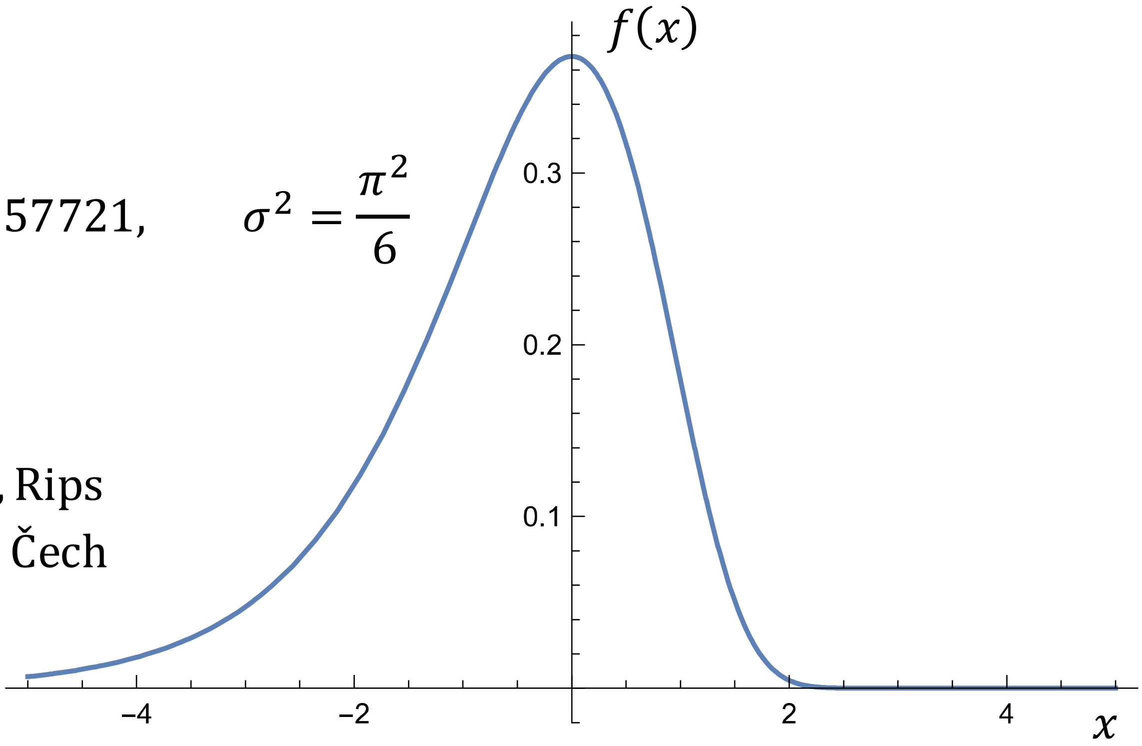
$$\mathrm{x} = \frac{(\rho - \bar{\rho})}{\beta} - \gamma, \qquad \bar{\rho} = \frac{1}{|\mathrm{dgm}_k|} \sum_{p \in \mathrm{dgm}_k} \rho\,, \qquad \beta = \begin{cases} 1, \text{Rips} \\ 2, \text{Čech} \end{cases}$$

