The Geometry and Topology of Shape Patterns with Applications to Leukaemia

SMAI - SIGMA

Wednesday 06/12/2023

PhD (2019-2023)
defended 22/09/2023

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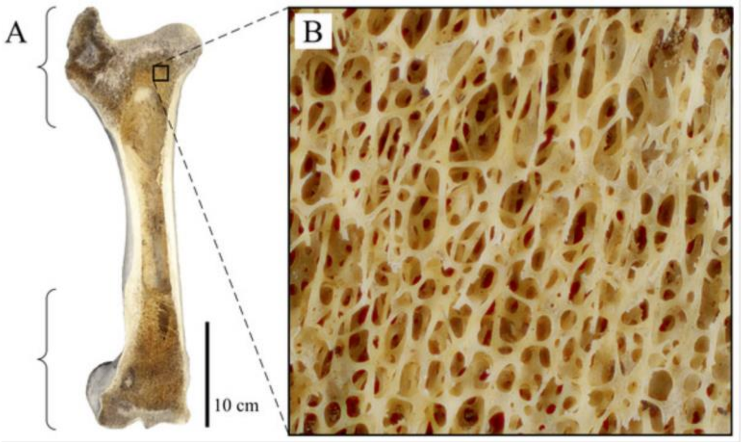
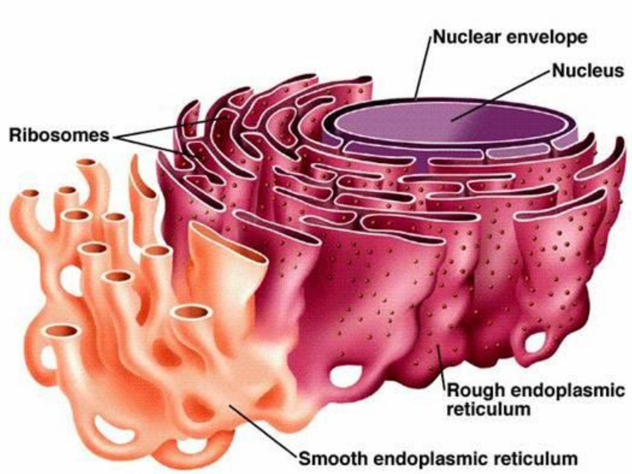
Introduction

Tubular and membranous shapes

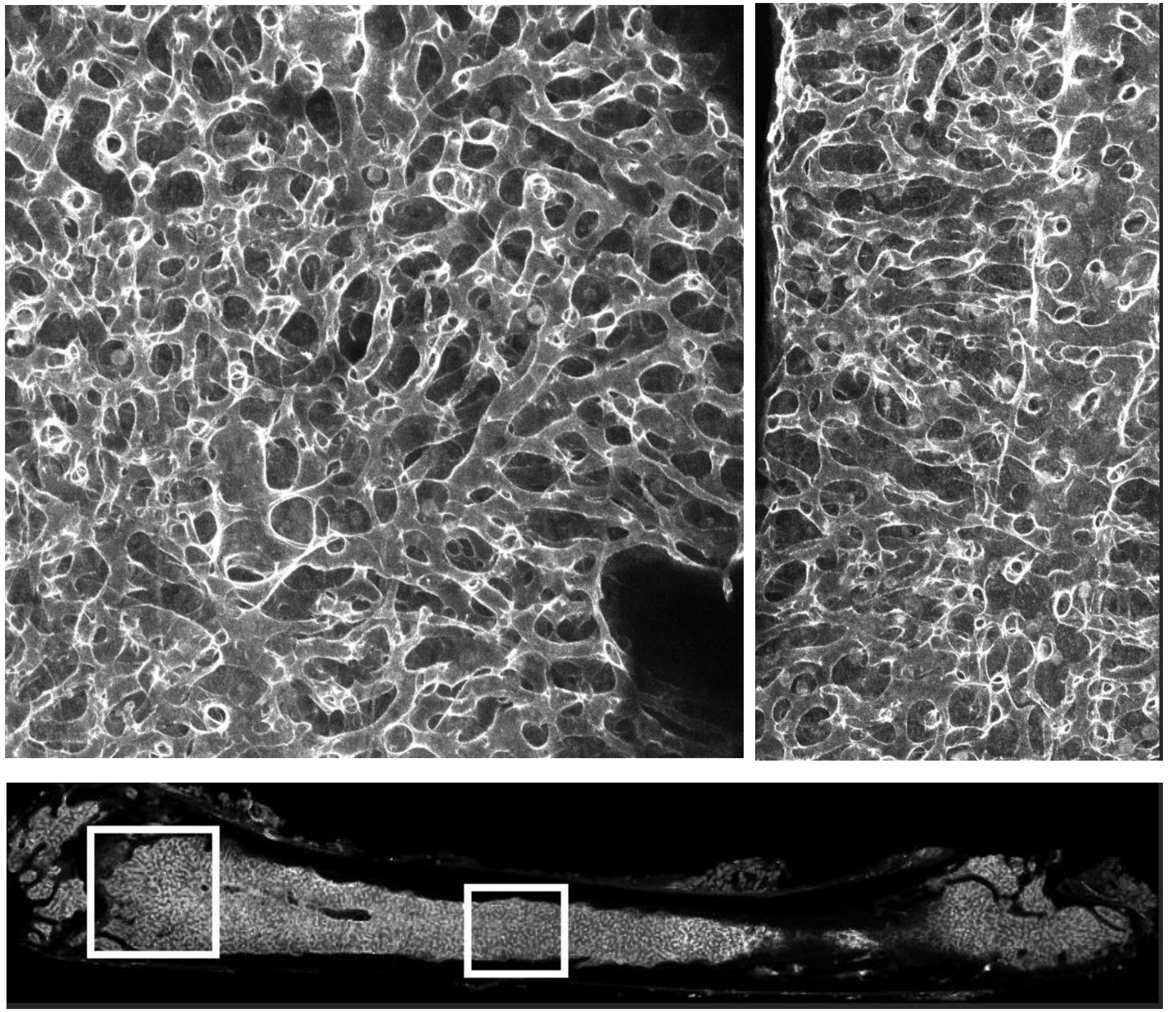


modified from Bishop et al., PeerJ (2018)

spongious bone



endoplasmic reticulum



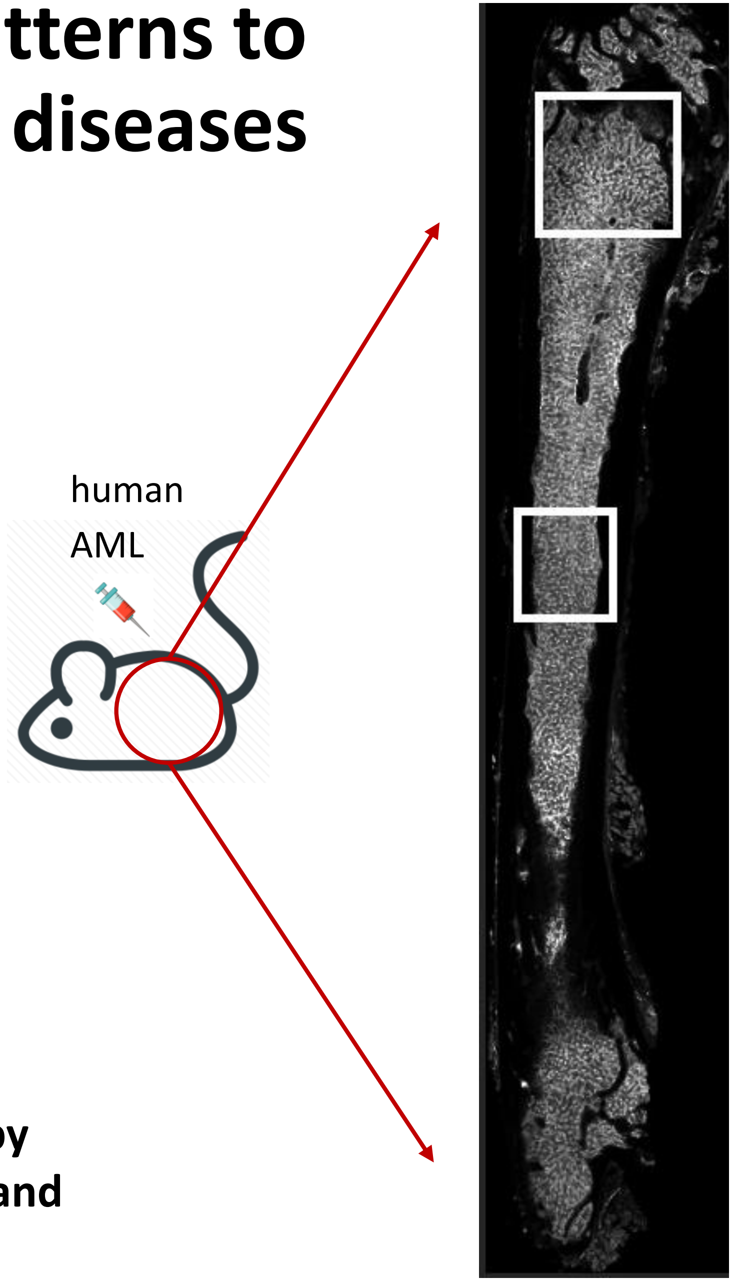
Data : Antoniana Batsivari and Dominique Bonnet

