Exploring biological shape analysis through topology, geometry and statistics

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

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Department of Computer Science

UNIVERSITY OF COPENHAGEN

Imaging research and pipeline

Research loop

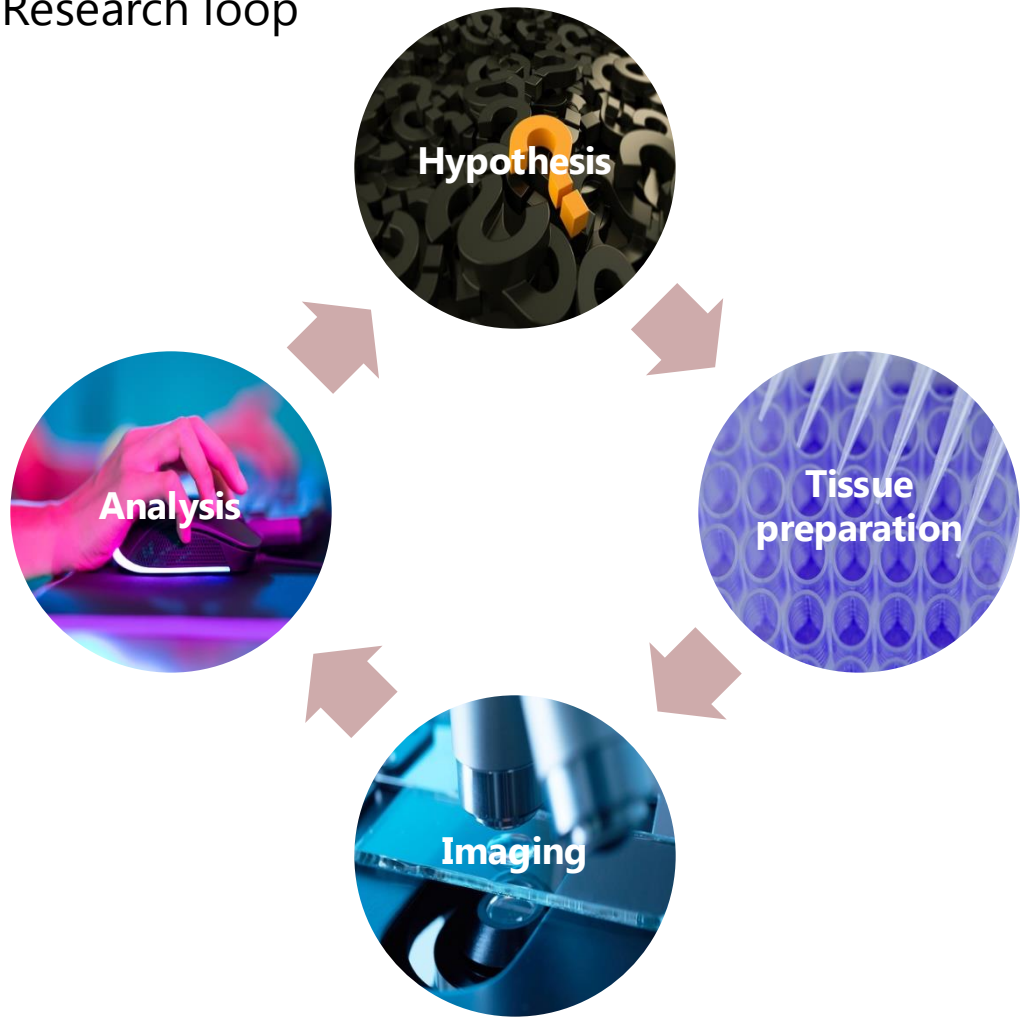
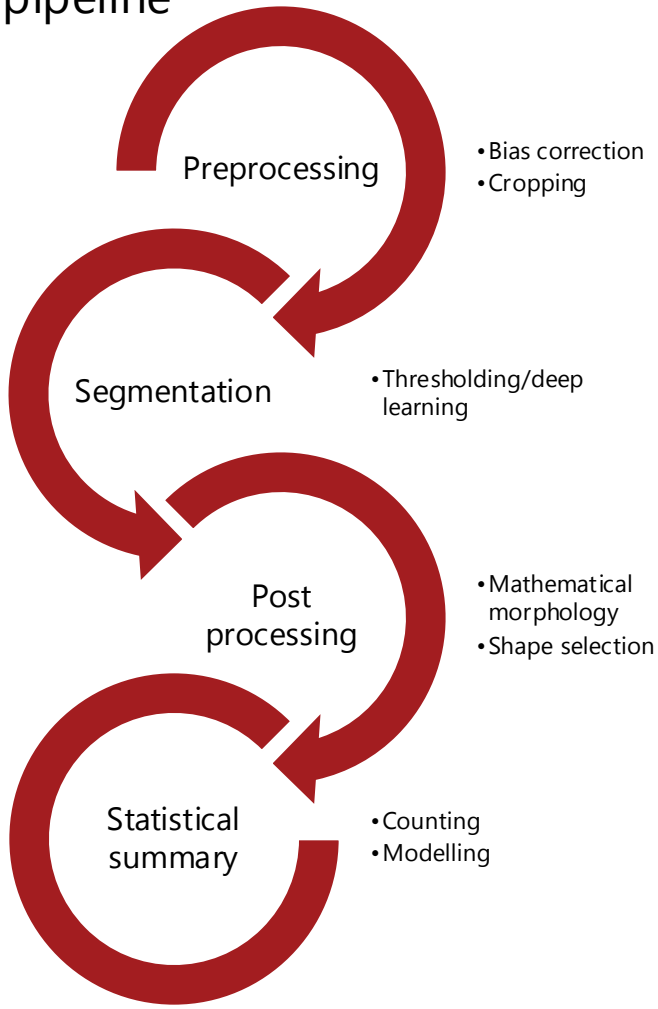


Image analysis pipeline



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

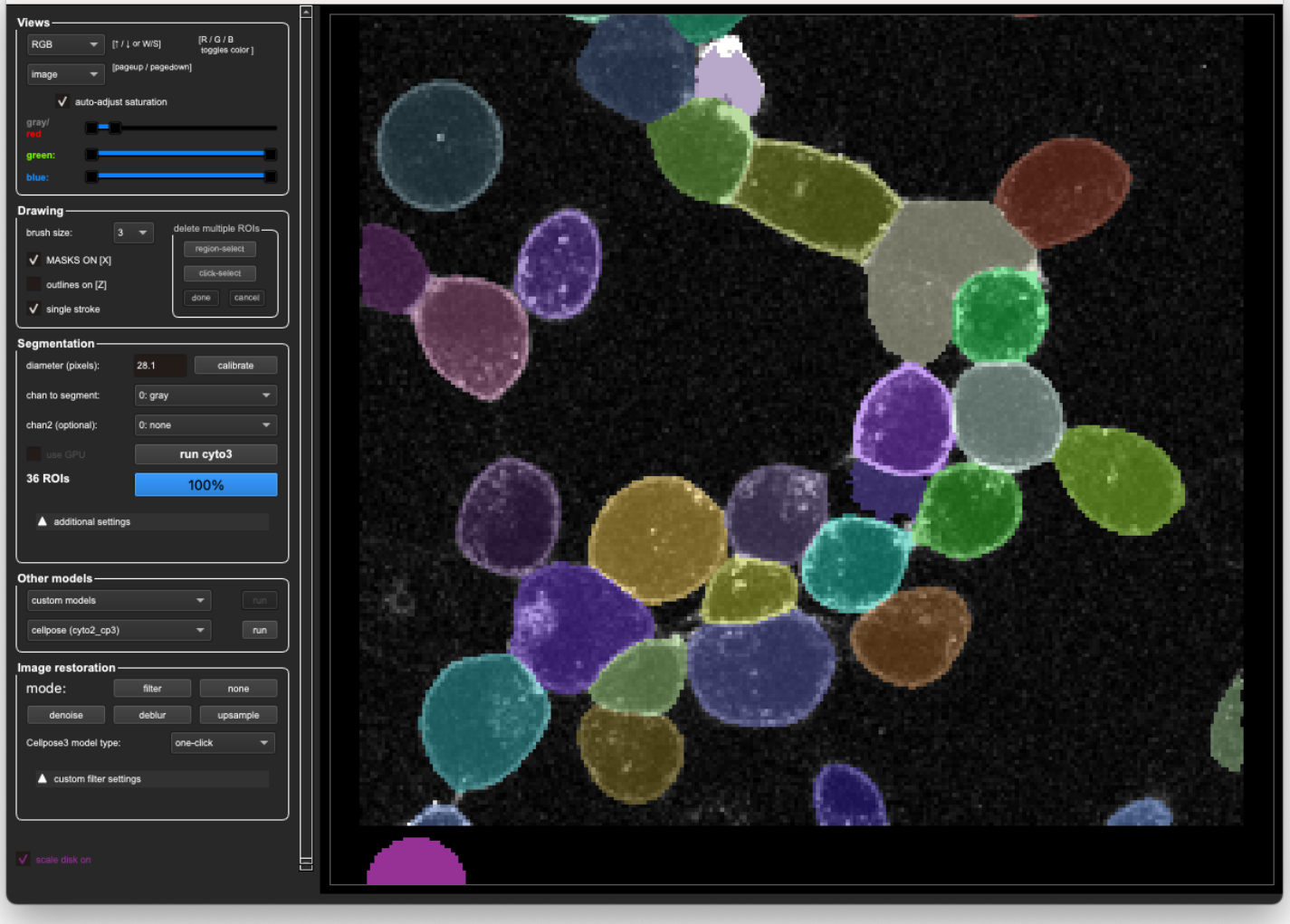
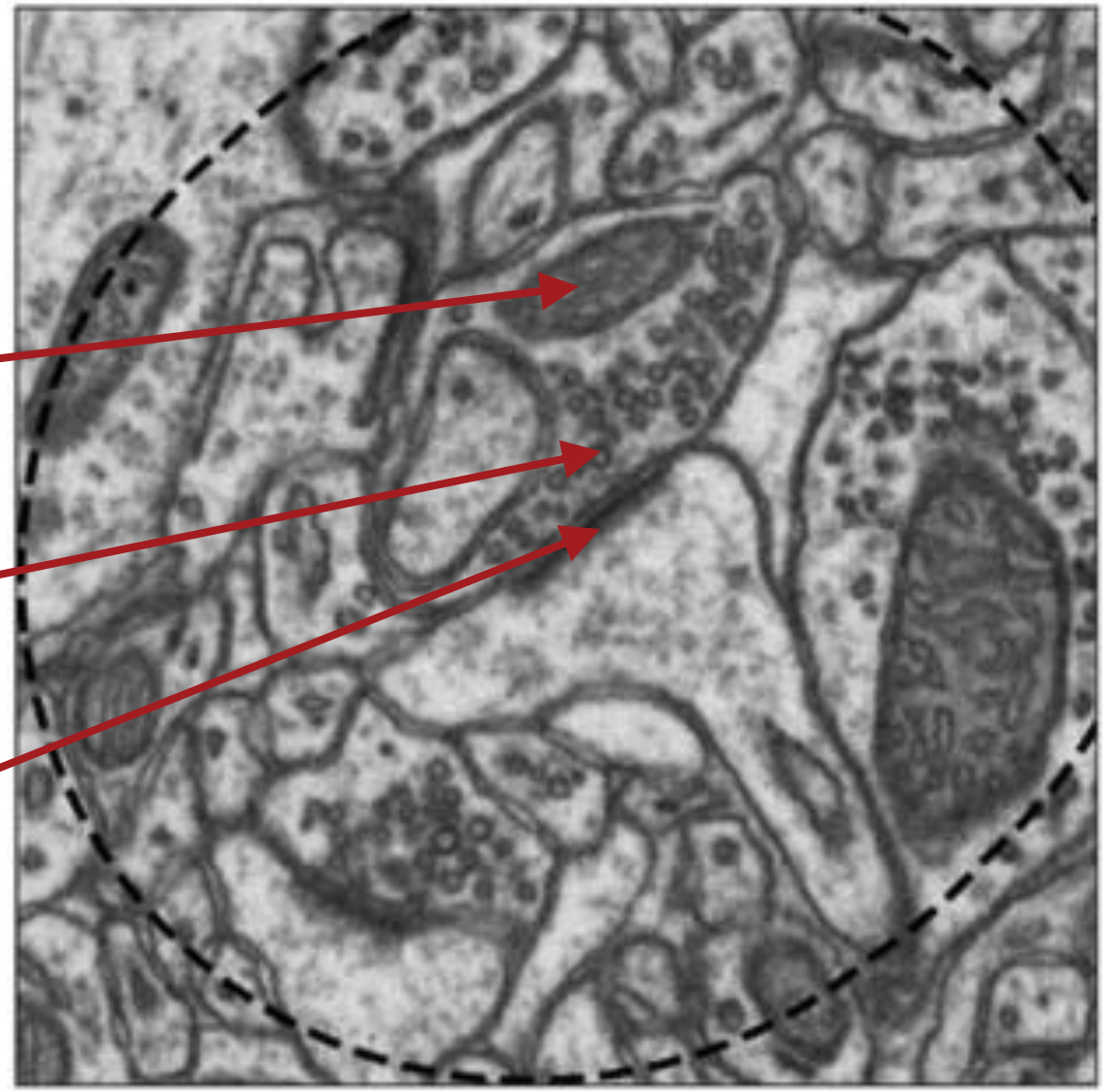


Image courtesy: Karen Martinez & Gabriella von Scheel von Rosing; AI: http://www.cellpose.org/

What to do next: Shape analysis

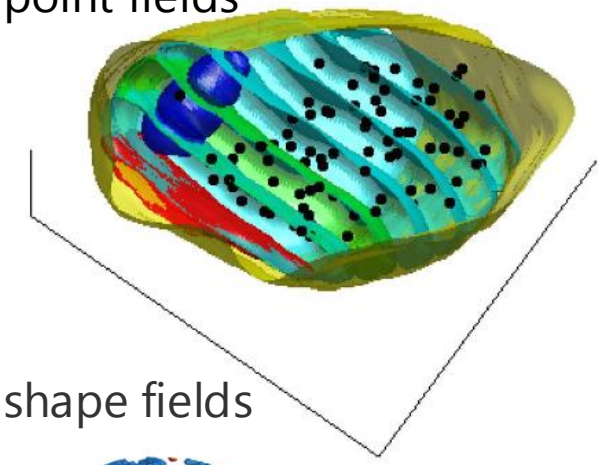
Focused ion-beam scanning electron microsopy (FIB-SEM)

Voxel size: (5 nm)^3

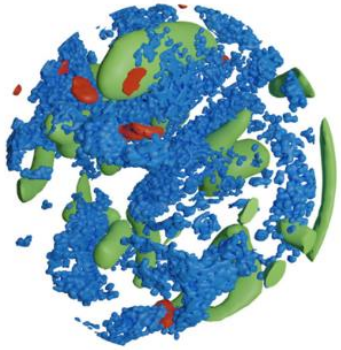


Graham Knott and Marco Cantoni. Electron microscopy dataset. https://cvlab.epfl.ch/data/ data-em/