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

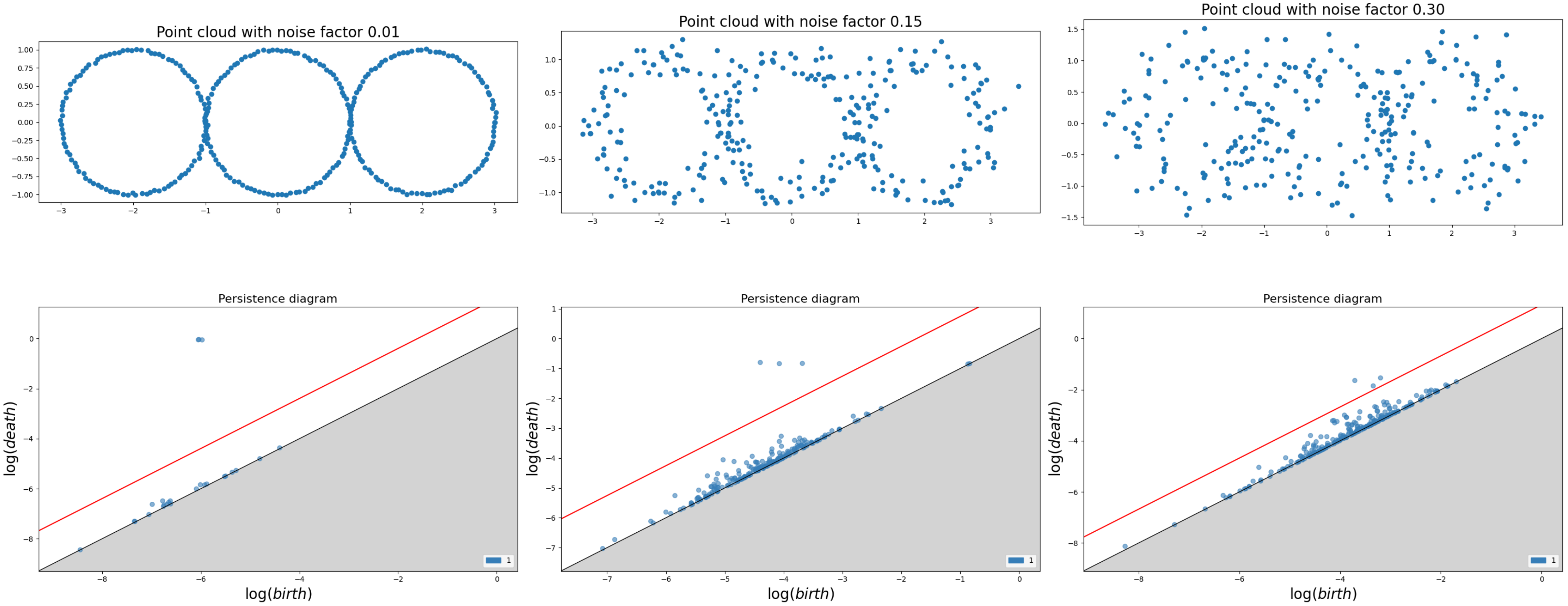
$$P(x \geq x_0 | x \text{ is noise}) = 1 - F(x) = e^{-e^{x_0}}$$

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

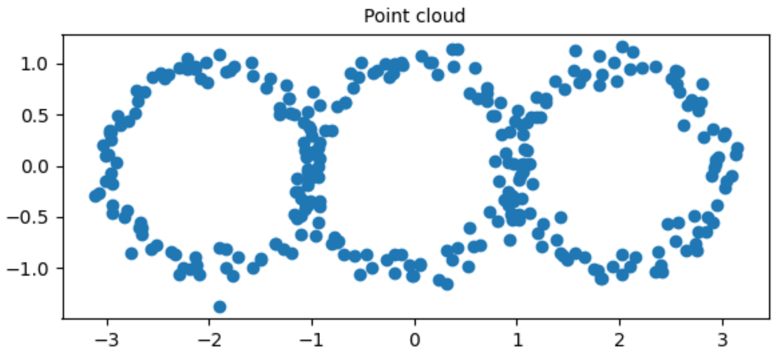
$$e^{\rho} = \ln \frac{r_{\text{death}}}{r_{\text{birth}}} = (-1)^{\beta} e^{\beta\gamma + \bar{\rho}} \left(\ln \frac{\alpha}{|\mathrm{dgm}_k|} \right)^{\beta}$$