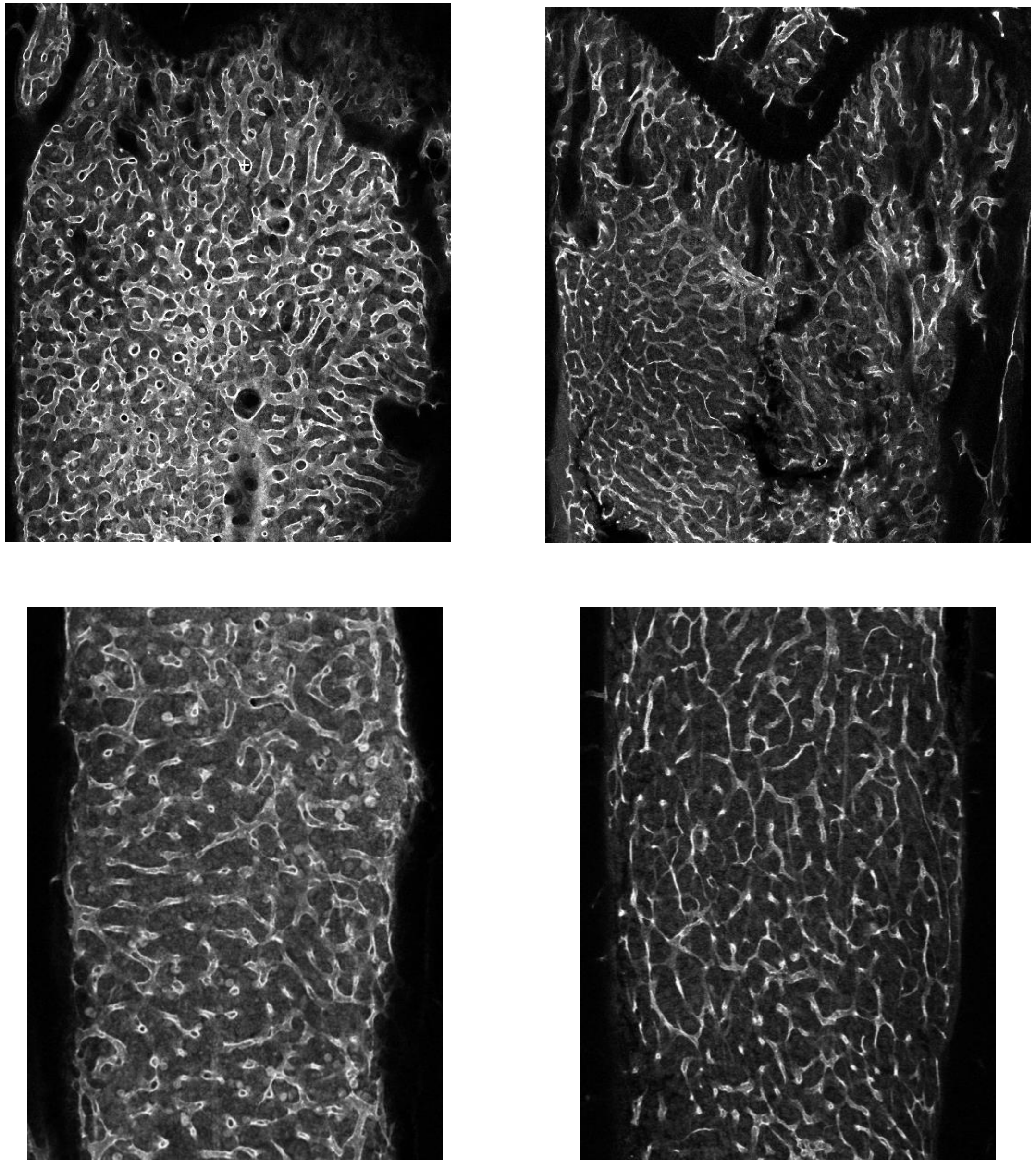
vascular network of the bone marrow

Quantify patterns to understand diseases

AML = Acute Myeloid Leukaemia

How does AML remodel bone marrow vessels?

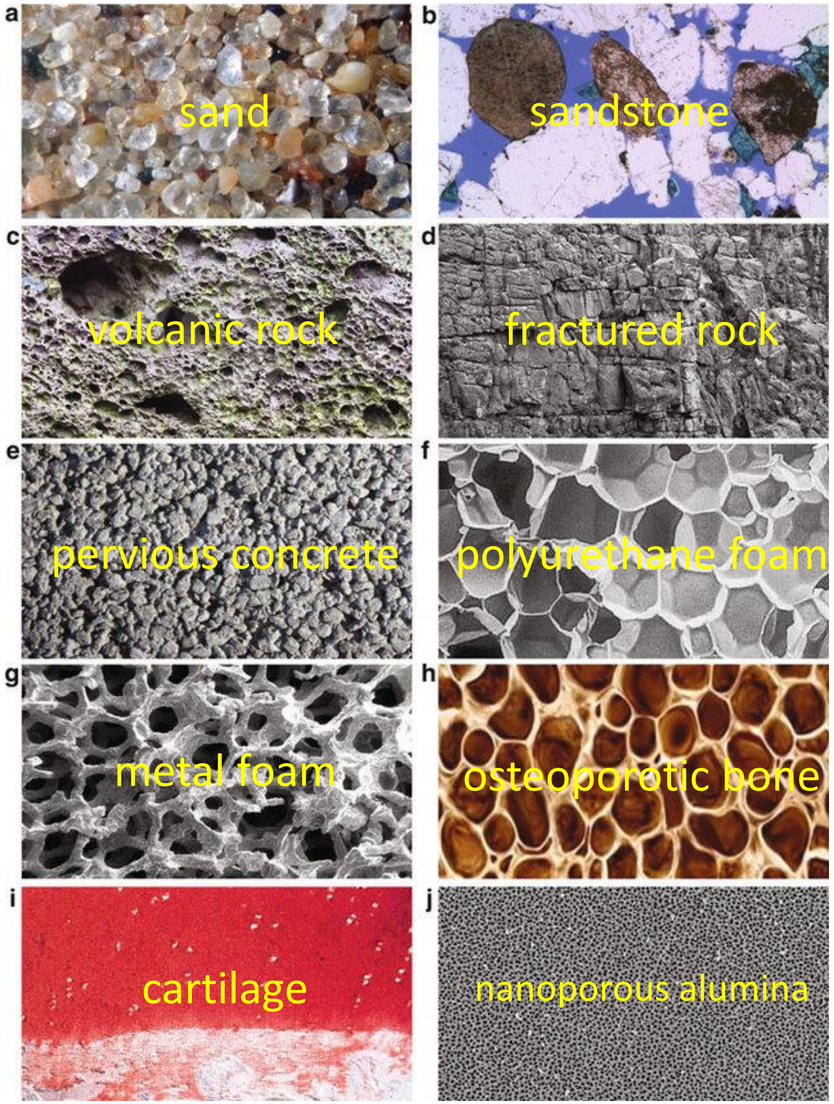




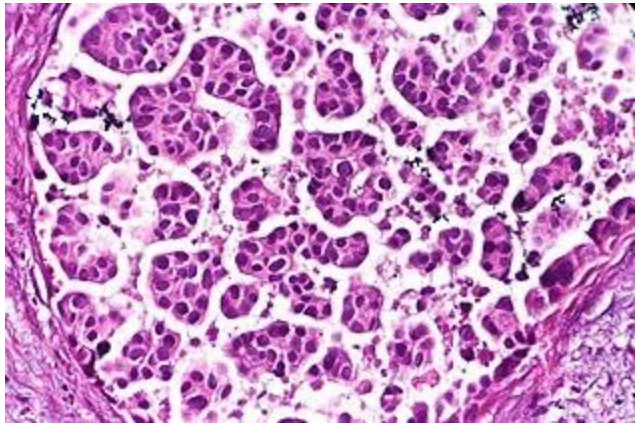
healthy | after engraftment

3D confocal images by Antoniana Batsivari and Dominique Bonnet

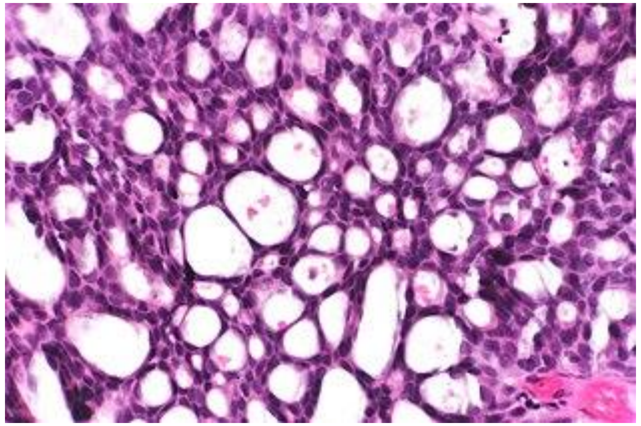
What is *texture* in shapes?