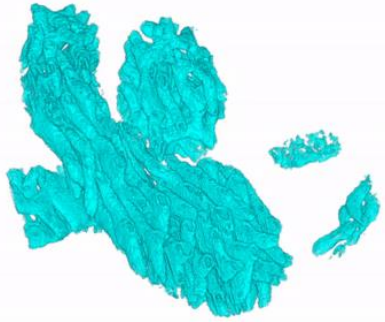
Spatial point fields



Spatial shape fields

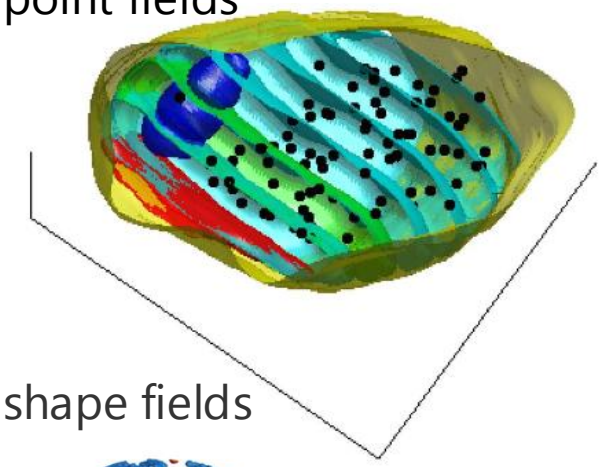


Topological data analysis

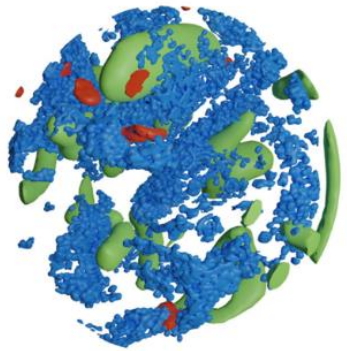


Literature

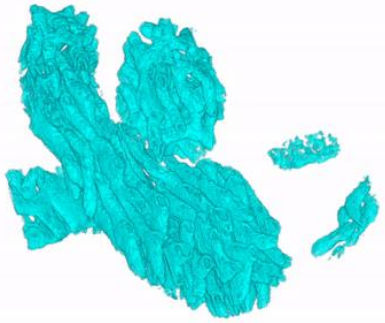
Spatial point fields



Spatial shape fields

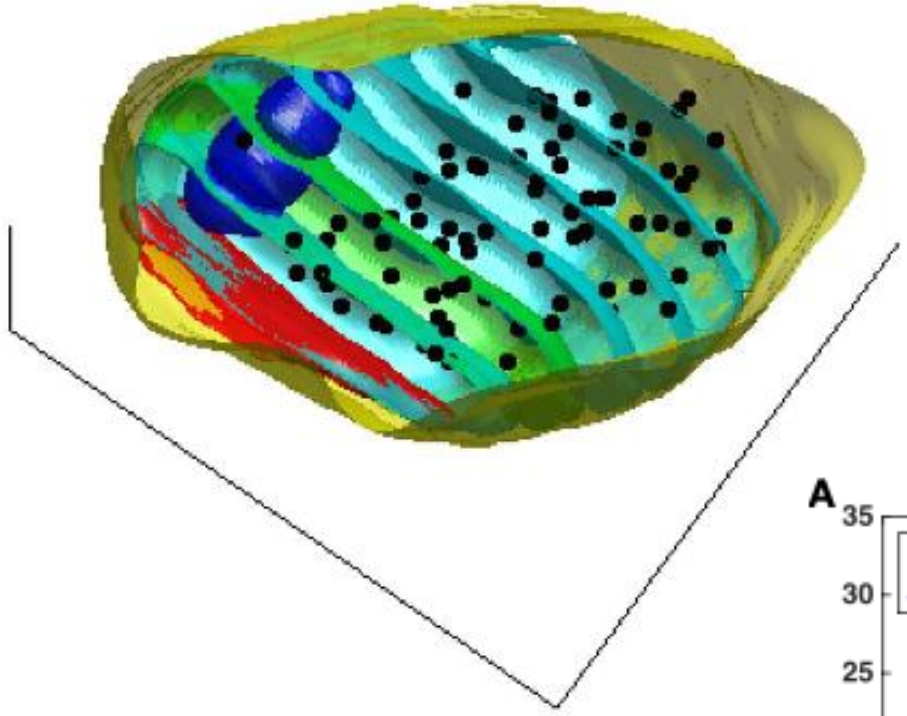


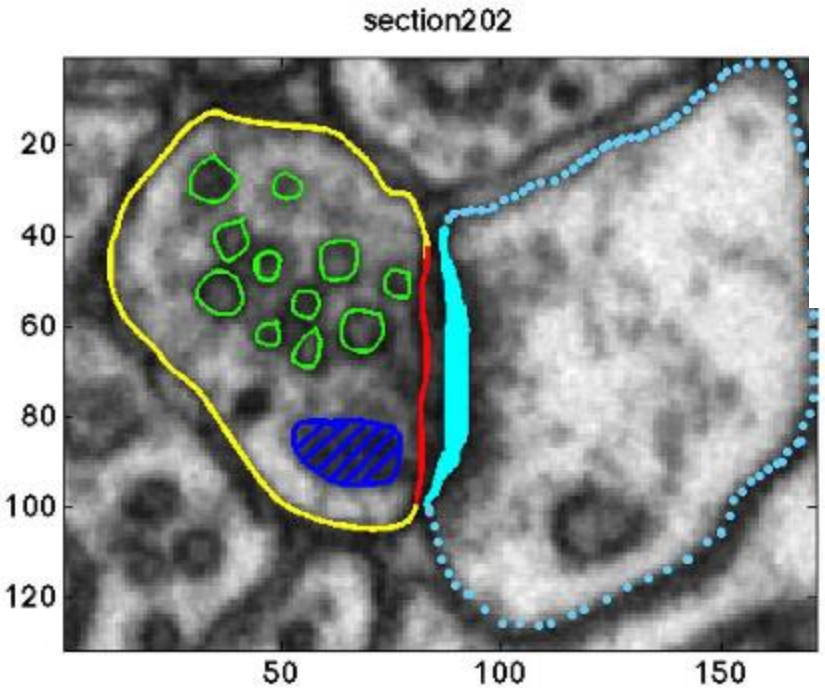
Topological data analysis

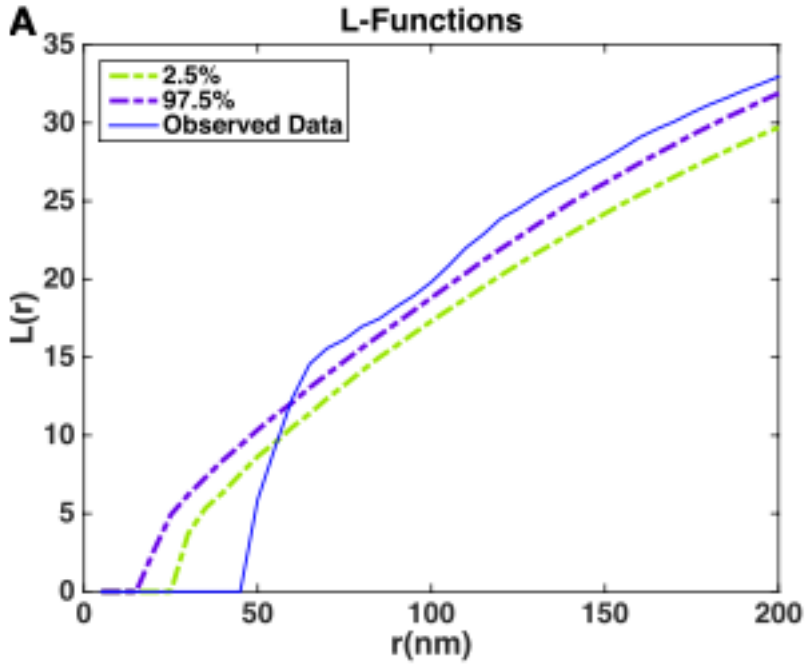


- Analysis of shape and spatial interaction of synaptic vesicles using data from focused ion beam scanning electron microscopy (FIB-SEM); M Khanmohammadi, RP Waagepetersen & J Sporring, Frontiers in Neuroanatomy, 2015
- Stoyan, D. (2006). Fundamentals of Point Process Statistics. In: Baddeley, A. et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





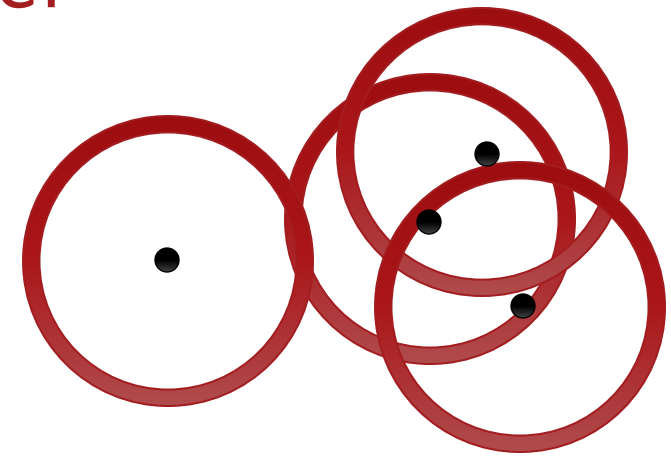


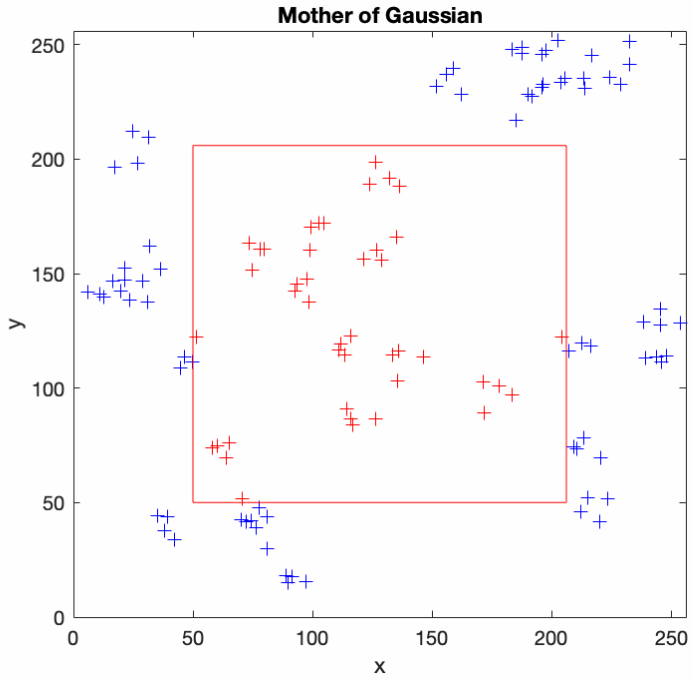
Analysis of shape and spatial interaction of synaptic vesicles using data from focused ion beam scanning electron microscopy (FIB-SEM); M Khanmohammadi, RP Waagepetersen & J Sporring, Frontiers in Neuroanatomy, 2015

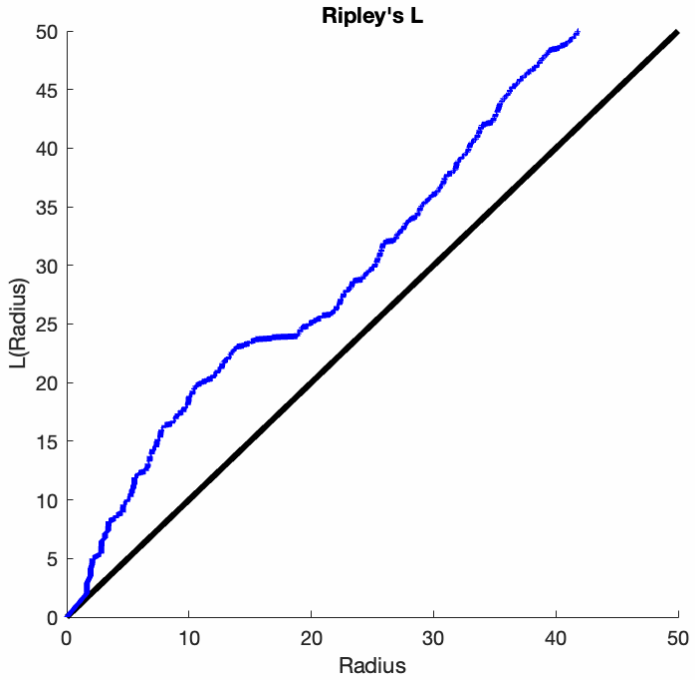
Ripley's K- and L-functions: expected number of neighboring points by radius