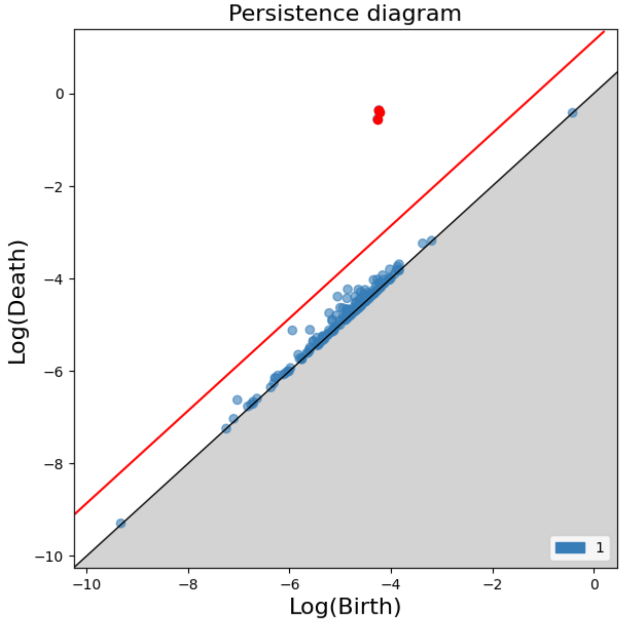


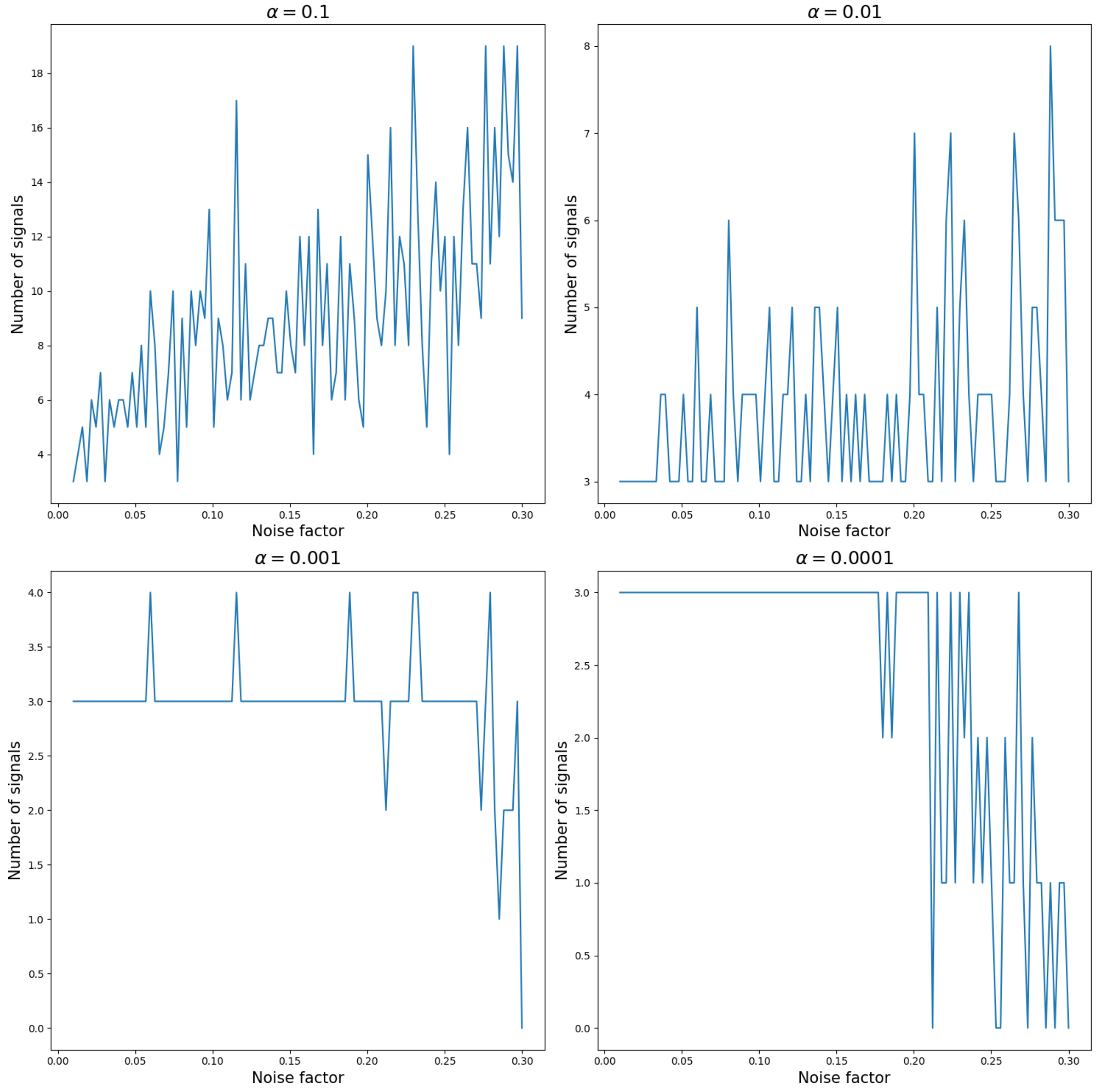
The universal distribution can separate very noisy cases