modified from Cheng, *Poroelasticity*, Springer (2016)



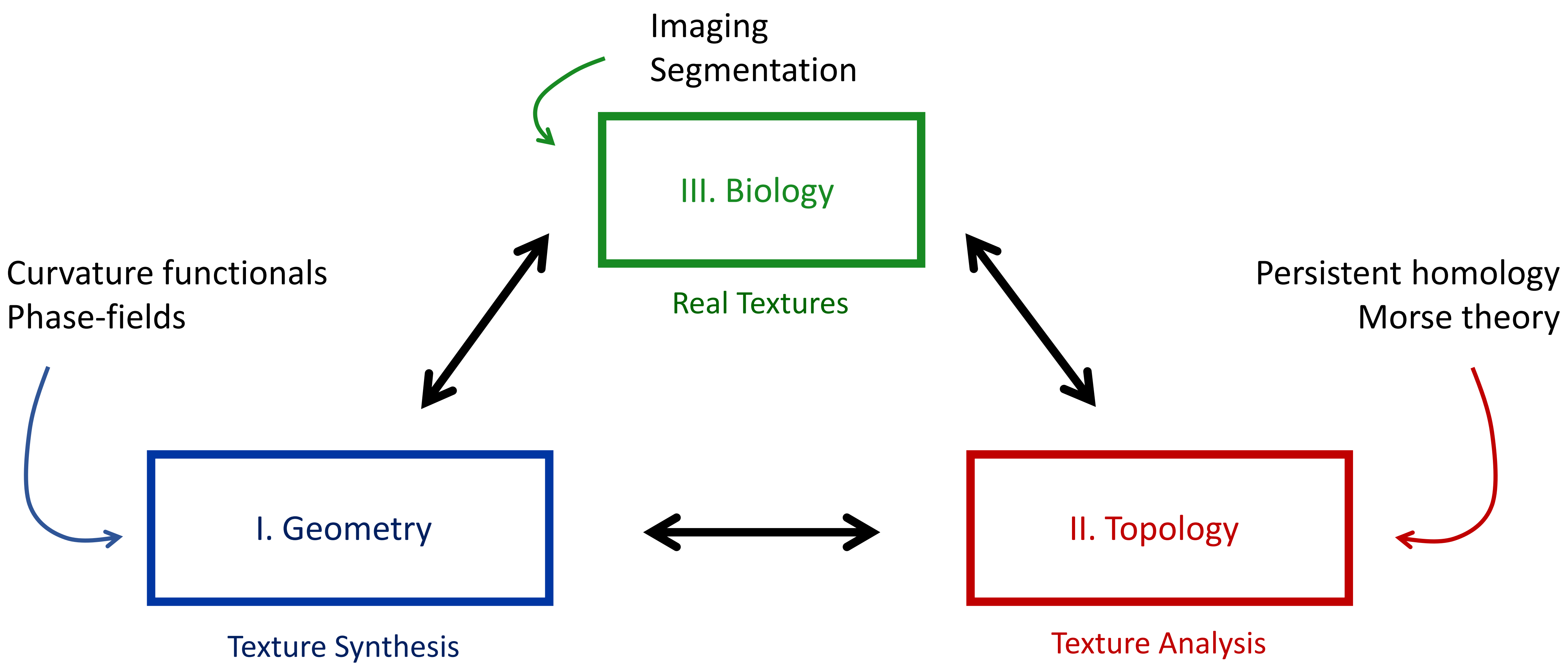
micropapillary

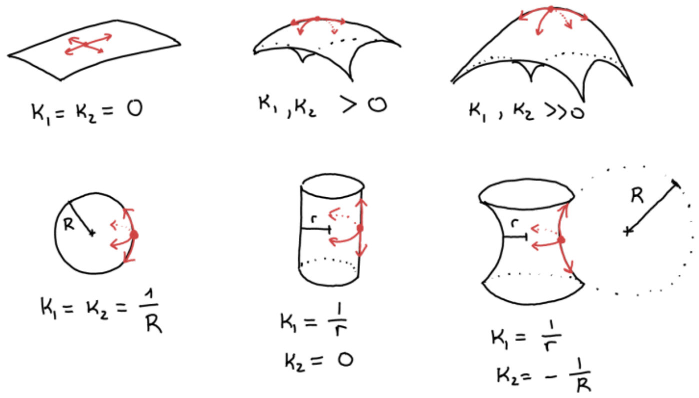


cribriform

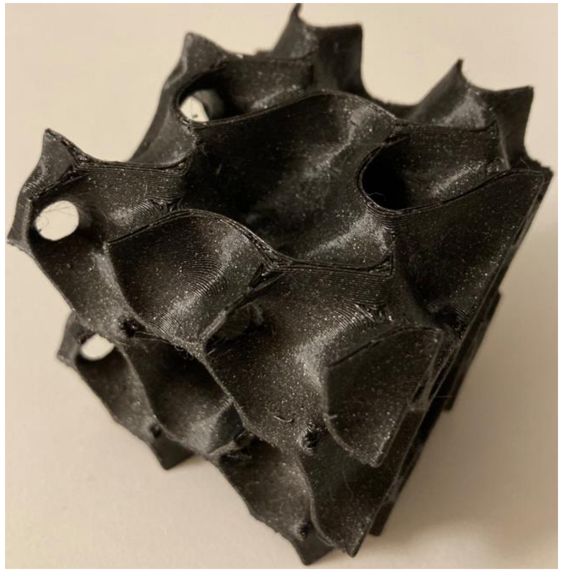
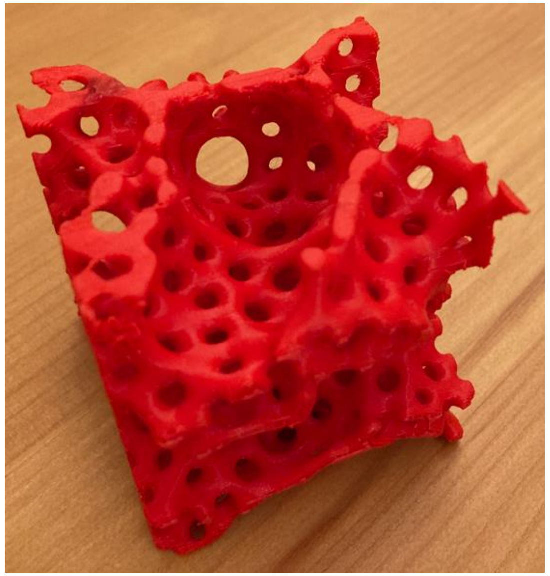
- **geometric** and **topological** features
- how to **model** / **quantify** texture?
- **computable** and **interpretable** outputs

The geometry and topology of *texture* in shapes



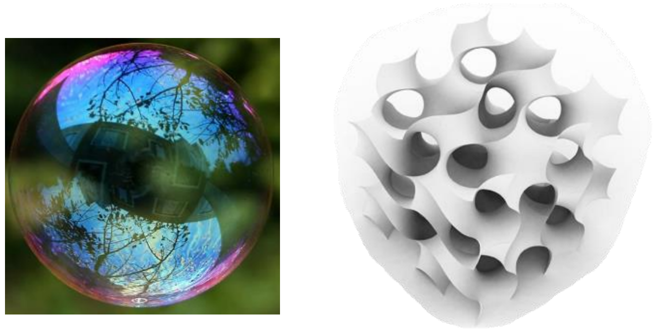


I. Curvatubes


Generation of Tubular and Membranous Shape Textures with Curvature Functionals, Anna Song, *J Math Imaging Vis* (2021)

Energy-minimizing surfaces



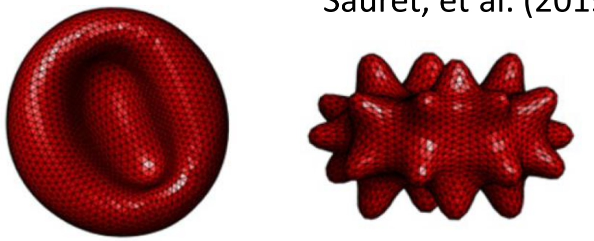
$$\mathbf{E}_A(\mathcal{S}) = \int_{\mathcal{S}} 1\, dA$$

area

$$\mathbf{E}_{\mathrm{W}}(\mathcal{S}) = \int_{\mathcal{S}} H^2\, dA$$

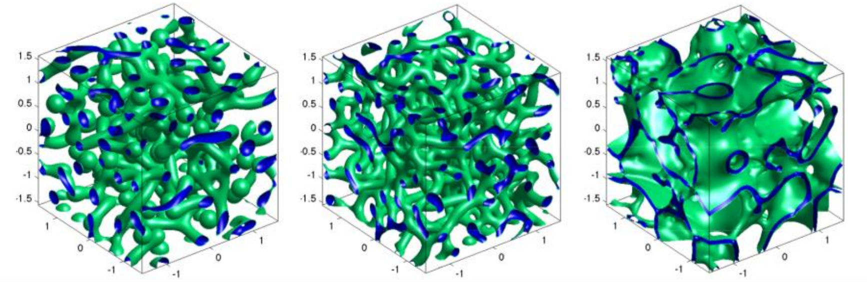
Willmore (1960')