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

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

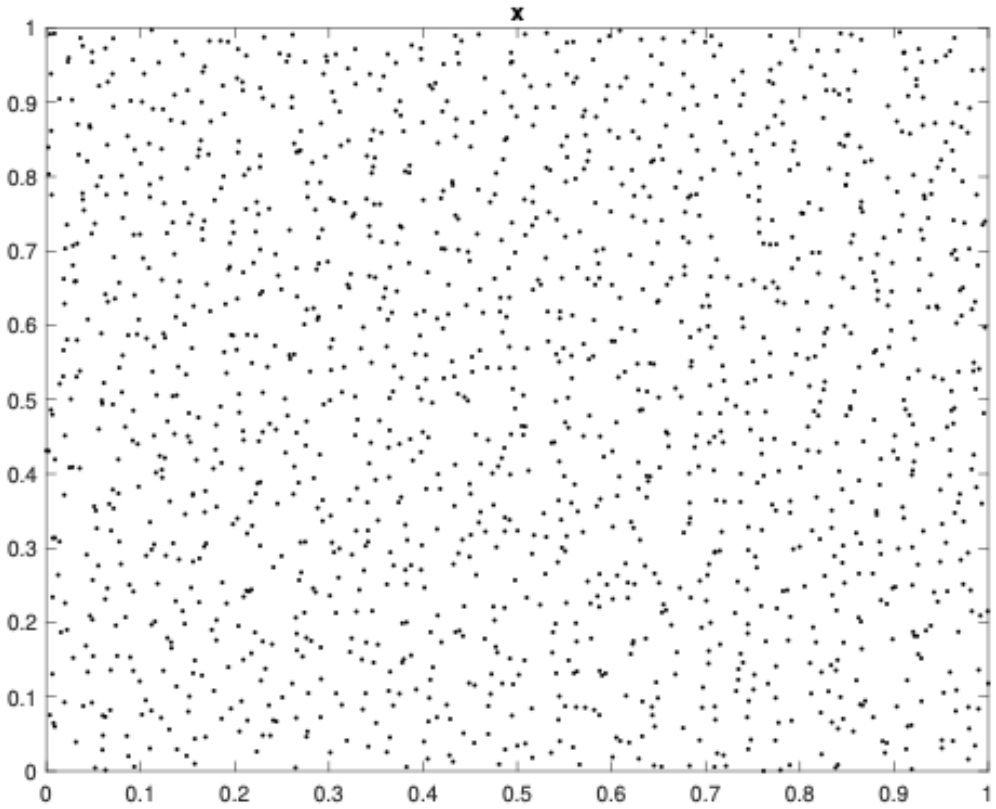


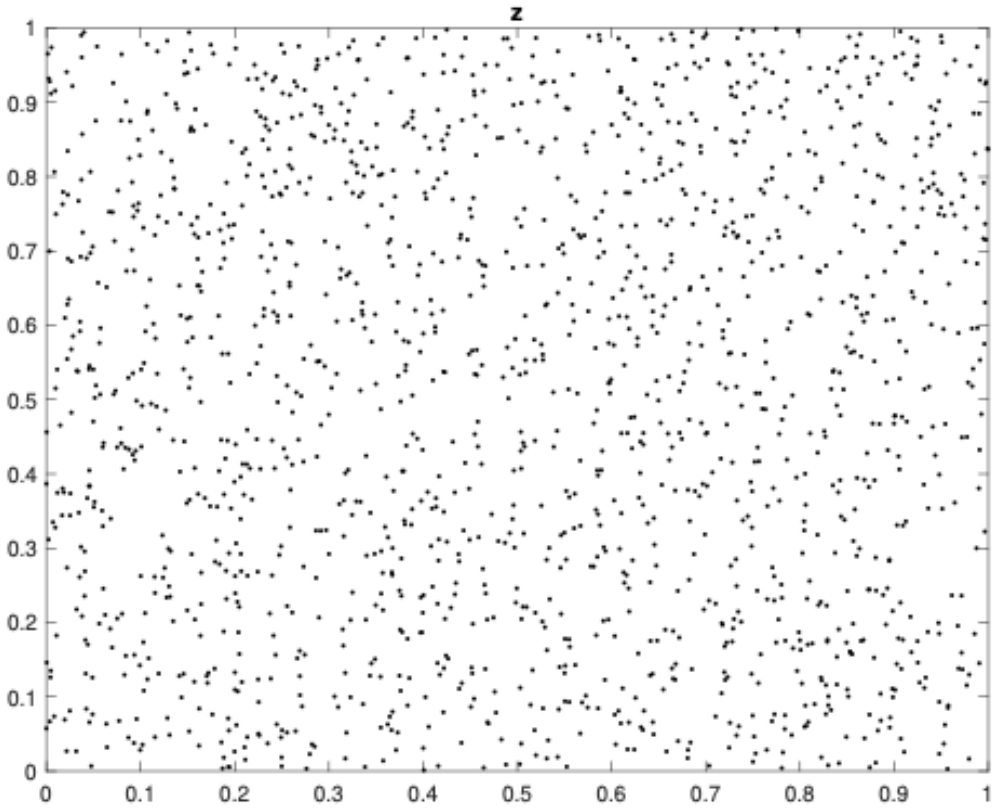




R and rpy2 demo: https://sporring.github.io/bia2024/ demoRpy2.py

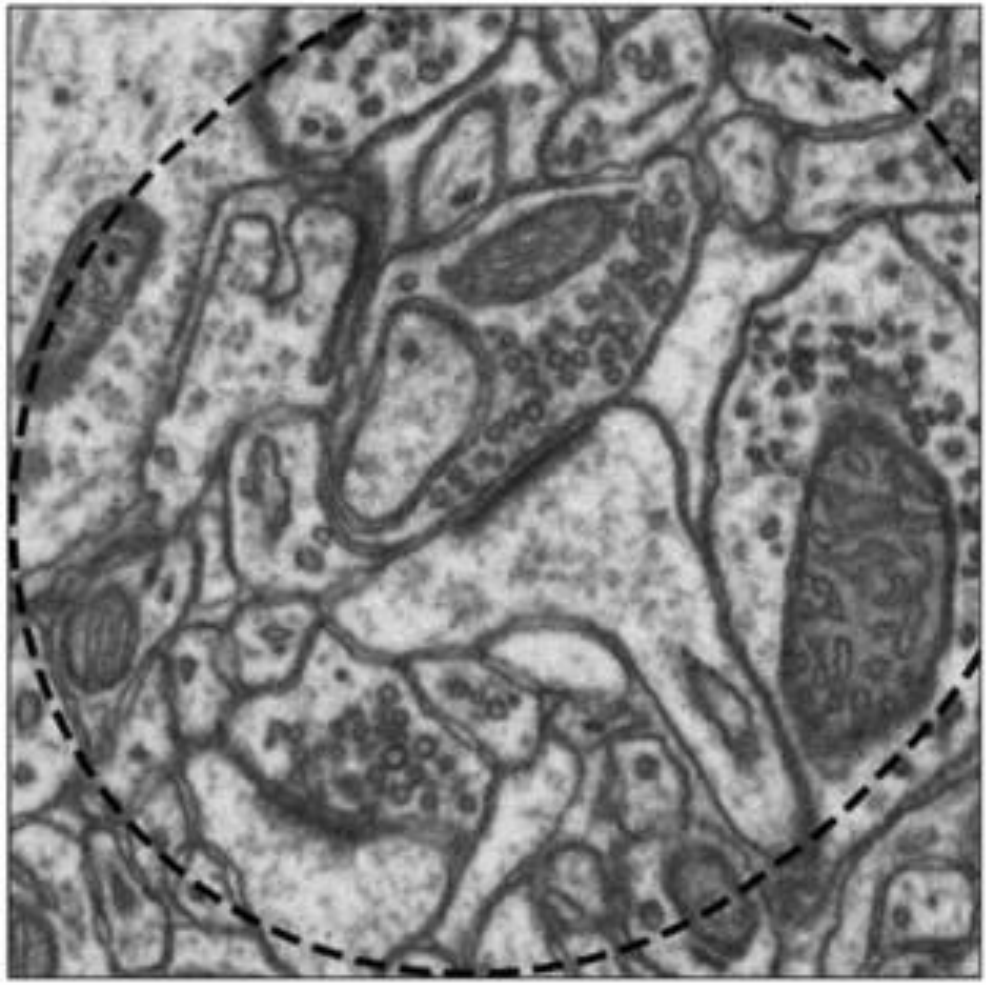
https://cran.r-project.org/
https://spatstat.org/
https://cran.r-project.org/web/packages/GET/vignettes/pointpatterns.pdf



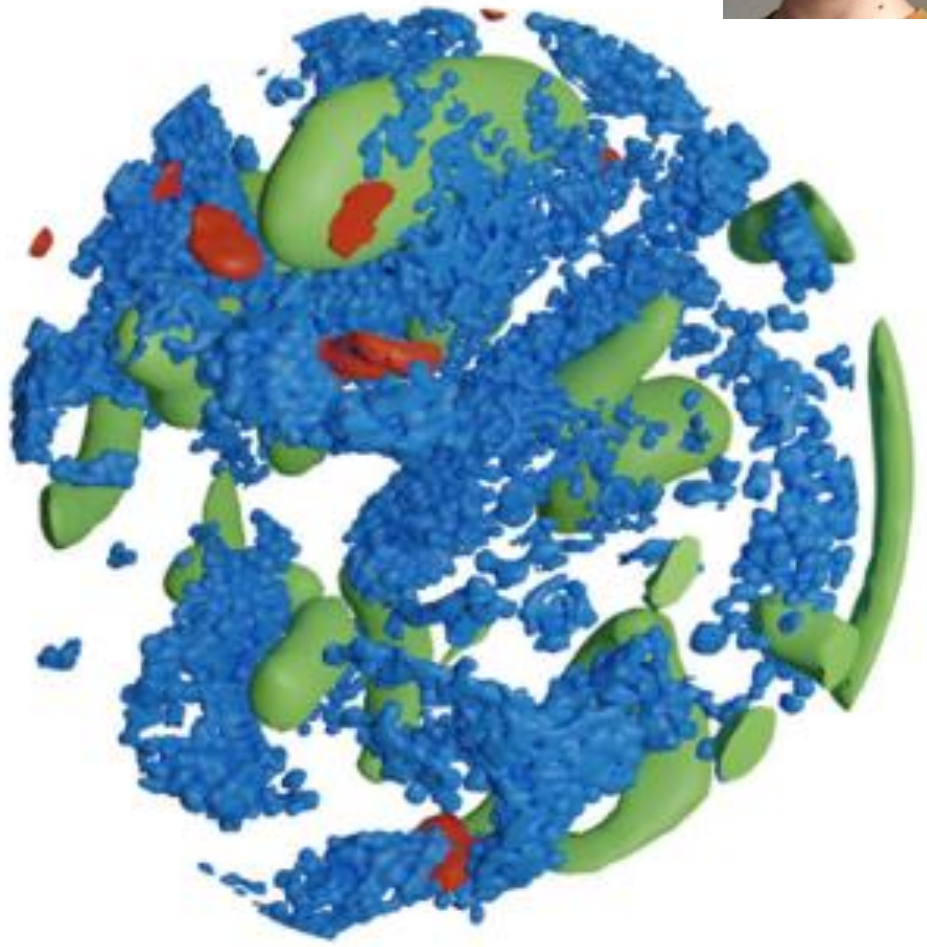


Exercise: Use GET's global_envelope_test to test whether x and/or z are likely to be random

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

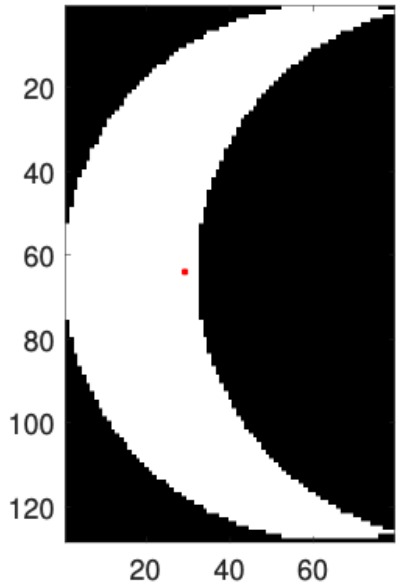


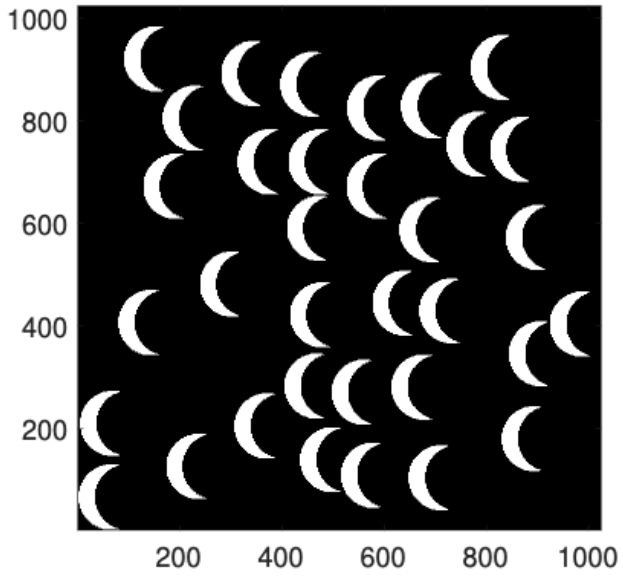
Deep Learning

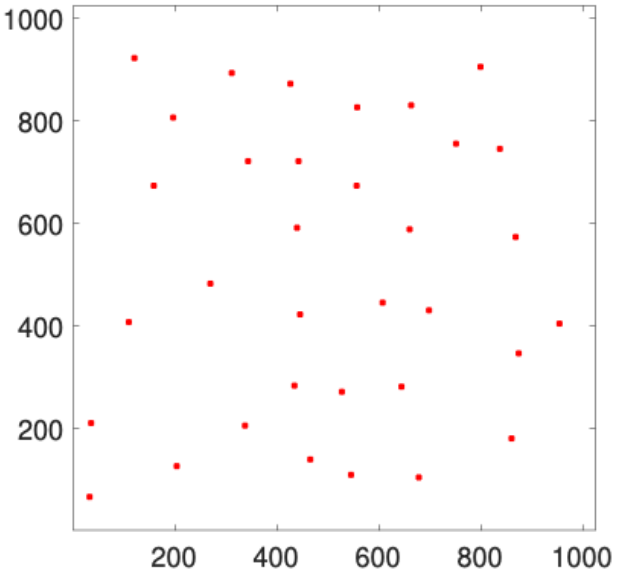


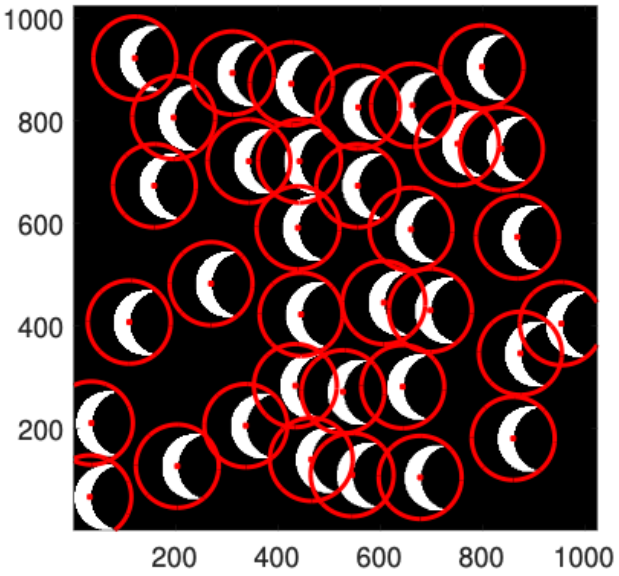
Measuring Shape Relations Using r-Parallel Sets; HJT Stephensen, AM Svane, CB Villanueva, SA Goldman, & J Sporring; Journal of mathematical imaging and vision, 2021