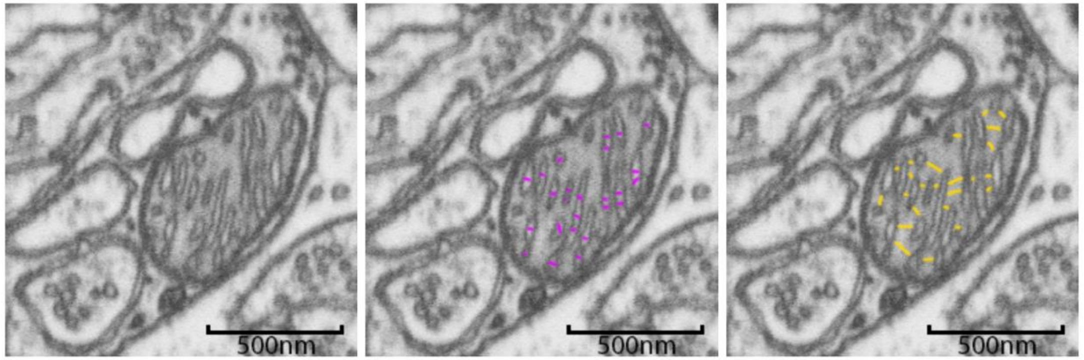
Family-wise error rate



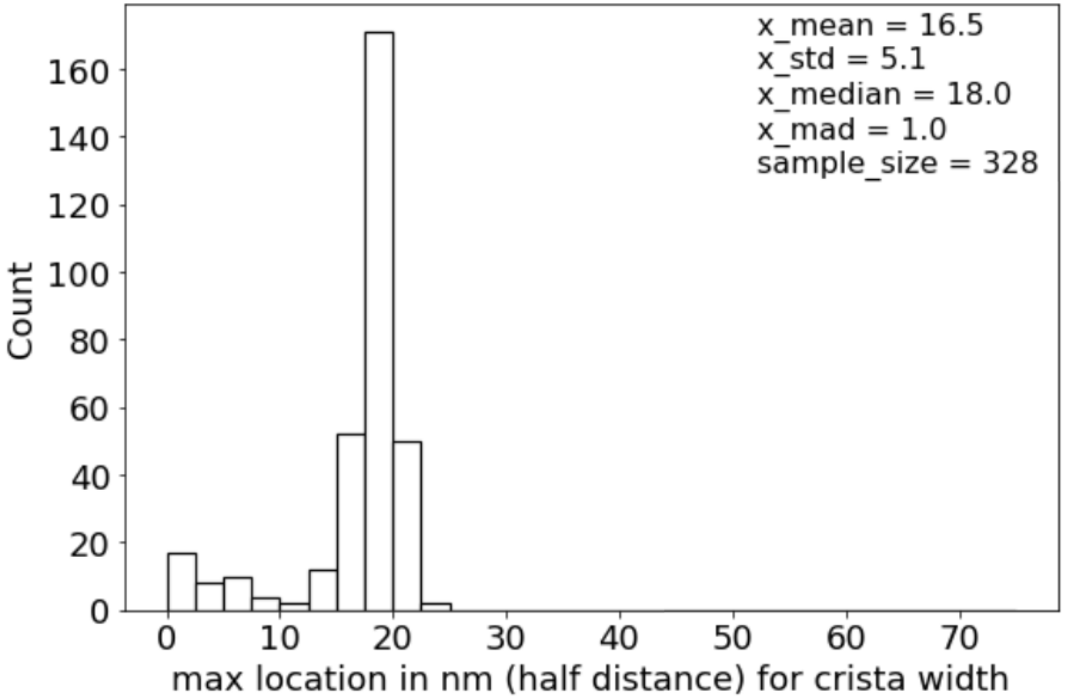




Persistent homology: Statistical measures on H_0

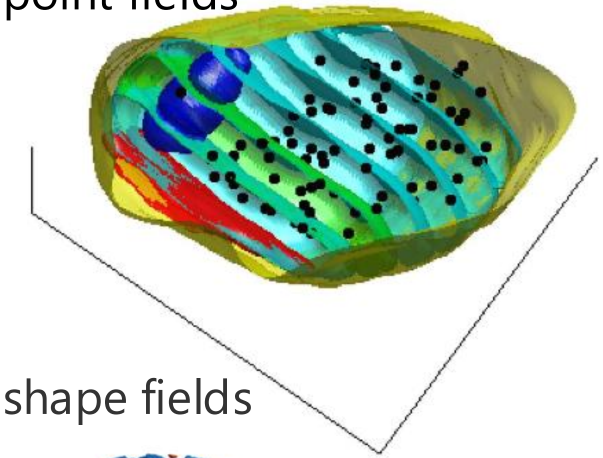


(a) (b) (c)



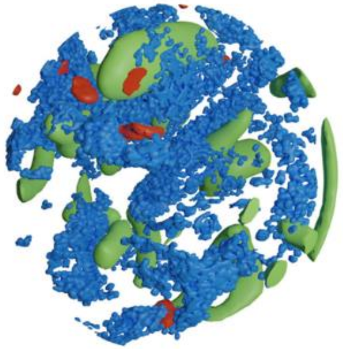
Statistical summary of object collections

Spatial point fields



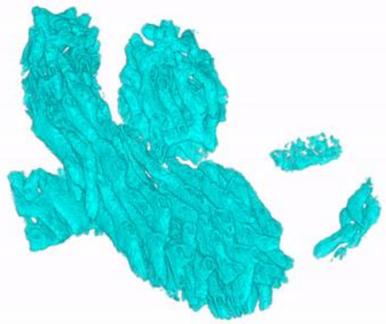
Pair correlation and Ripley's K functions summarizes 1st order point relations – e.g., do the vessicles cluster?