Geekiyanage, Balanant, Sauret, et al. (2019)



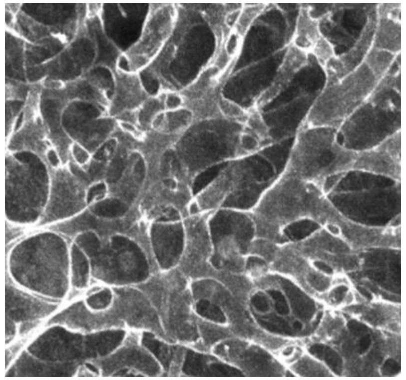
$$\mathbf{E}_{\mathrm{H}}(\mathcal{S}) = \int_{\mathcal{S}} \left(\frac{\chi_b}{2}(H - H_0)^2 + \chi_G K \right) dA$$

Helfrich (1970') and beyond



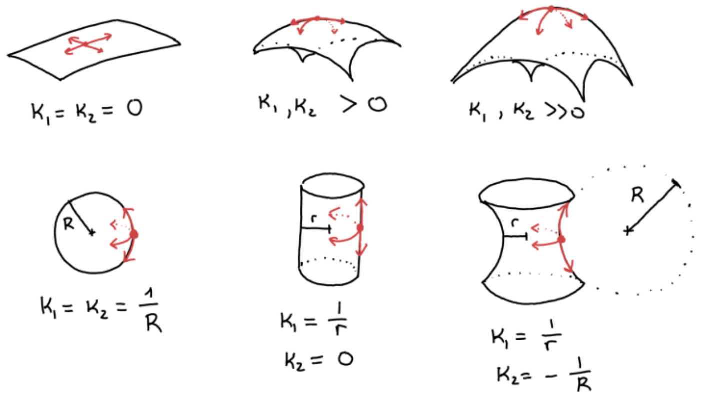
Kraitzman & Promislow (2014)

FCH model (2012)
not curvature-based



General 3D shapes?

Branching, tubular, membranous, porous, spherical…

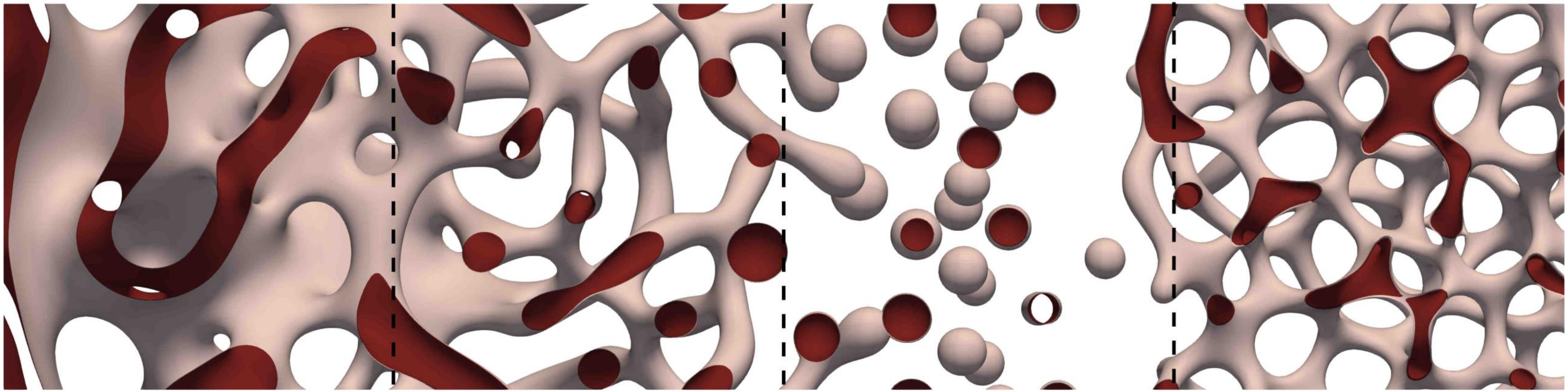


"Curvatubes" functional

$$\mathbf{F}(S) = \int_S p(\kappa_1, \kappa_2)\, dA$$

$$p(x,y) = \sum_{|\alpha| \le 2} a_\alpha (x,y)^\alpha$$

can be asymmetric



$H^2 + \kappa_1^2 + \kappa_2^2$

$(H-20)^2 + 5\,\kappa_2^2$

$(H-25)^2 + (\kappa_1 - 12.5)^2$
$+(\kappa_2 - 12.5)^2$

$(H-45)^2 + (\kappa_1 - 45)^2$
$+10\,\kappa_2^2$

Main contributions

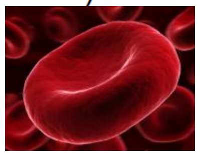
$$\mathbf{E}_A(\mathcal{S}) = \int_{\mathcal{S}} 1 \, dA$$

minimal surfaces (1750')

$$\mathbf{E}_{\mathrm{W}}(\mathcal{S}) = \int_{\mathcal{S}} H^2 \, dA$$

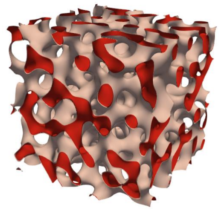
Willmore (1960')

$$\mathbf{E}_{\mathrm{H}}(\mathcal{S}) = \int_{\mathcal{S}} \left(\frac{\chi_b}{2}(H - H_0)^2 + \chi_G K \right) dA$$



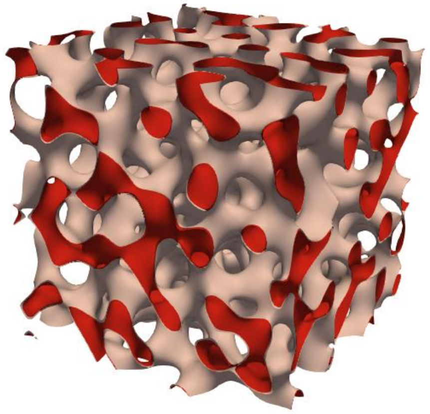
Helfrich (1970')

$$\mathbf{F}(\mathcal{S}) = \int_{\mathcal{S}} p(\kappa_1, \kappa_2) \, dA$$

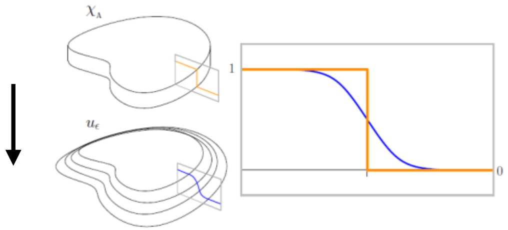


Curvatubes (2021)

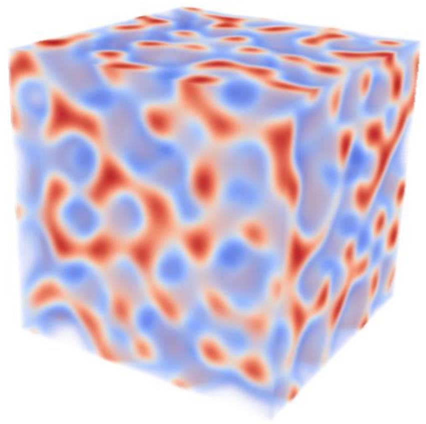
$$\mathbf{F}(\mathcal{S}) = \int_{\mathcal{S}} p(\kappa_1, \kappa_2) \, dA$$



2D surface energy
hard to simulate



$$\mathcal{E}_\epsilon(u) = \int_{\Omega} p(\kappa_{1,u}^{\epsilon}, \kappa_{2,u}^{\epsilon}) \, \epsilon |\nabla u|^2 \, dx$$



3D phase-field energy
GPU-friendly

https://github.com/annasongmaths/curvatubes

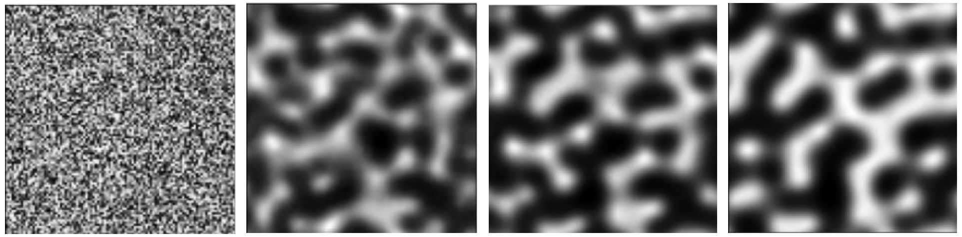
Algorithm

curvatubes

parameters inside energy

$$\dot{u} = \Delta \frac{\partial \mathcal{F}_\epsilon}{\partial u}$$

random initialization



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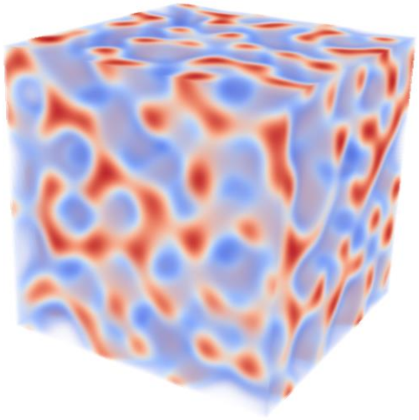
phase-field



$$\mathcal{F}_\epsilon(u) = \int_\Omega \Big[\frac{a_{2,0} + a_{0,2} - a_{1,1}}{2\epsilon} \|\mathcal{M}_u^\epsilon\|^2 + \frac{a_{1,1}}{2\epsilon} (\mathrm{Tr}\mathcal{M}_u^\epsilon)^2 + \frac{a_{2,0} - a_{0,2}}{2\epsilon} \mathrm{Tr}\mathcal{M}_u^\epsilon \sqrt{(2\|\mathcal{M}_u^\epsilon\|^2 - (\mathrm{Tr}\mathcal{M}_u^\epsilon)^2)^+} + \frac{a_{1,0} + a_{0,1}}{2} |\nabla u| \mathrm{Tr}\mathcal{M}_u^\epsilon + \frac{a_{1,0} - a_{0,1}}{2} |\nabla u| \sqrt{(2\|\mathcal{M}_u^\epsilon\|^2 - (\mathrm{Tr}\mathcal{M}_u^\epsilon)^2)^+} + a_{0,0}\, \epsilon |\nabla u|^2 \Big] \, dx.$$