Not all shapes are well summarized as a reference point

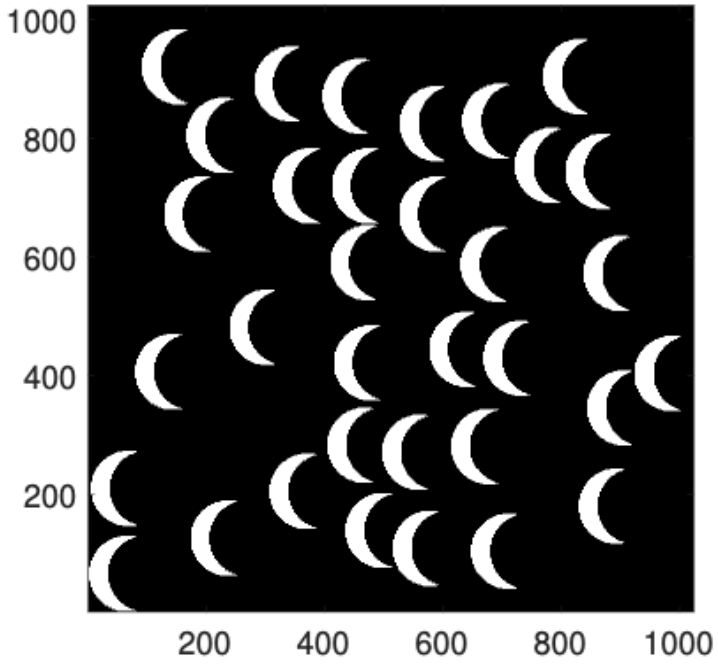


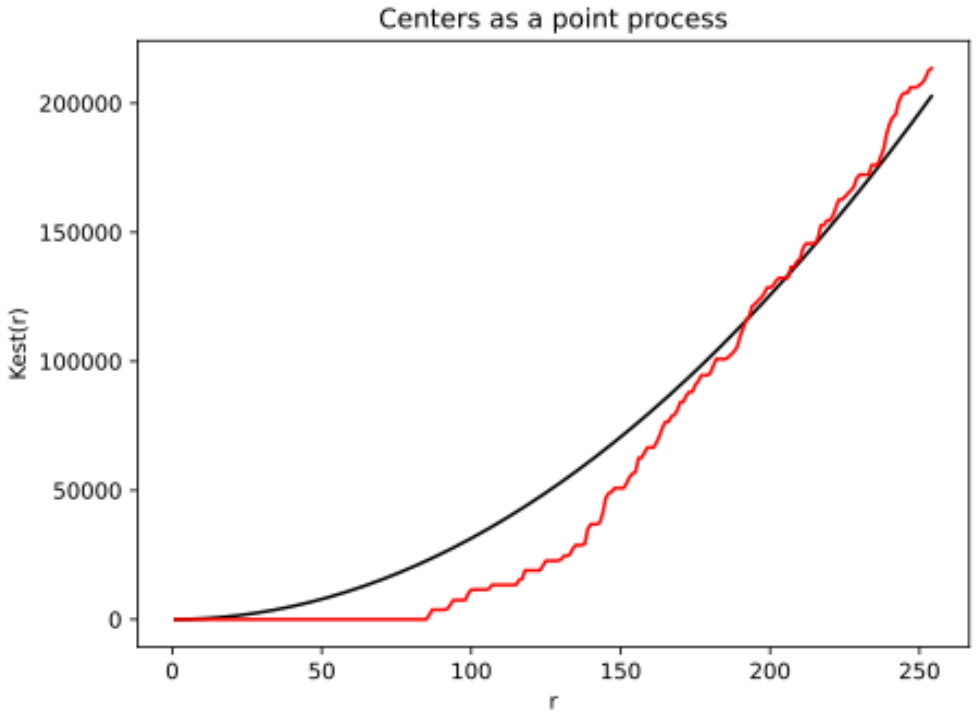


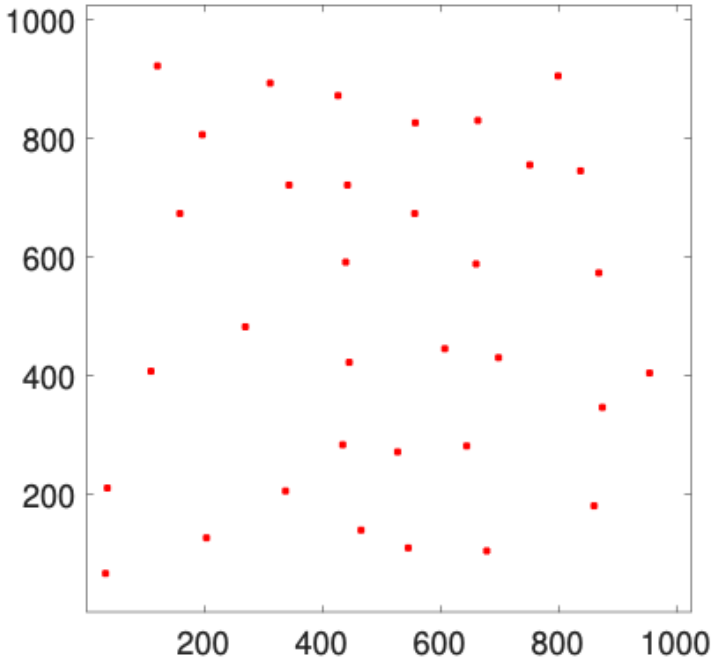




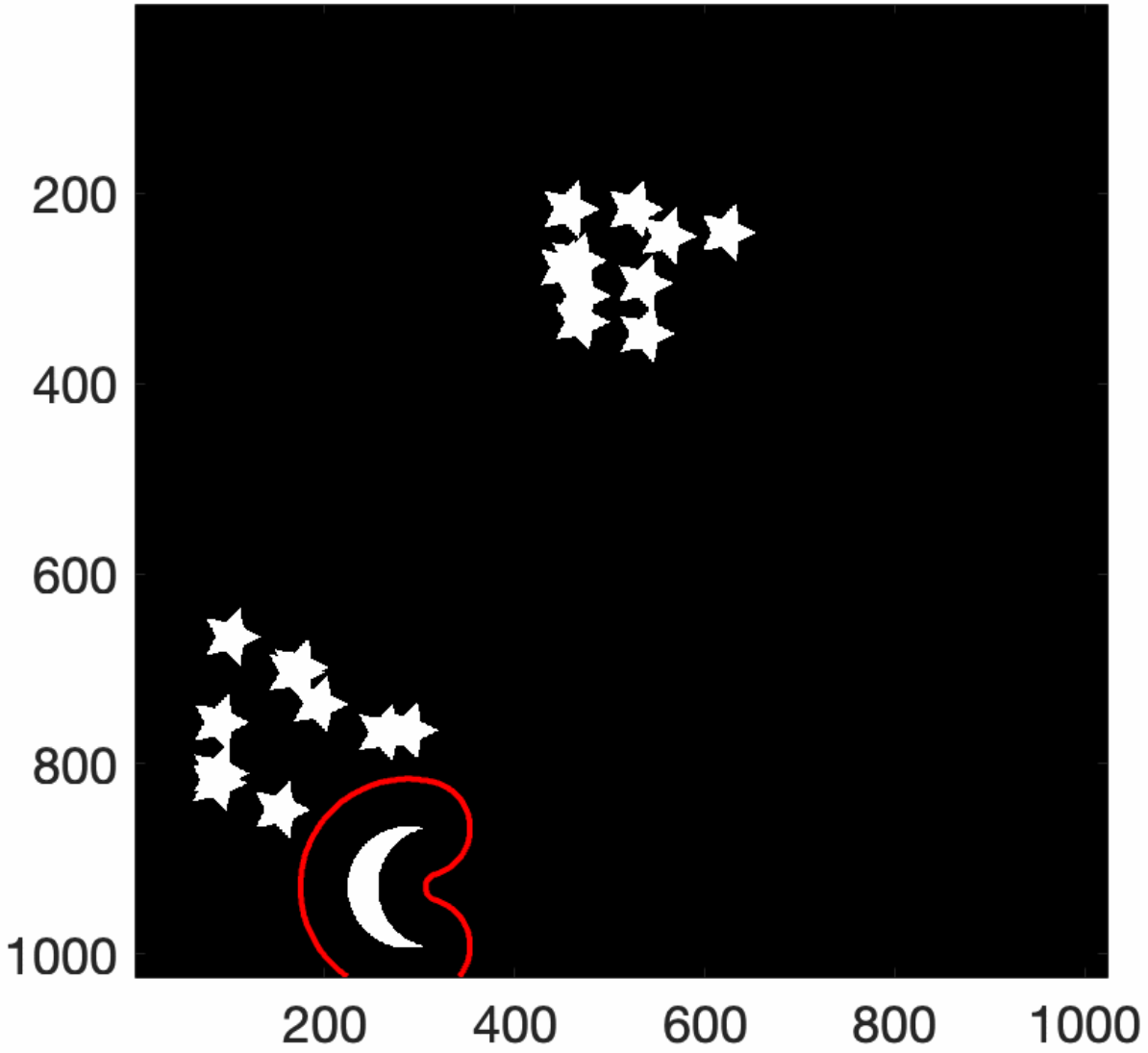
Ripley's K-function indicates strong repulsion



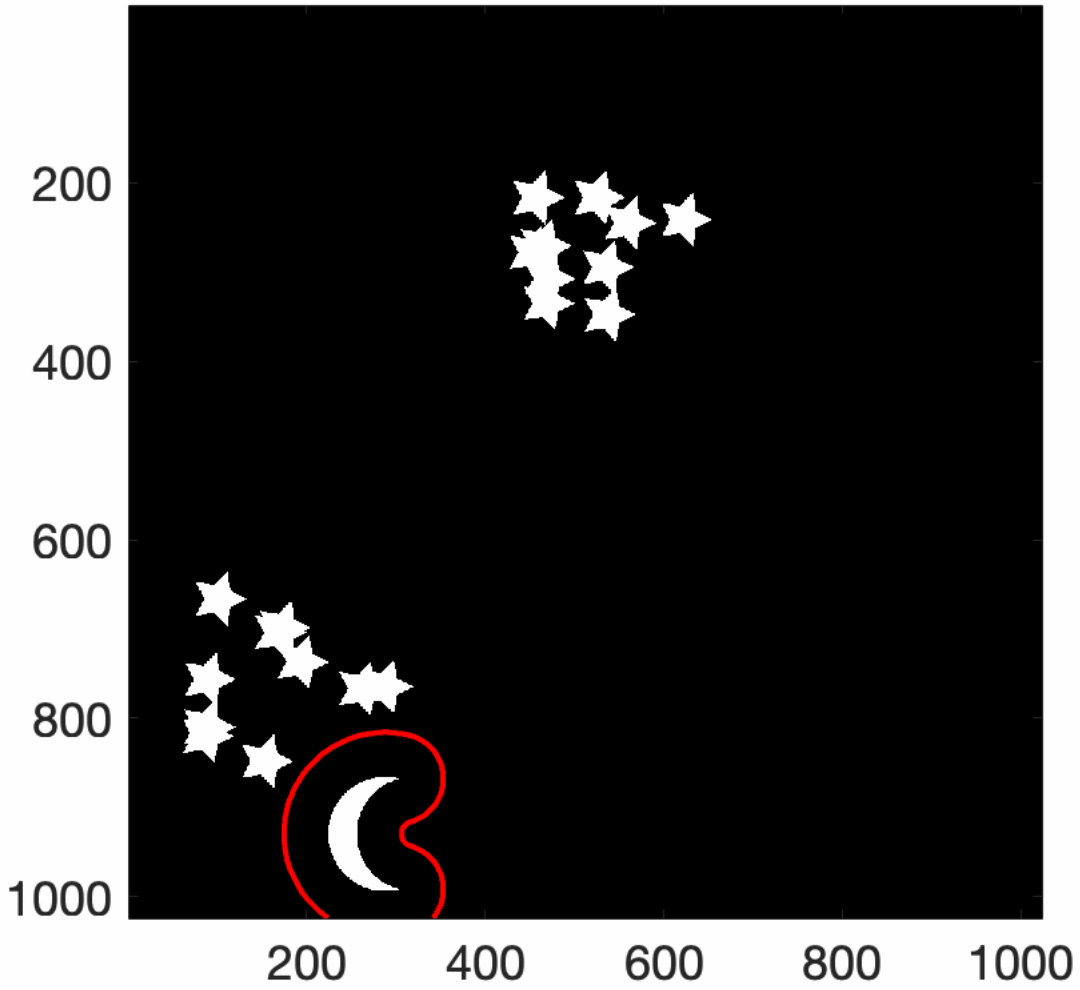


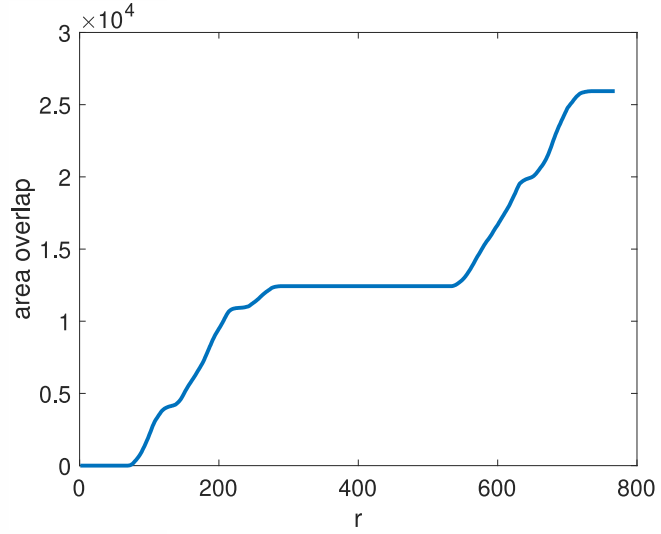


Shape relation measures = Interaction with distance fields



Shape relation measures: Some characteristic functions

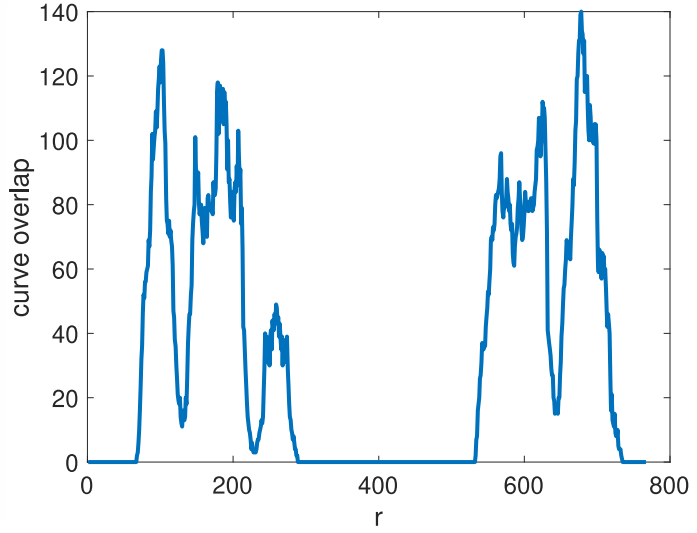


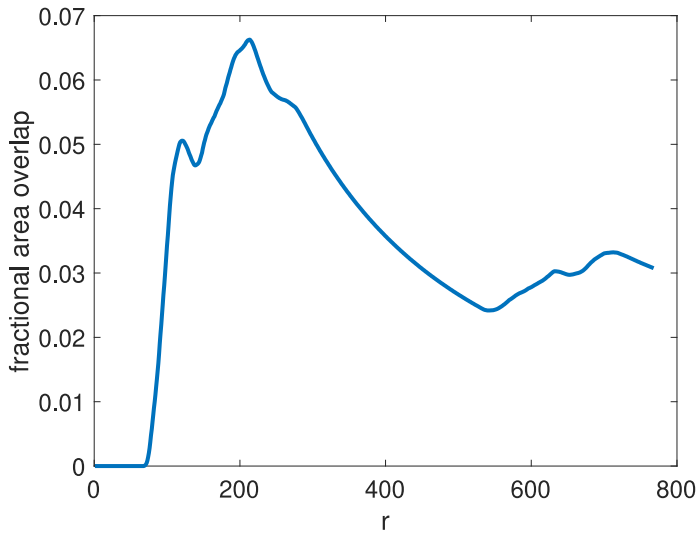


$$\mu_{00}(r) = \mathcal{H}(X \cap Y^r)$$

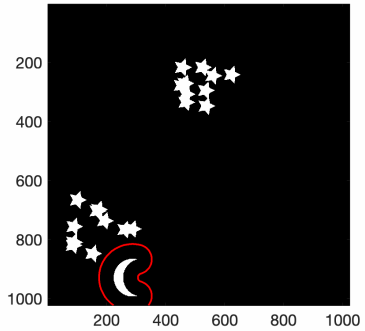
$$g_{00}(r) = \frac{d\mu_{00}(r)}{dr} = \mu_{01}(r)$$

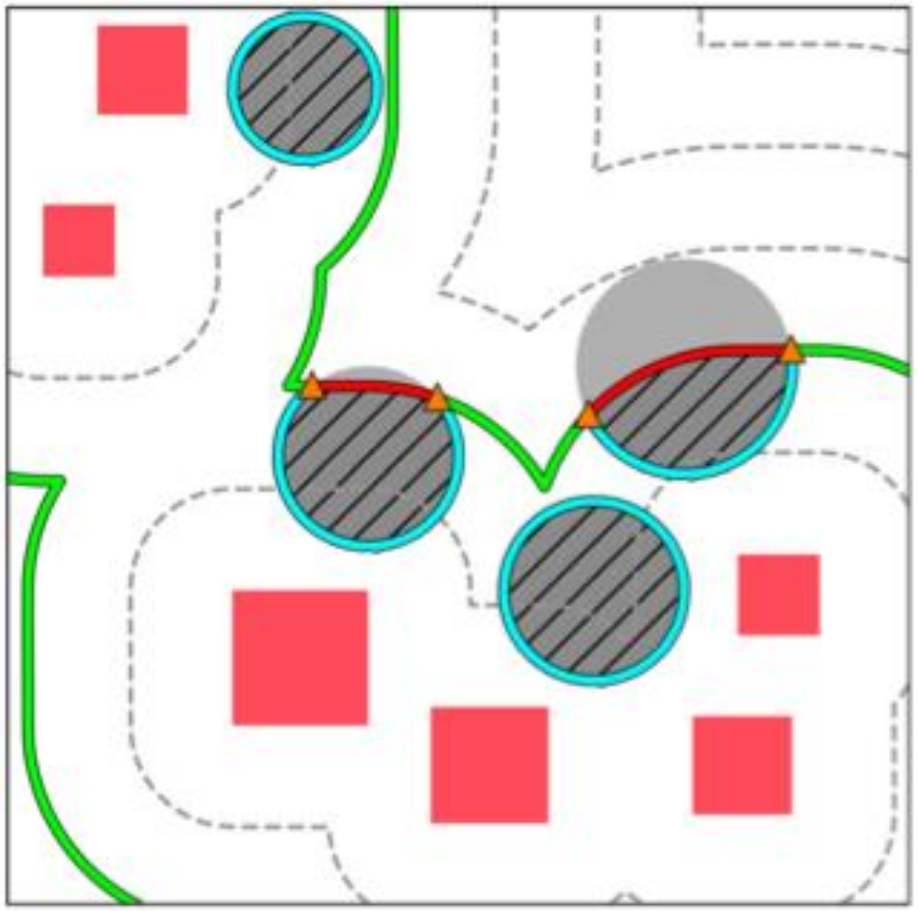
$$f_{00}(r) = \frac{\mu_{00}(r)}{\mathcal{H}(Y^r)}$$