Spatial shape fields



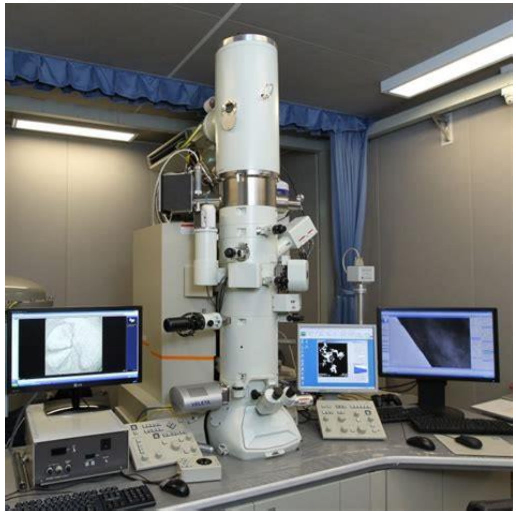
Hausdorf measures on overlaping sets extends notion of points to shapes – e.g., are mitochondria seen close to the synapse?

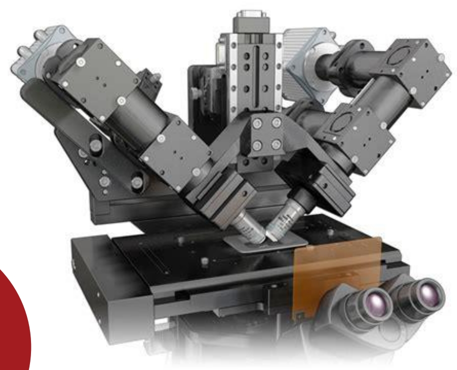
Topological data analysis

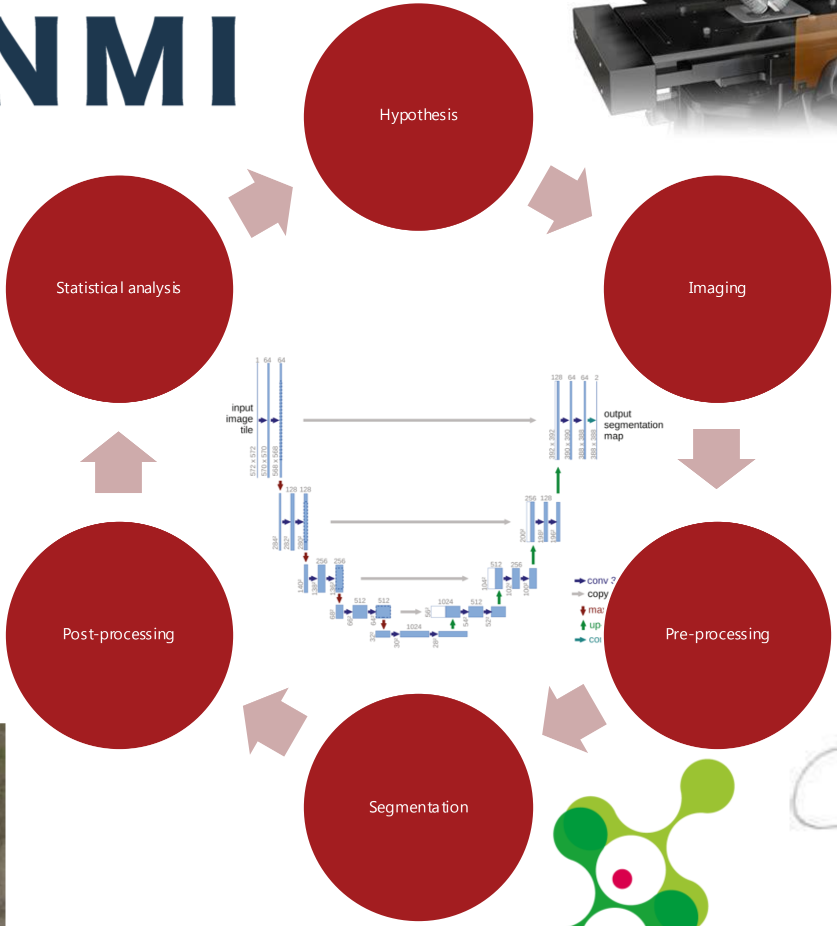


Filtrations brings topological concepts to measurements - e.g., what is the average tubular radius of complicated objects

BNMI







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