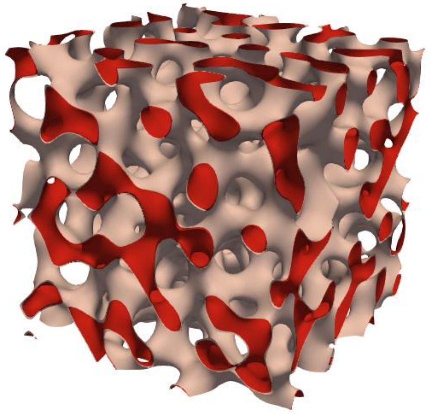
similarity with Cahn-Hilliard flow

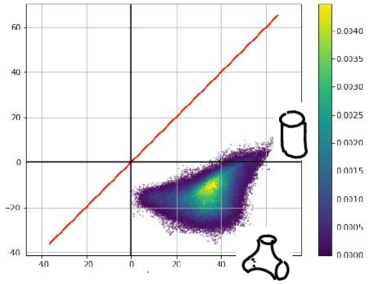
$$\dot{u} = \Delta \left(\frac{u^3 - u}{\epsilon} - \epsilon \Delta u \right) = \Delta \frac{\partial \mathcal{E}_A}{\partial u}$$

Pytorch + GPU
Adam or L-BFGS

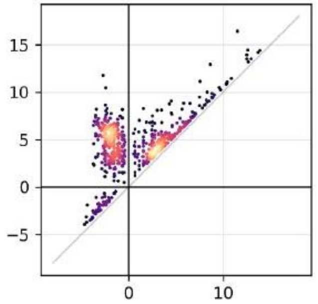
outputs

surface





curvature diagram

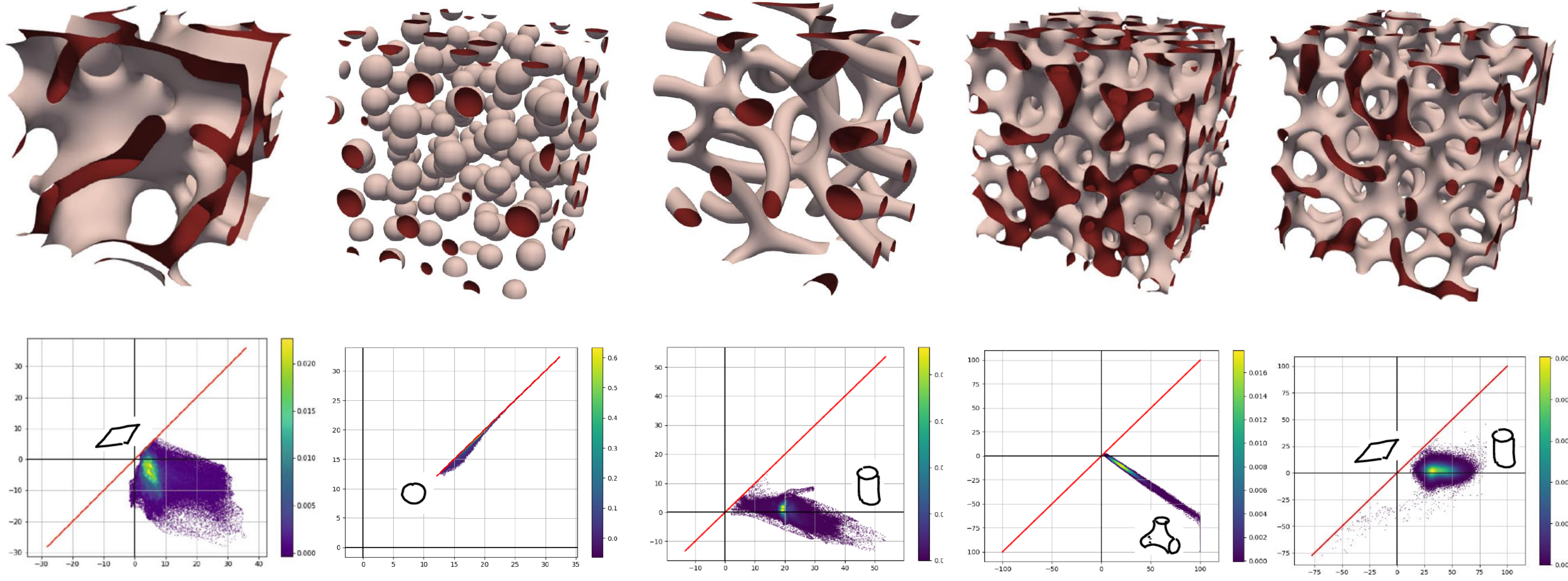


persistence diagram

other features...

Basic shape textures

Natural form $h_2(H - H_0)^2 + k_1 K + \alpha(\kappa_1 - \kappa_1^0)^2 + \beta(\kappa_2 - \kappa_2^0)^2$



$H^2 + \kappa_1^2 + \kappa_2^2$

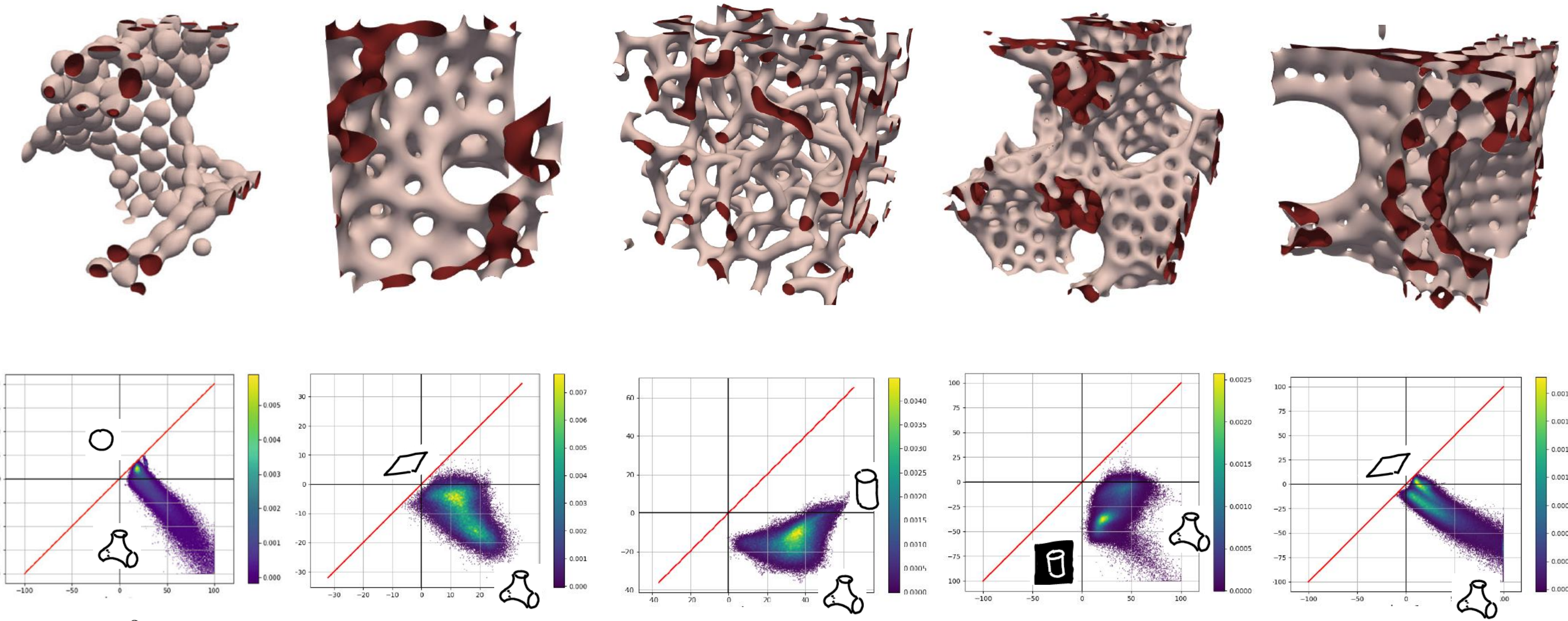
$(H - 25)^2 + (\kappa_1 - 12.5)^2 + (\kappa_2 - 12.5)^2$