There can be only 4





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

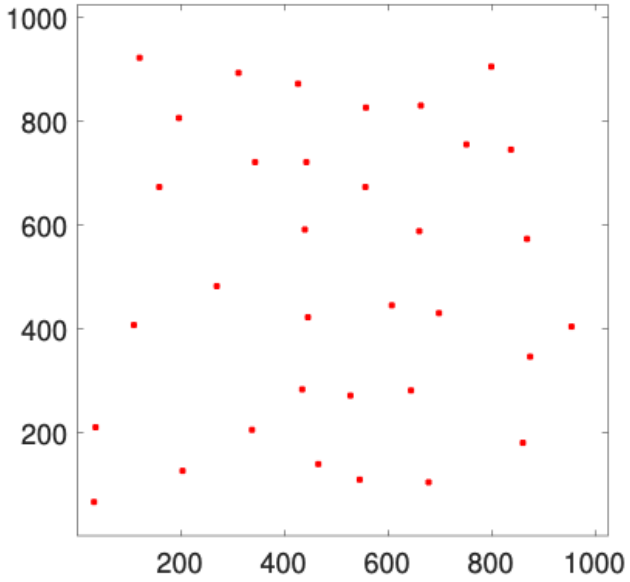
$$\mu_{\varepsilon,\varepsilon'}(X, Y^r) = \mathcal{H}^{d-\varepsilon-\varepsilon'}(\partial^\varepsilon X \cap \partial^{\varepsilon'} Y^r) \ . \quad (2)$$

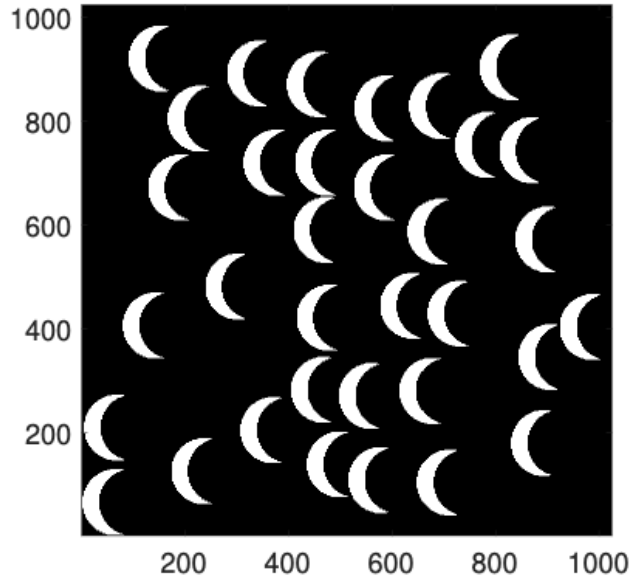
$d=2$	$(\varepsilon,\varepsilon')$	$\mathcal{H}^{d-\varepsilon-\varepsilon'}$	$\partial^\varepsilon X \cap \partial^{\varepsilon'} Y^r$	Interpretation of $\mu_{\varepsilon,\varepsilon'}(X,Y^r)$
	$(0,0)$	Area	$X \cap Y^r$	Area of intersection
	$(0,1)$	Curve length	$X \cap \partial Y^r$	Boundary length 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

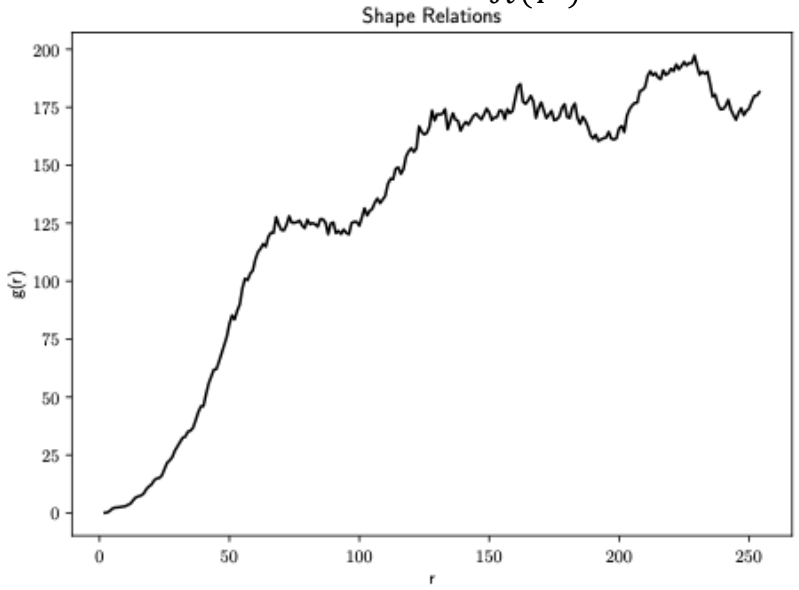
https://lab.compute.dtu.dk/QIM/tools/relationalshapemeasure

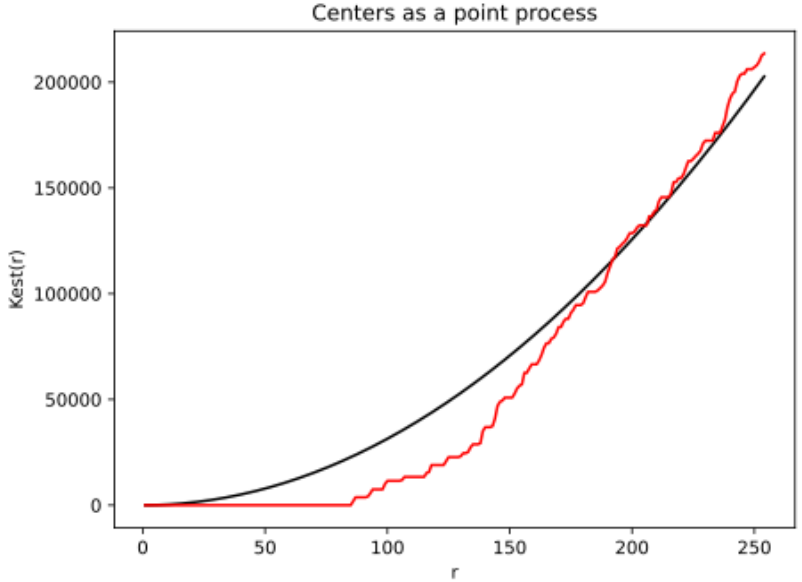
Spatial point fields vs. shape fields

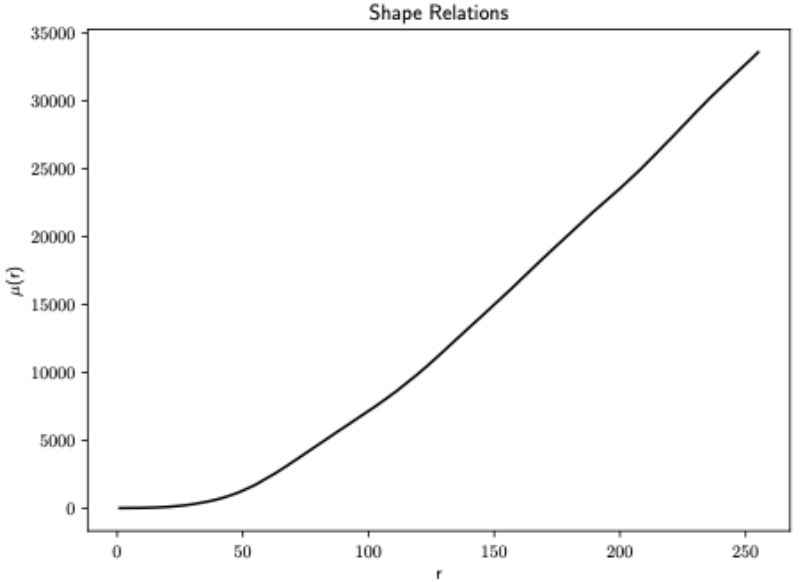
$$\mu_{00}(r) = \mathcal{H}(X \cap Y^r)$$
$$g_{00}(r) = \frac{d\mu_{00}(r)}{dr} = \mu_{01}(r)$$
$$f_{00}(r) = \frac{\mu_{00}(r)}{\mathcal{H}(Y^r)}$$

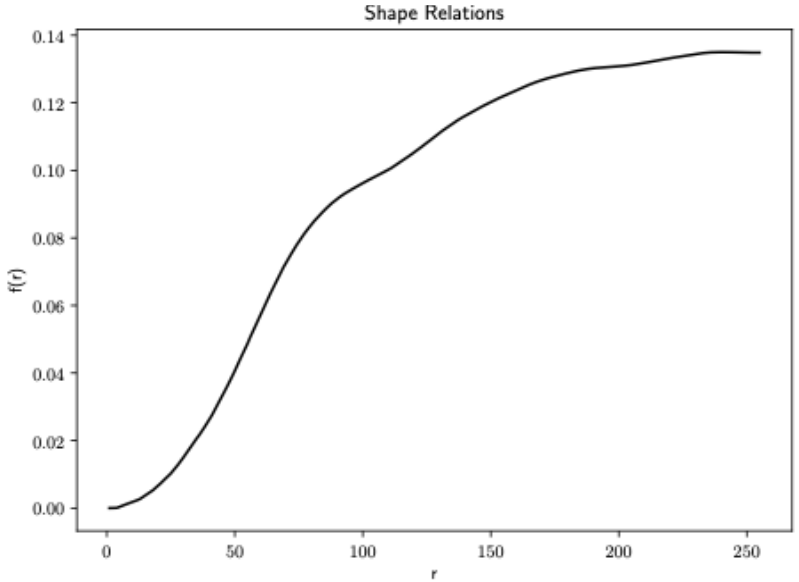




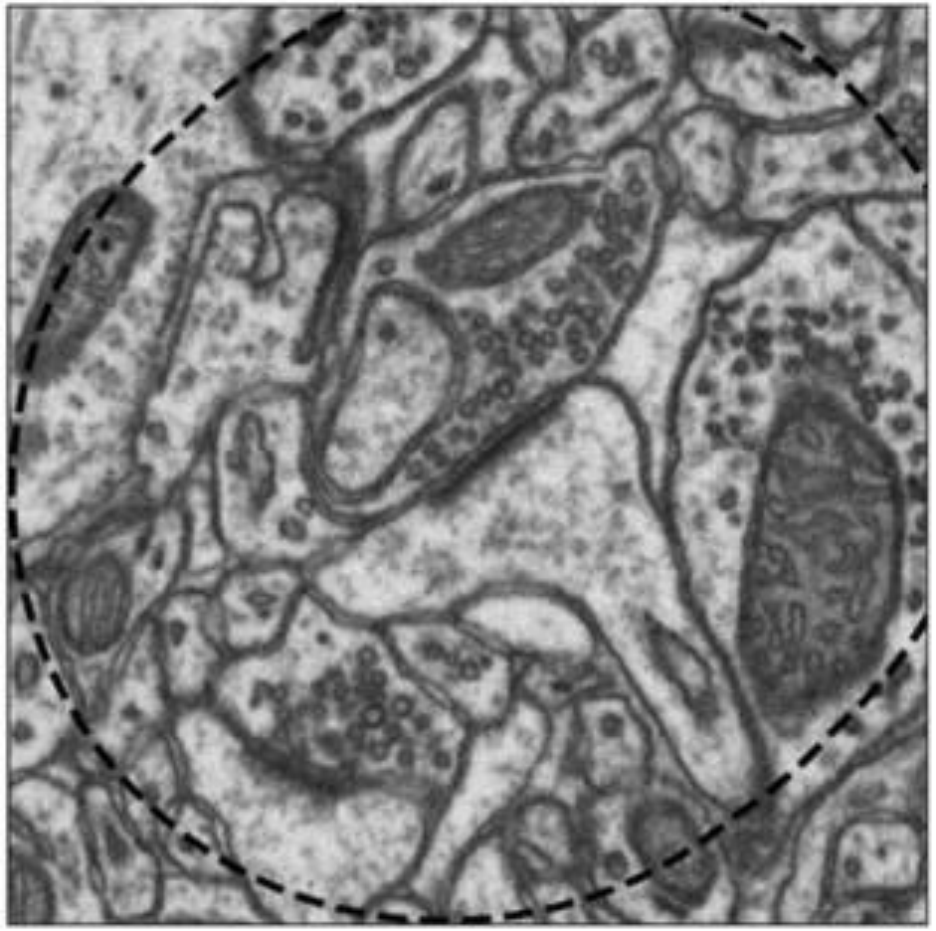




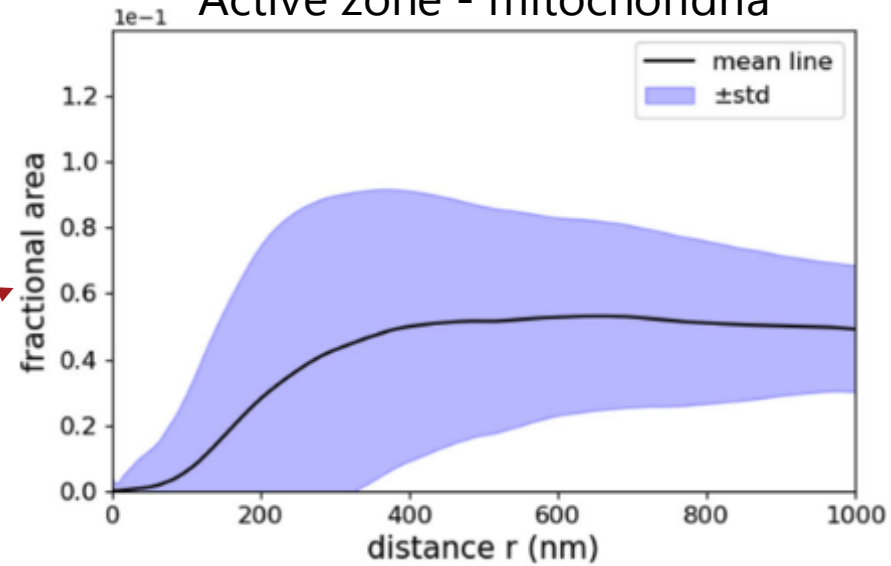




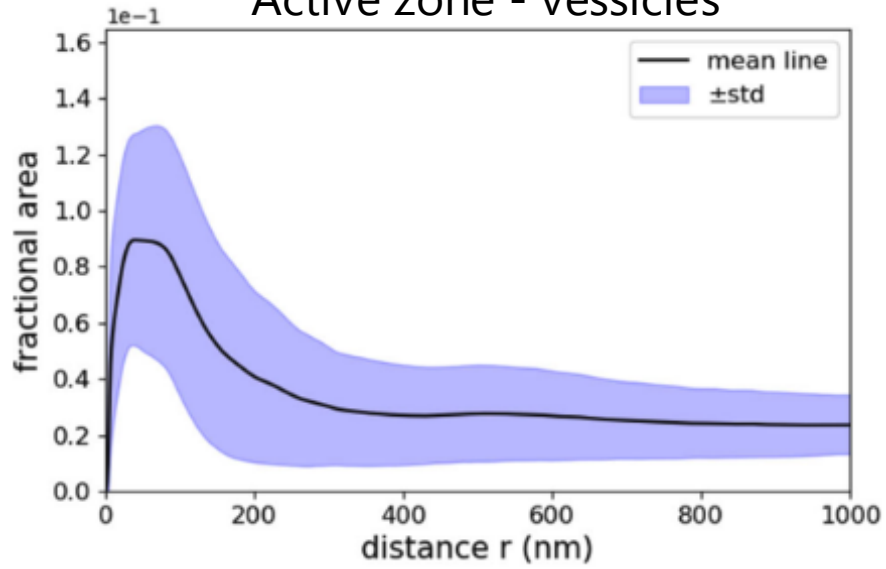
Shape relations for statistical summary of families of shapes and their relations