$(H - 20)^2 + 5\kappa_2^2$

$(H - 5)^2 + 0.8K + \kappa_2^2$

(no natural form)

Complex shape textures

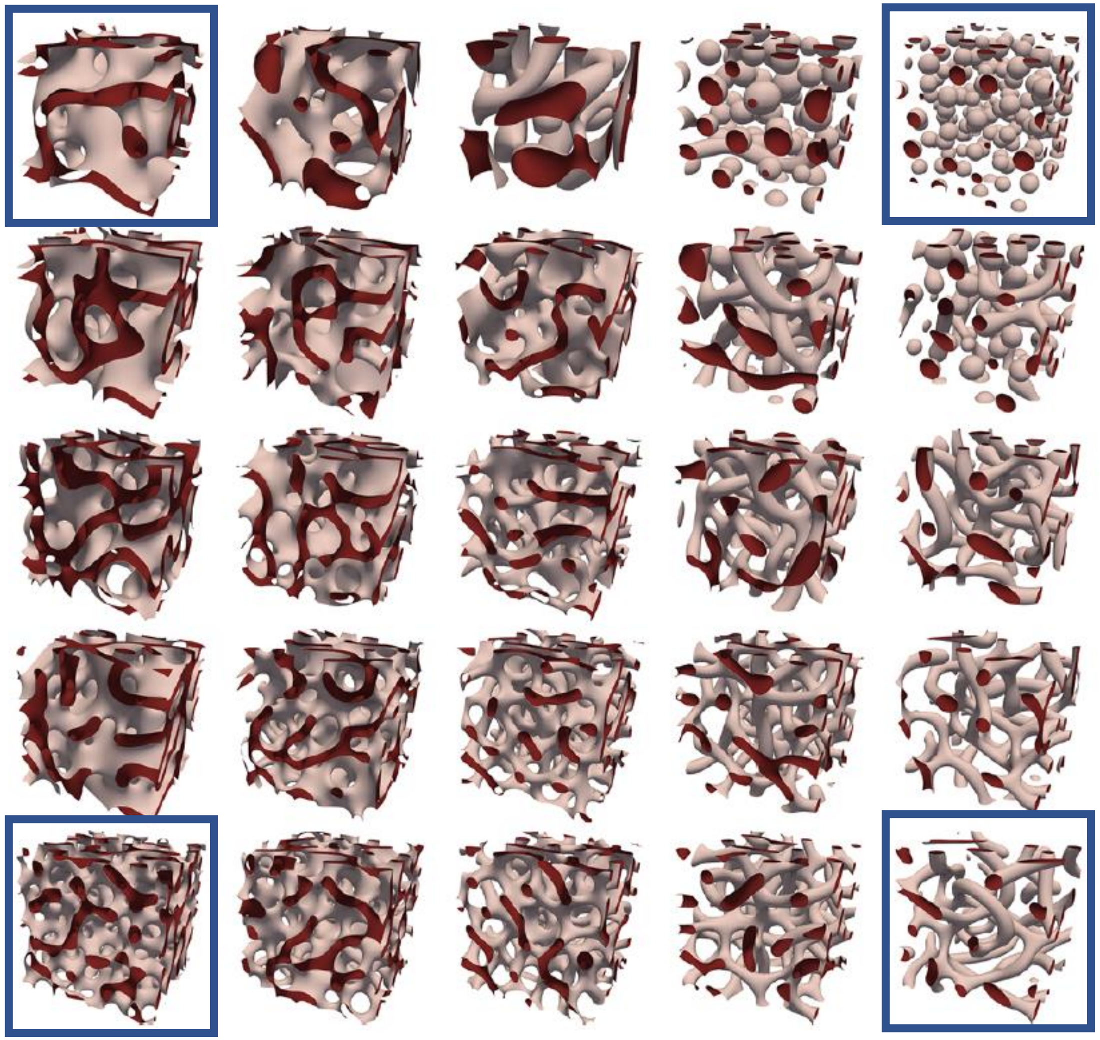


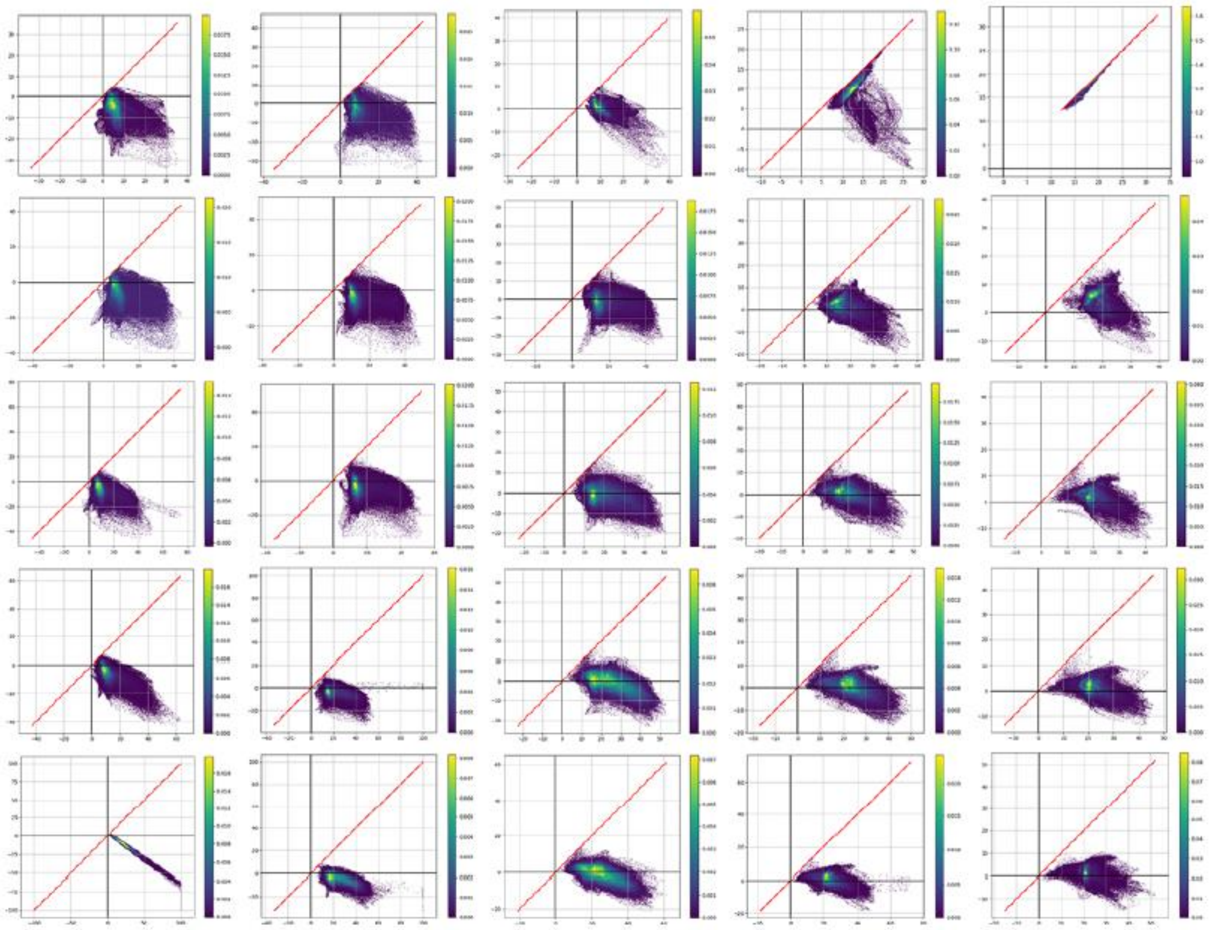
$(H - 28)^2 + 1.55K$ (no natural form) (no natural form) (no natural form) (no natural form)