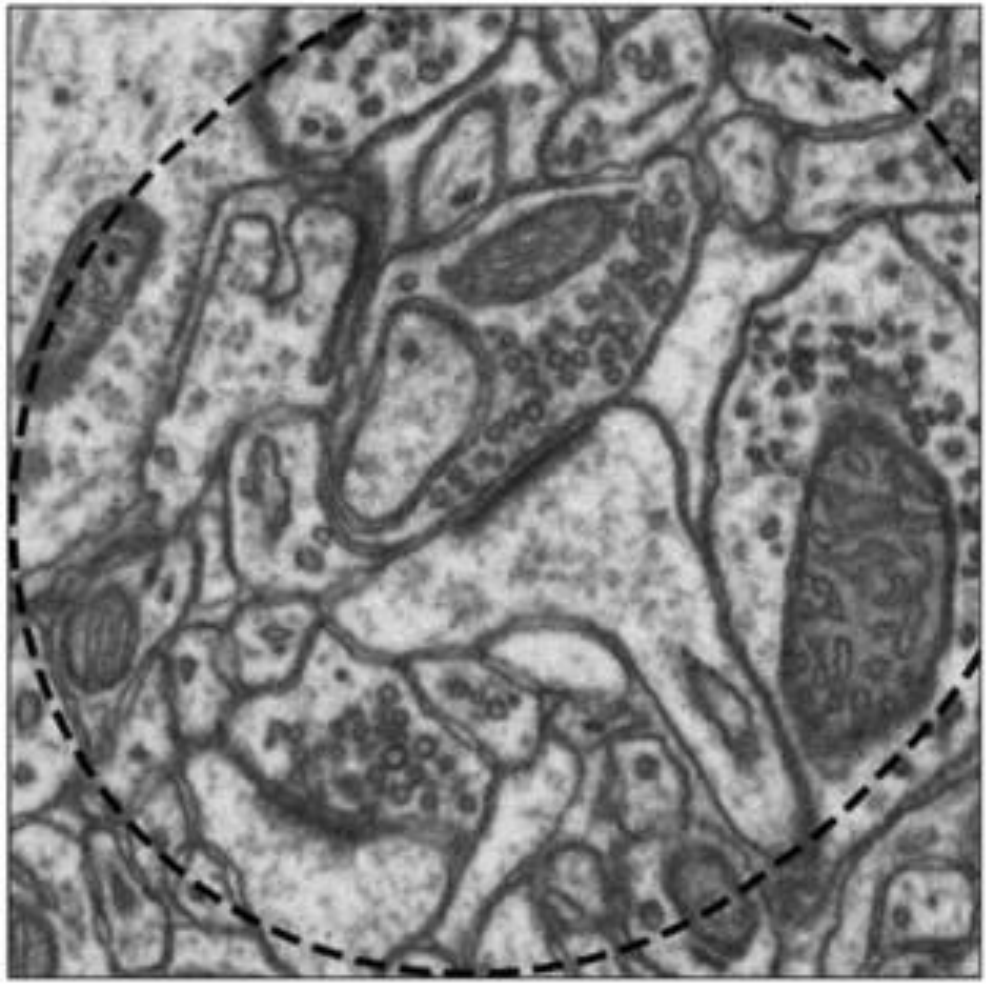
Active zone - mitochondria



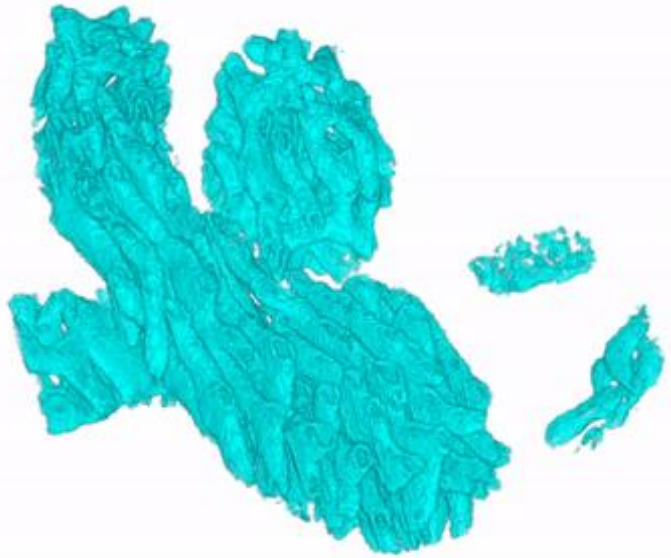
Active zone - vessicles



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



Deep Learning

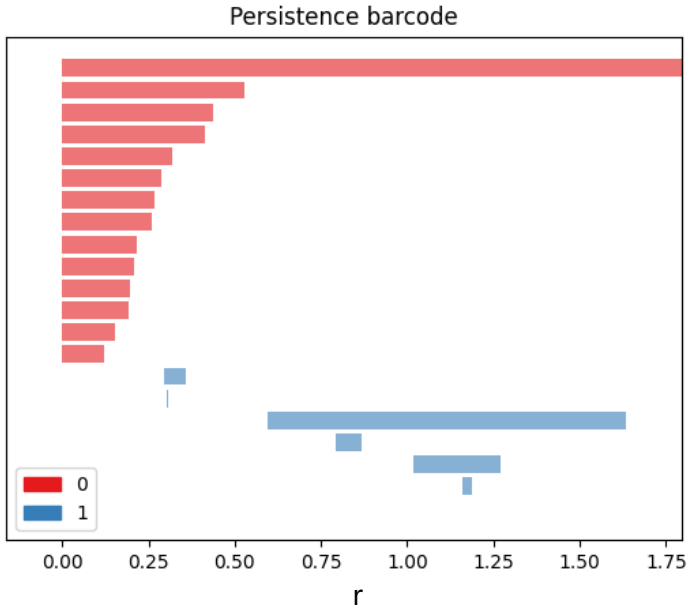


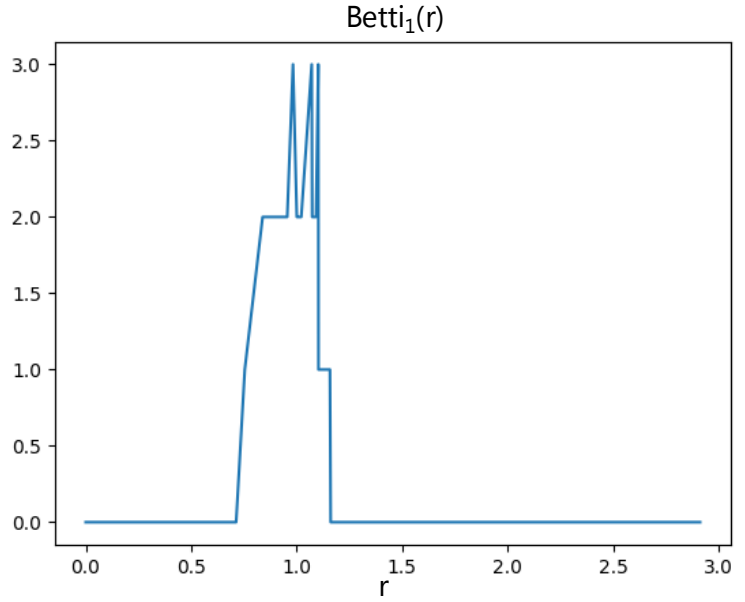
Extracting Mitochondrial Cristae Characteristics from 3D Focused Ion Beam Scanning Electron Microscopy Data, C Wang, L Østergaard, S Hasselholt, & J Sporring, to appear in Communications Biology, 2024

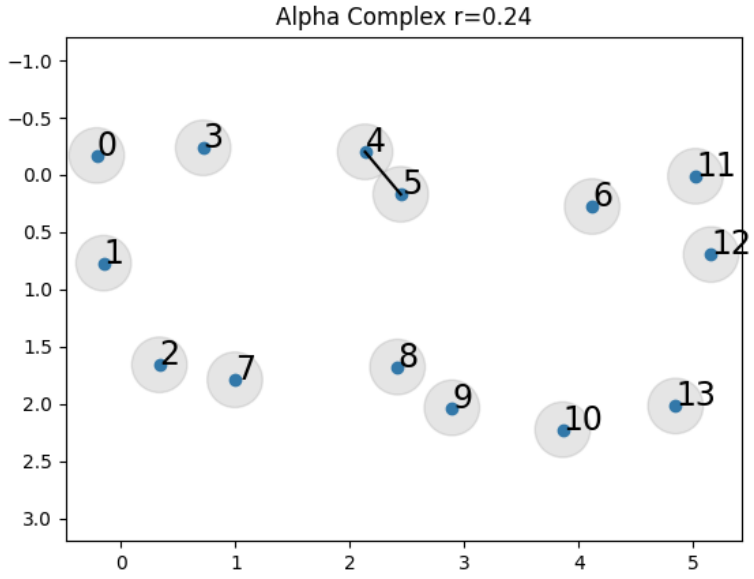
Persistent homology and friends

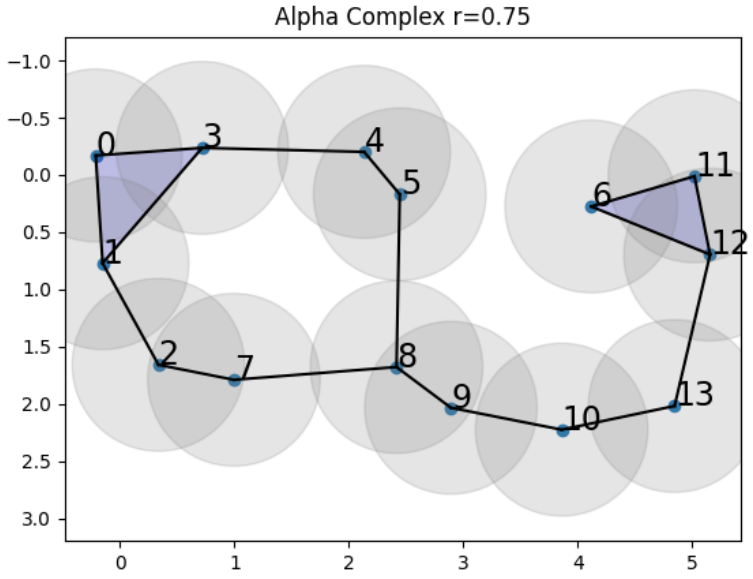
Simplex $\sigma = [x_0, x_1, \ldots x_k]$ is in the alpha complex if

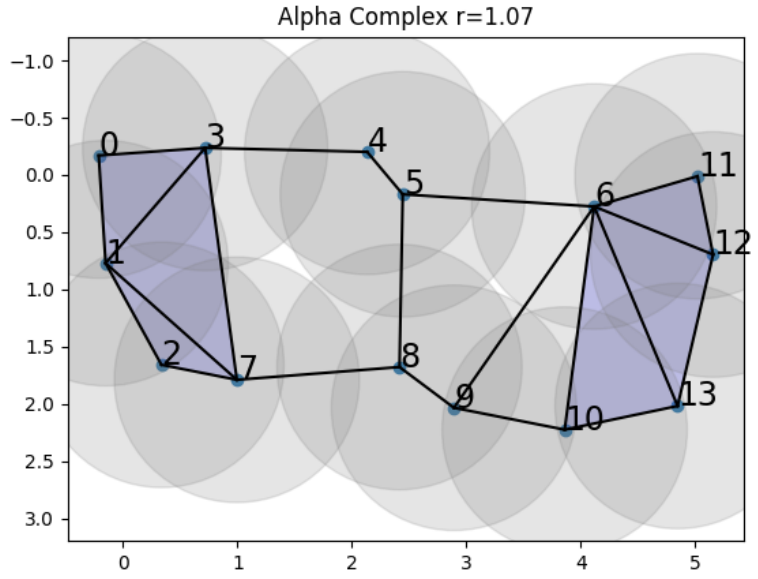
$$\bigcap_{x_i \in \sigma} B(x_i, r) \neq \emptyset$$



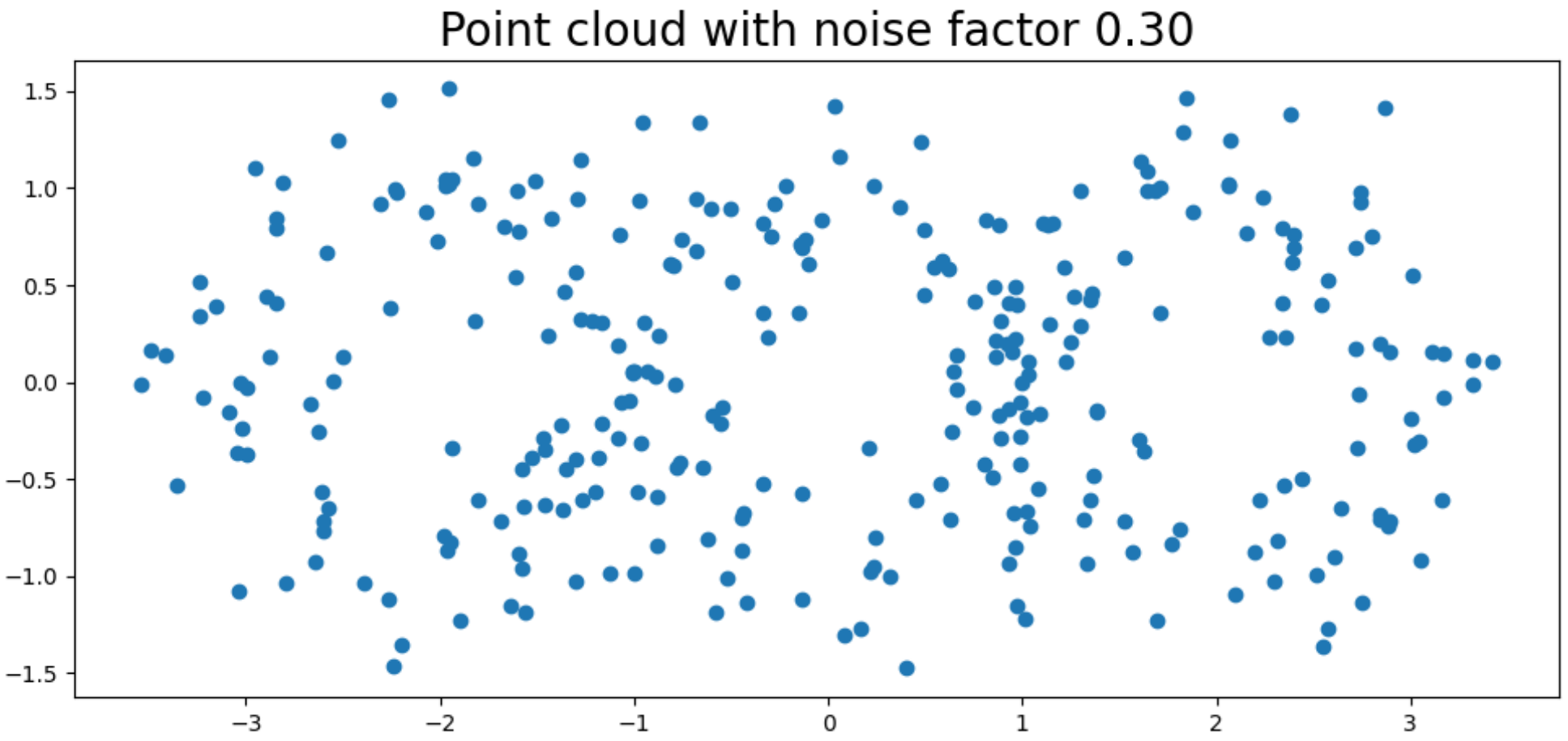






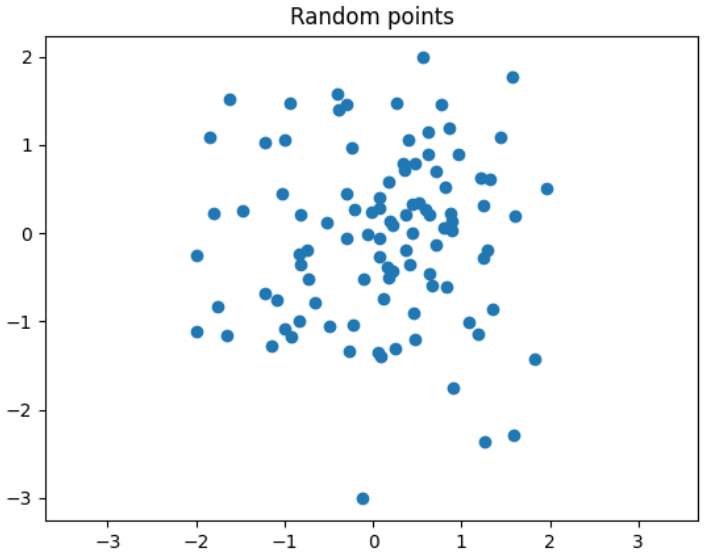


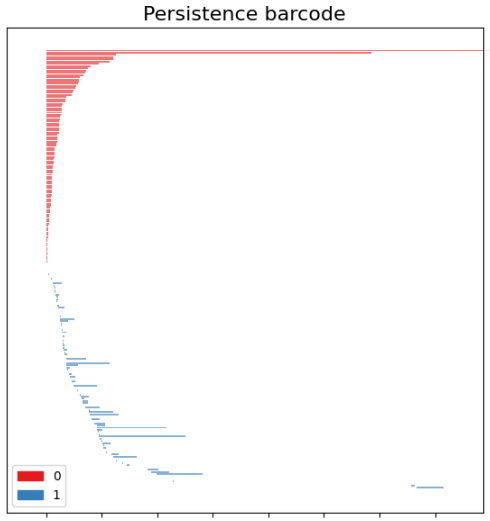
Persistence under noise: $\mathrm{dgm} = \mathrm{dgm}^{\mathrm{Signal}} \cup \mathrm{dgm}^{\mathrm{Noise}}$