Continuity of shapes and of textures

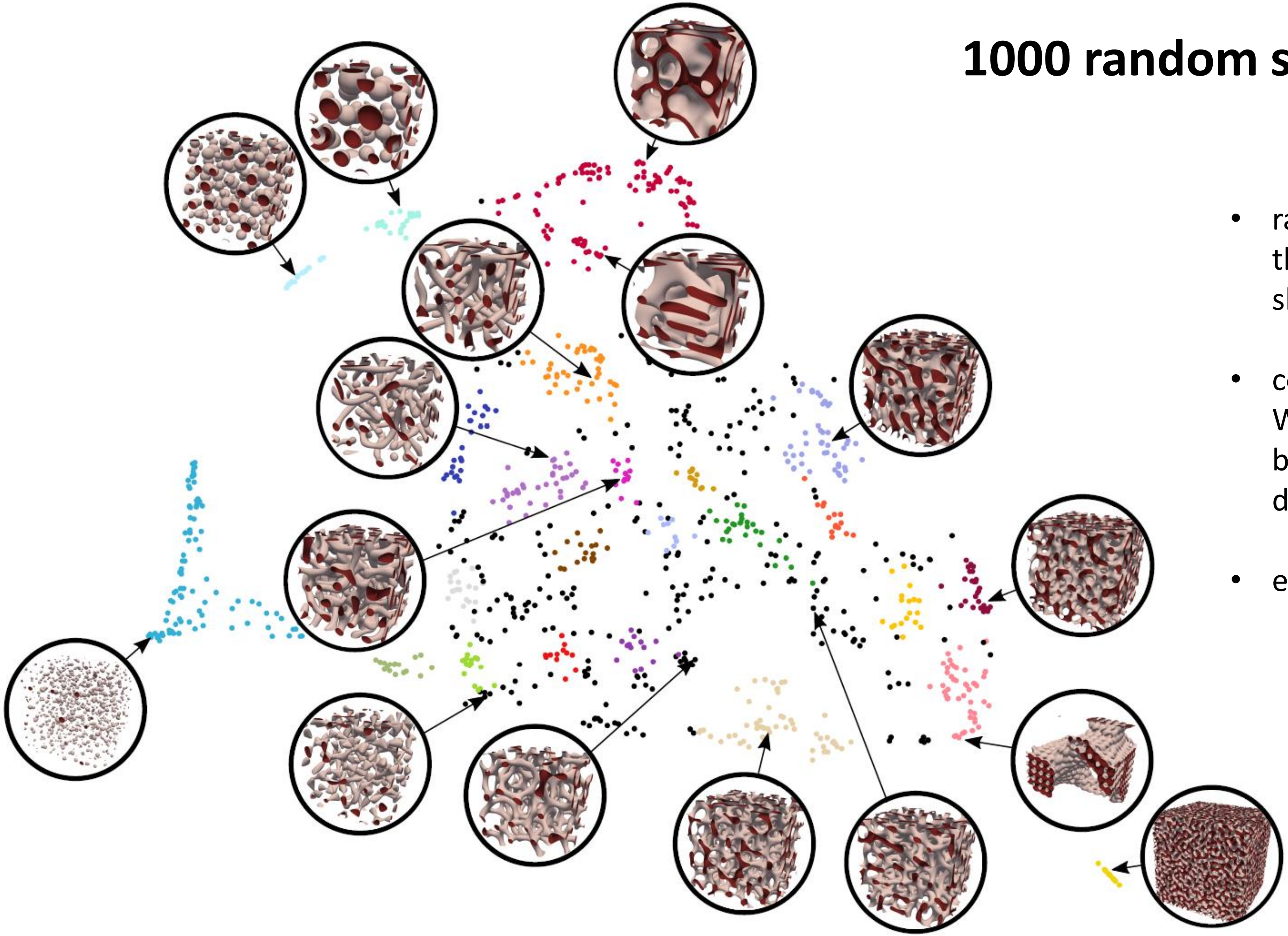
same initialization
different energies

bilinear interpolation between 4 shape parameters leads to continuum of morphologies



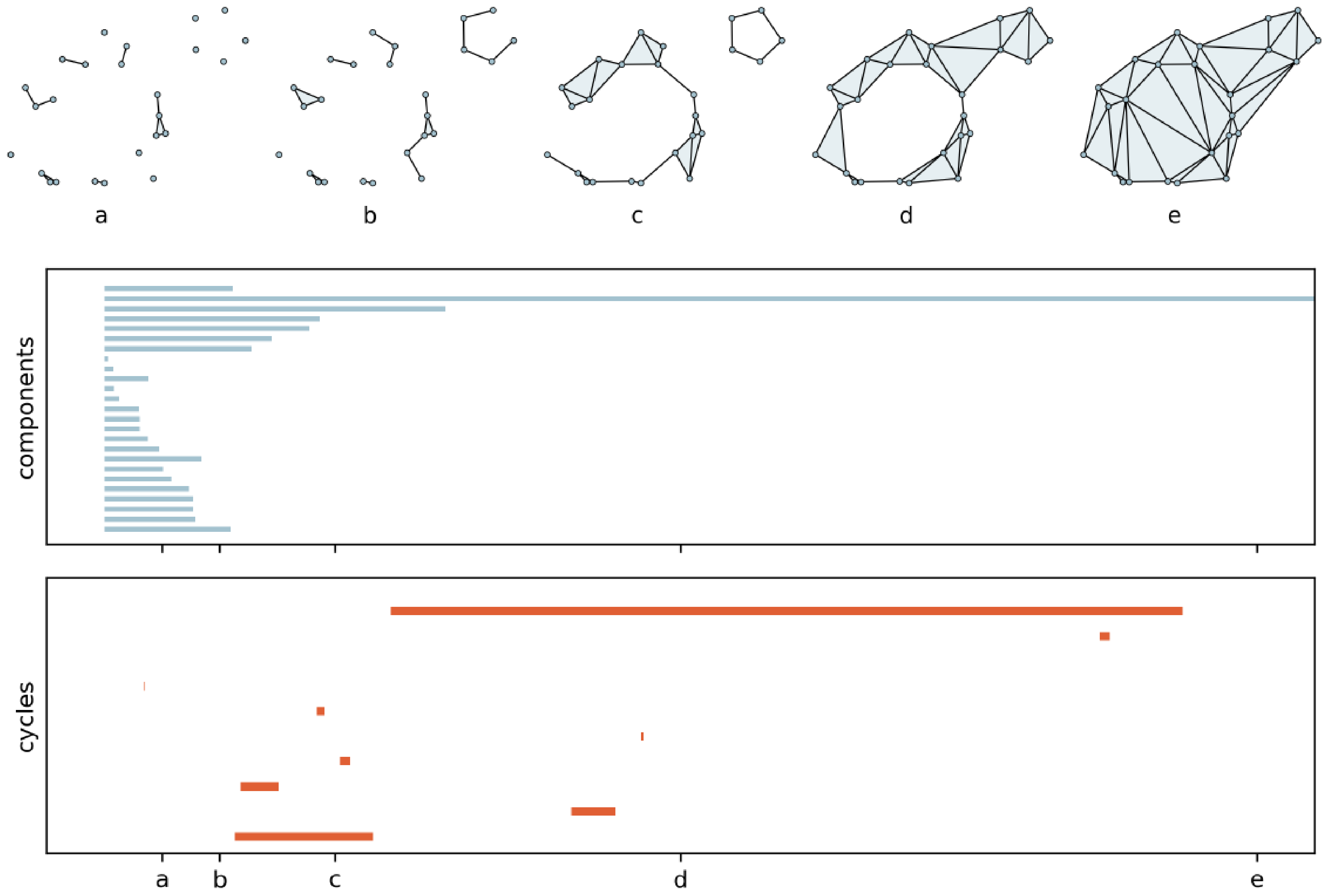


1000 random shapes in UMAP



- randomly chosen coeffs, then accept only “valid” shapes
- compute pairwise Wasserstein distances between curvature diagrams
- embed in 2D using UMAP

II. Signed distance persistent homology (SDPH)



Persistent homology :