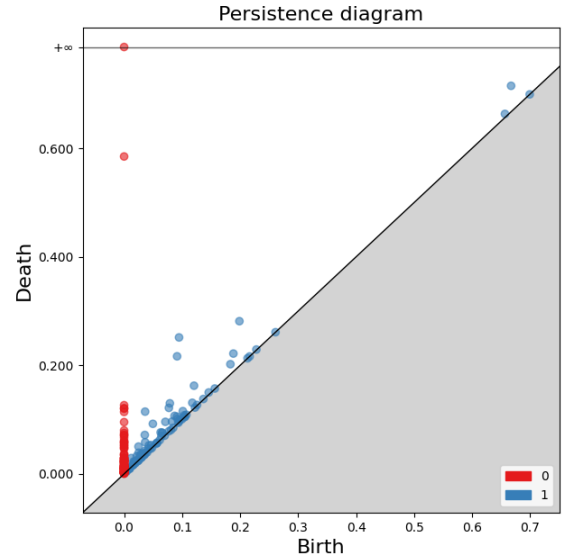


Pure noise

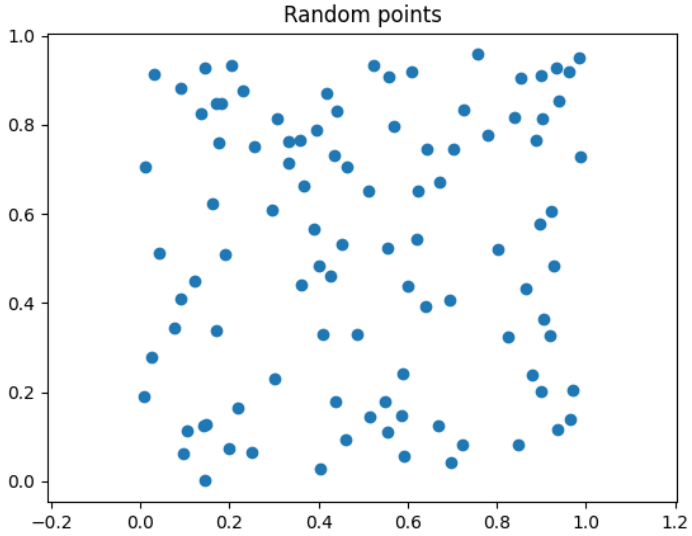
Normal

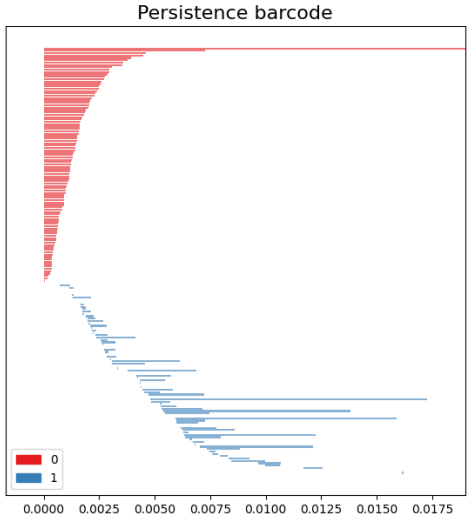


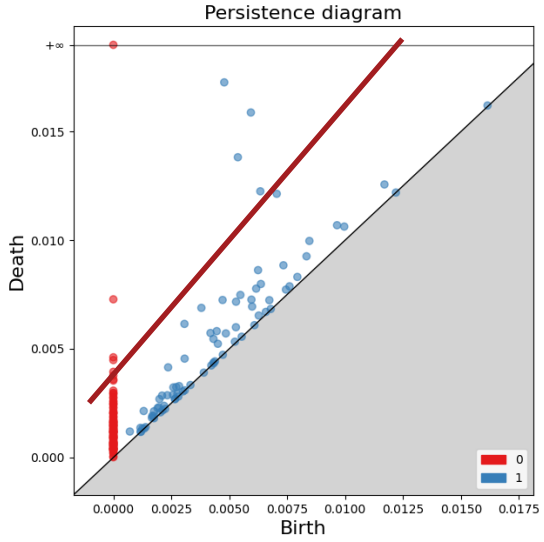




Uniform







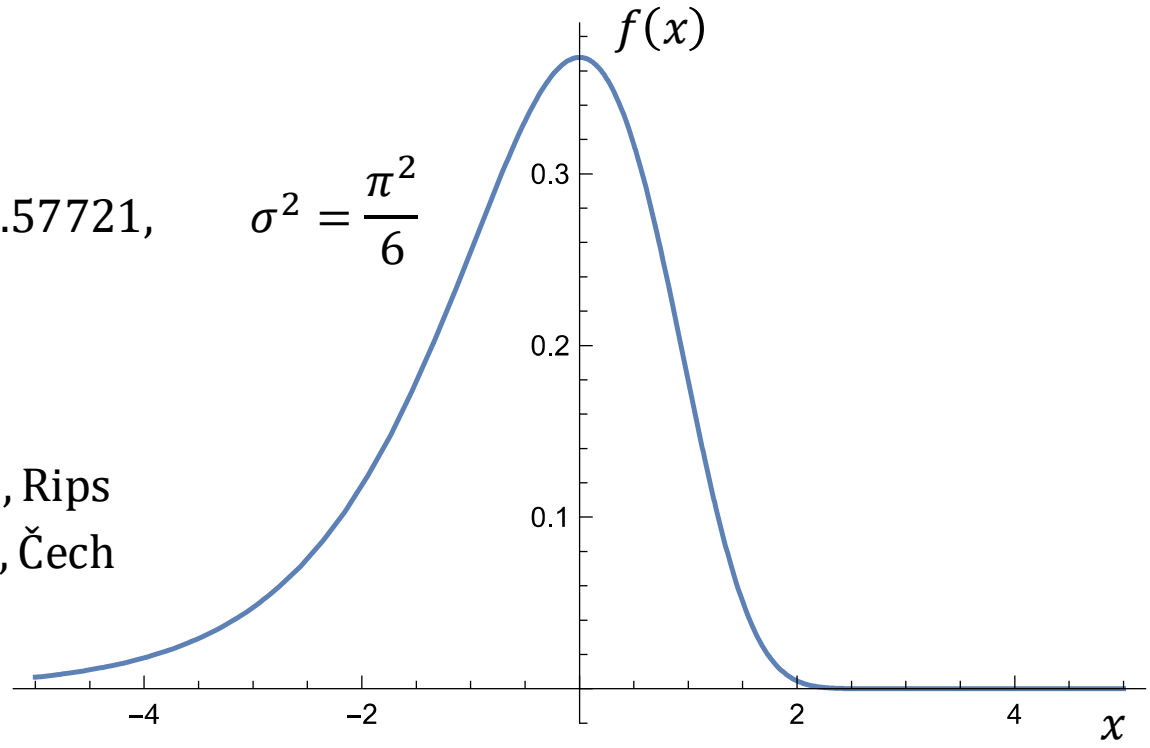
Bobrowski & Skraba, "A universal null-distribution for topological data analysis", Nature/Scientific Reports, 2023

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:

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

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

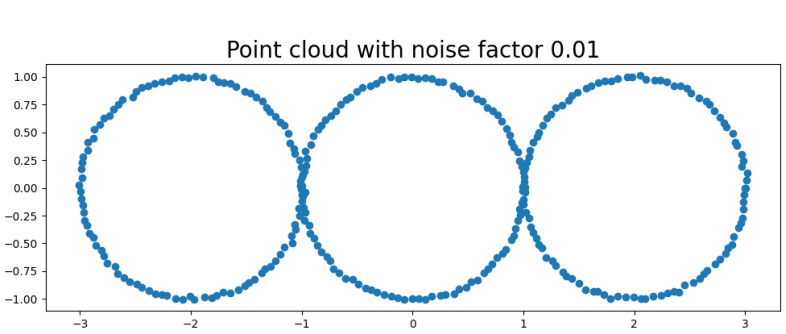
Bonferroni testing (family-wise error rate $< \alpha$):

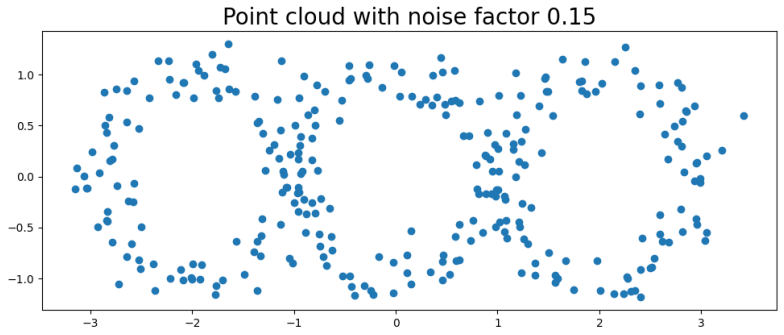
$$P(x \geq x_0 | x \text{ is noise}) = 1 - F(x) = e^{-e^{x_0}}$$

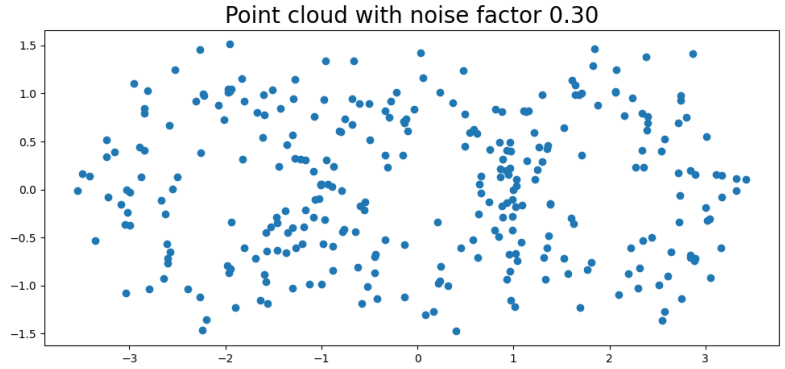
$$\mathrm{dgm}_k^{\text{Signal}}(\alpha) = \left\{ p \in \mathrm{dgm}_k \colon e^{-e^x} < \frac{\alpha}{|\mathrm{dgm}_k|} \right\}$$

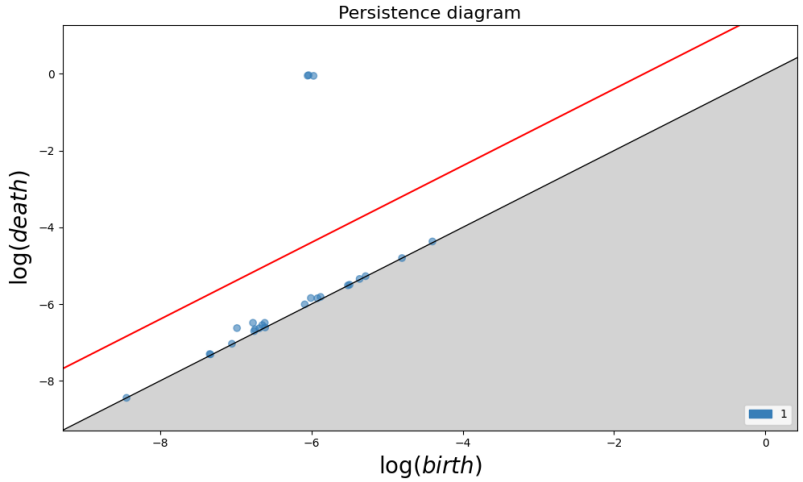
$$e^{\rho} = \ln\frac{r_{\text{death}}}{r_{\text{birth}}} = (-1)^{\beta} e^{\beta\gamma + \bar{\rho}} \left(\ln\frac{\alpha}{|\mathrm{dgm}_k|}\right)^{\beta}$$

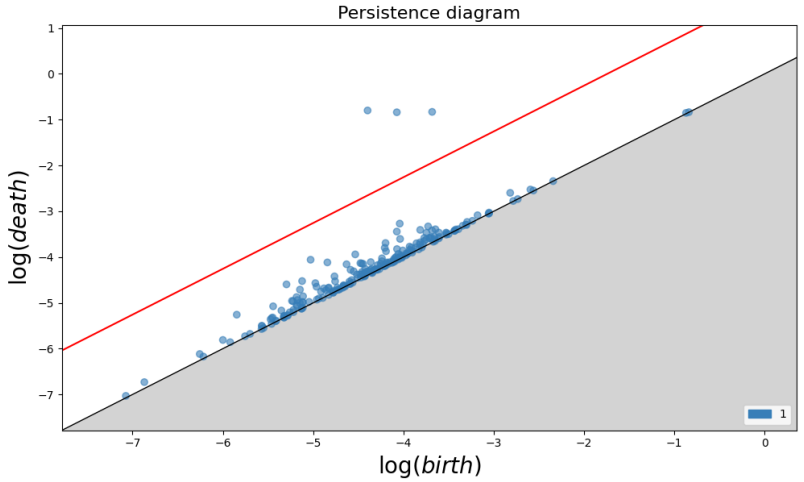
The universal distribution can separate very noisy cases

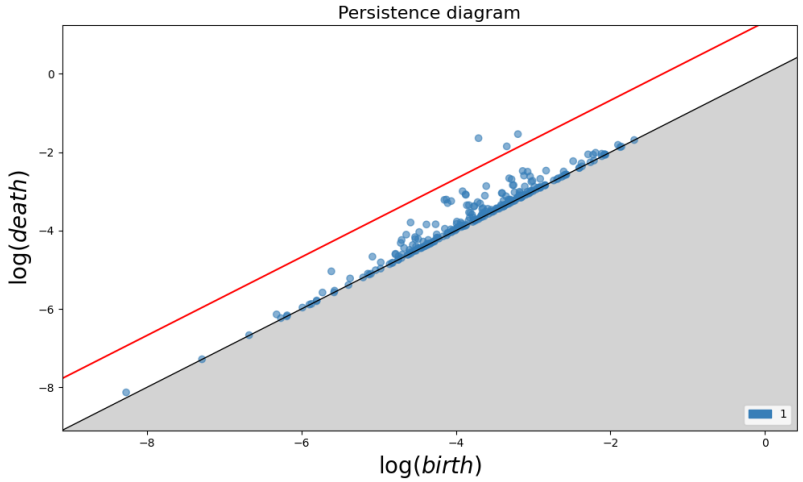




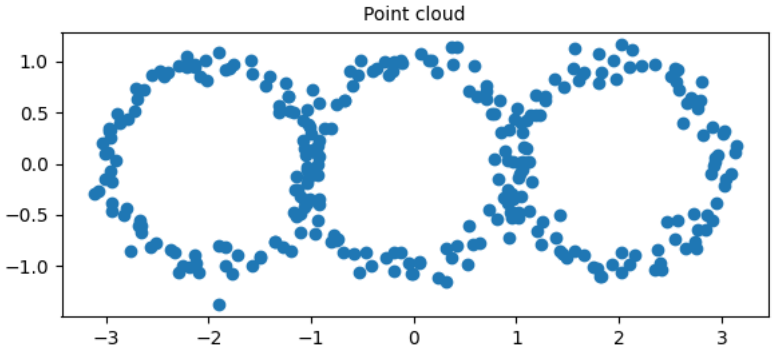


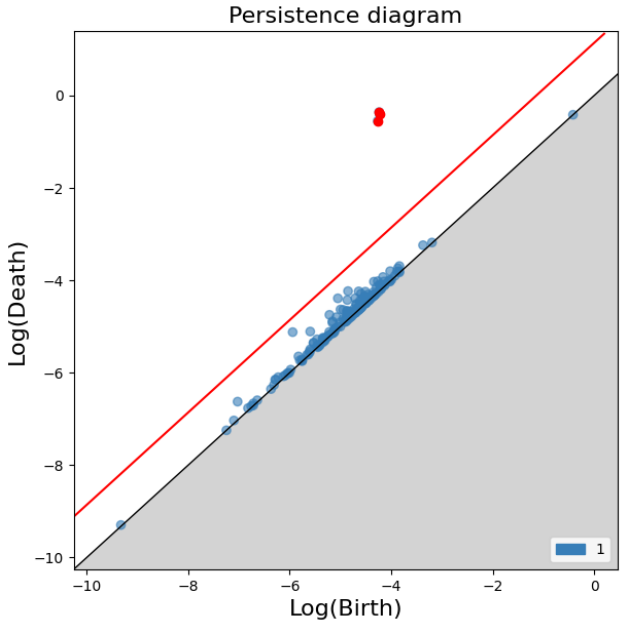


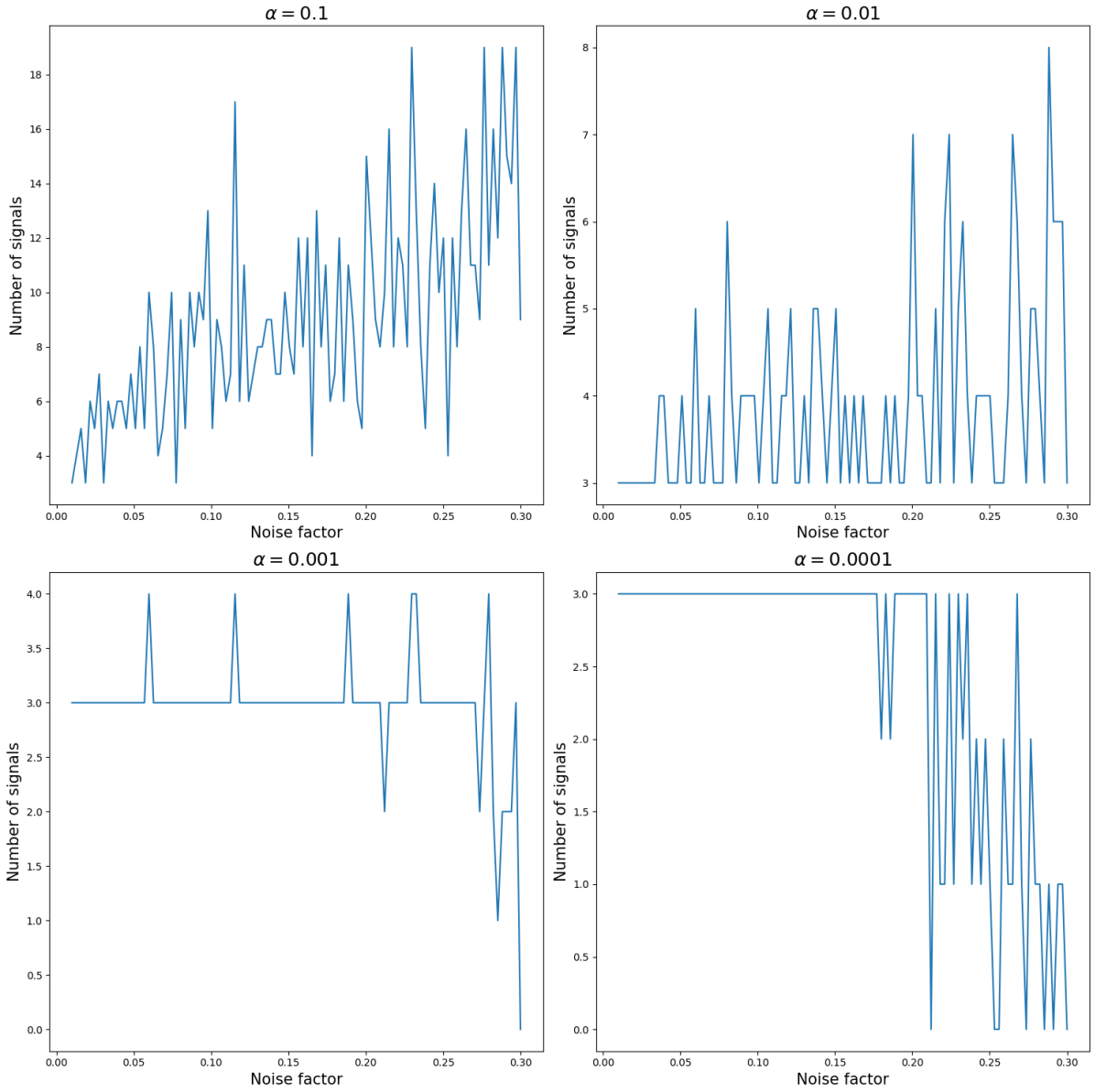




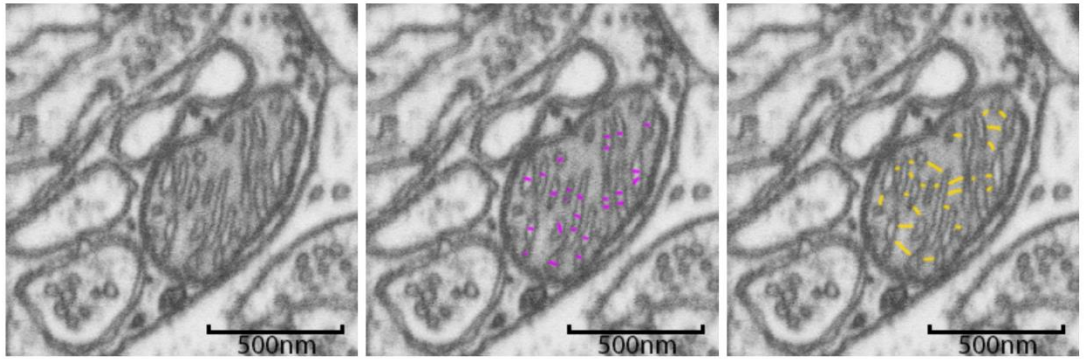
Family-wise error rate



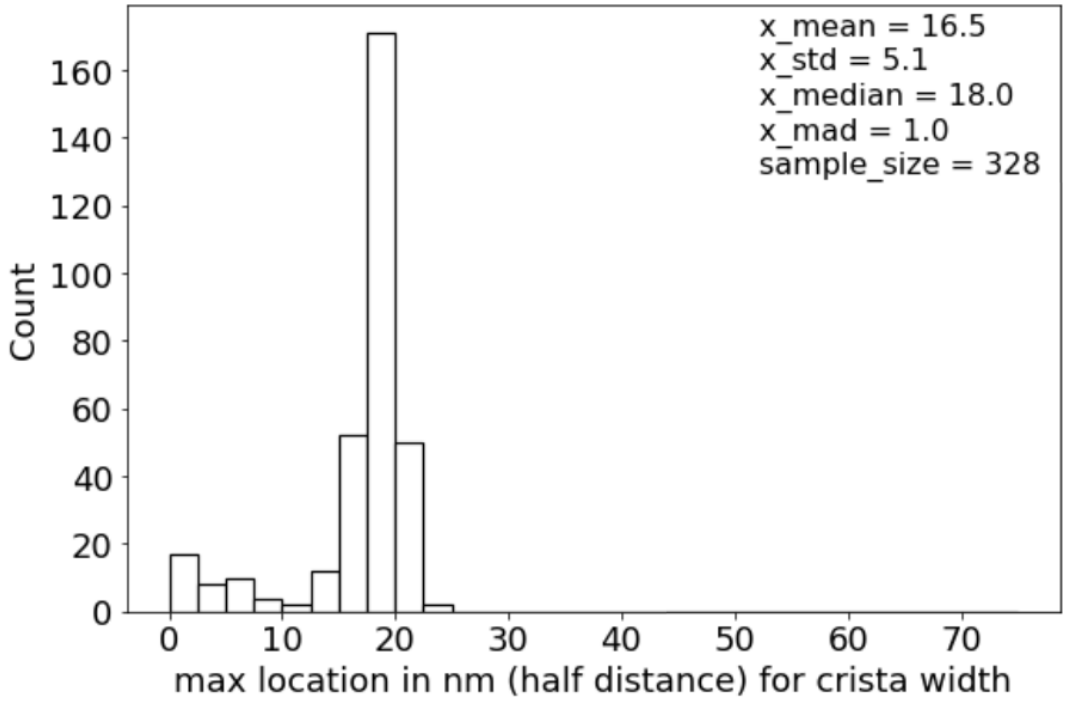




Persistent homology: Statistical measures on H_0

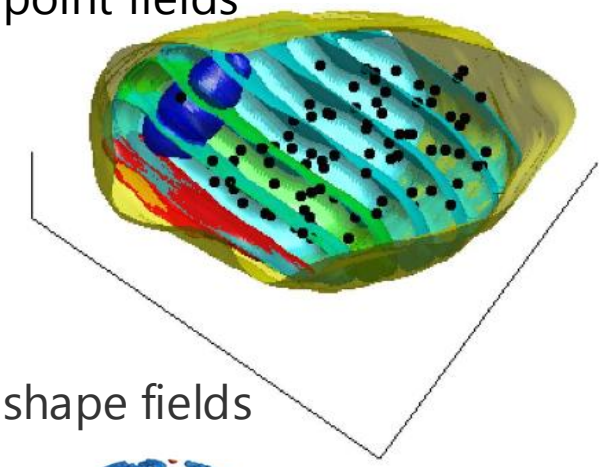


(a) (b) (c)



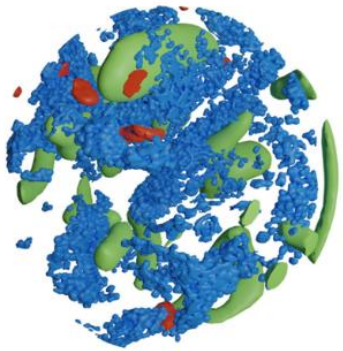
Statistical summary of object collections

Spatial point fields



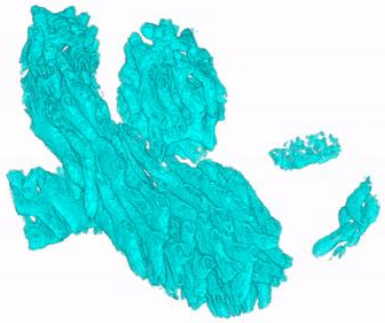
Pair correlation and Ripley's K functions summarizes 1st order point relations – e.g., do the vessicles cluster?

Spatial shape fields



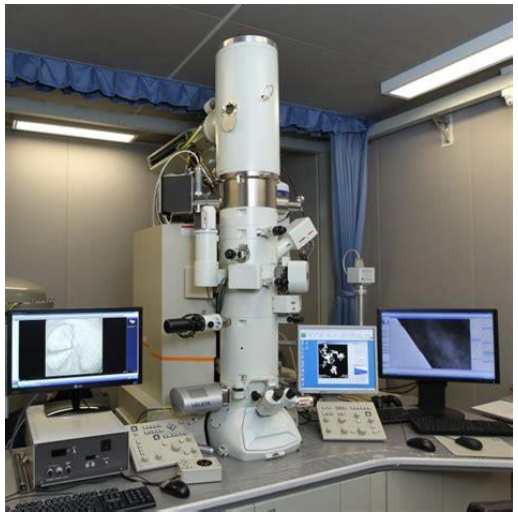
Hausdorf measures on overlaping sets extends notion of points to shapes – e.g., are mitochondria seen close to the synapse?

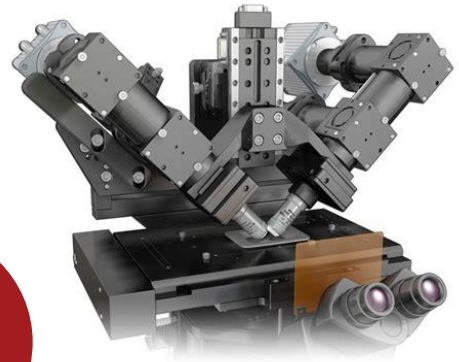
Topological data analysis



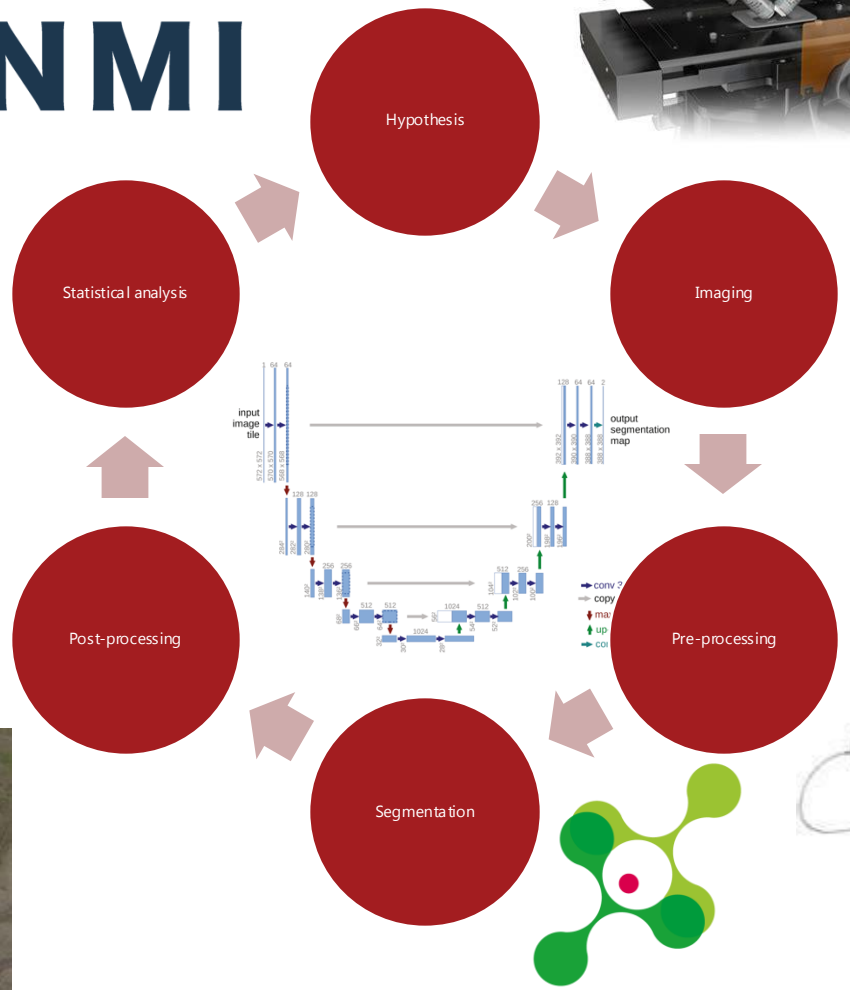
Filtrations brings topological concepts to measurements - e.g., what is the average tubular radius of complicated objects

BNMI





DANISH BIOIMAGING NETWORK



EURO BIOIMAGING
Image life, discover the future