- tracks evolution of topological features

- summarizes birth-death times in barcodes

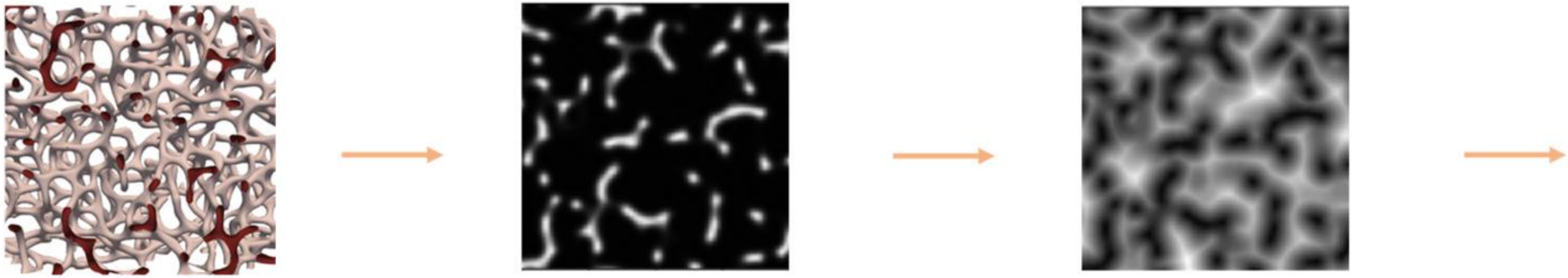
PH0: components

PH1: cycles

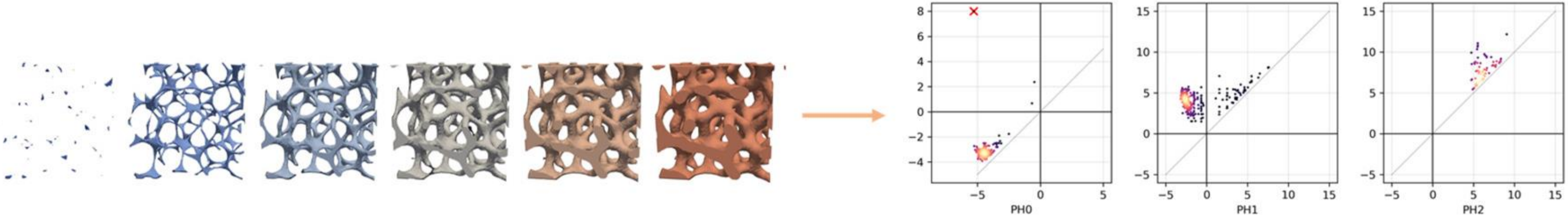
PH2: cavities

PHk: k-dim holes

SDPH method

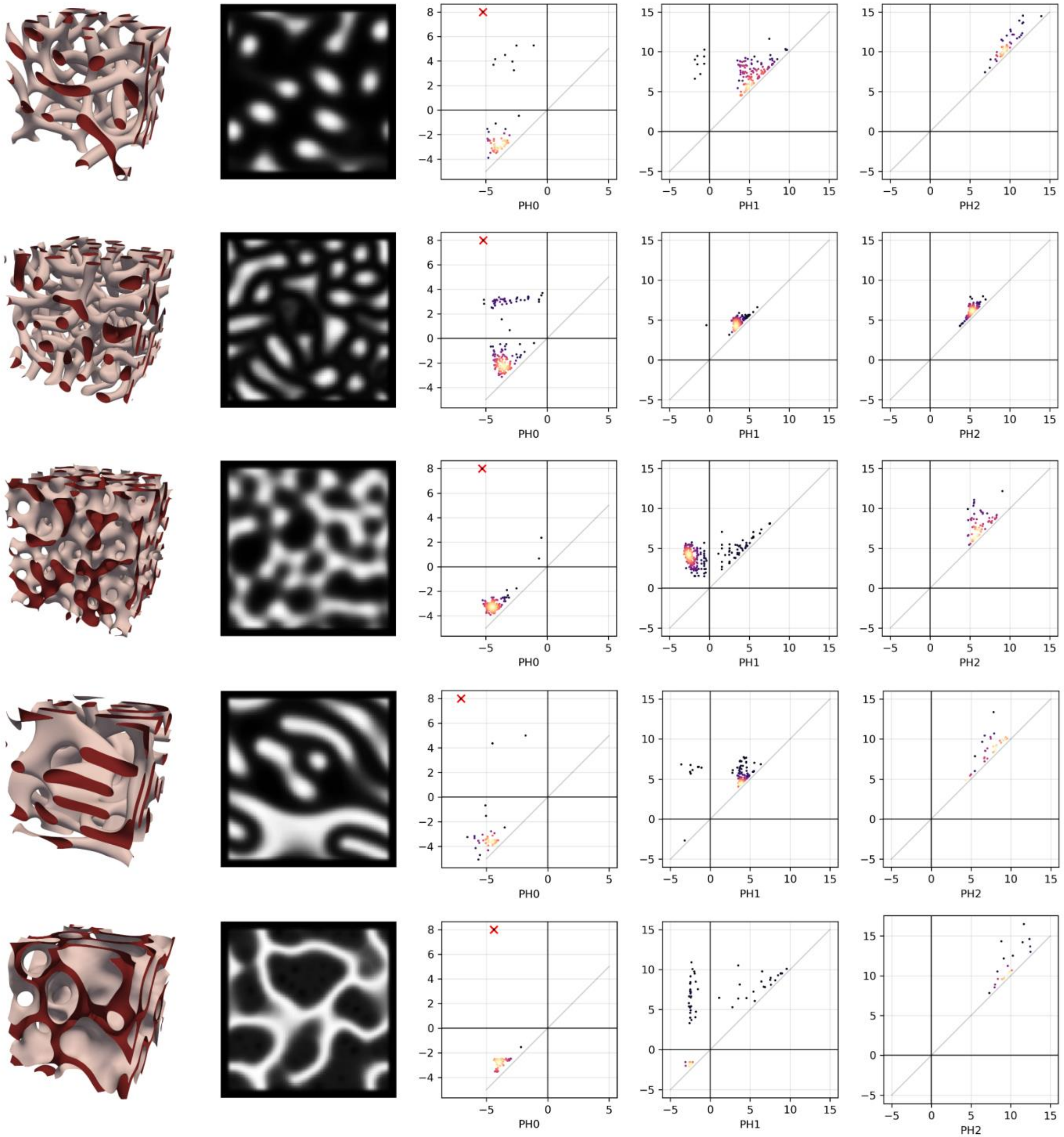


(1) 3D shape (2) segmentation (3) signed distance field



(4) sublevel set filtration (5) persistence diagrams PH0, PH1, PH2

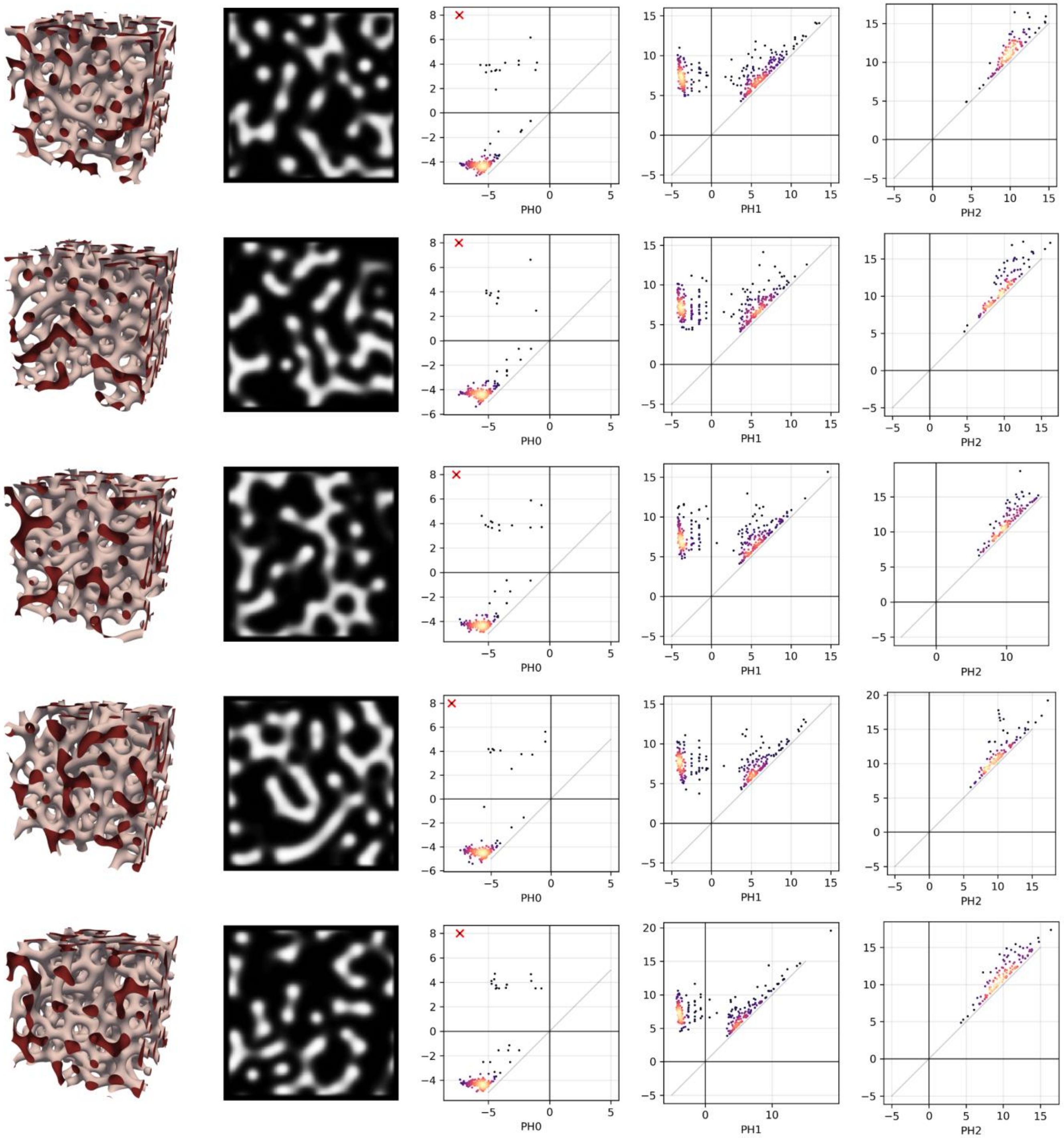
- five curvatubes shapes
- objective quantification
- SDPH easily discriminates



- same parameters, different initializations

- SDPH quantifies texture, does not care about geometric realization

- **stability** of SDPH wrt texture



Theoretical investigation

Generalized Morse Theory of Distance Functions to Surfaces for Persistent Homology
Anna Song, Ka Man Yim, and Anthea Monod (arxiv, 2023)

Setting

SDPH used by (Delgado-Friedrichs *et al.*, 2014, 2015; Herring *et al.*, 2019; Moon *et al.*, 2019; Pritchard *et al.*, 2023) in the discrete cubical setting. Here, we consider distance fields to smooth surfaces.

Let Ω^- be a bounded open set with C^k boundary $\mathcal{S} = \partial\Omega^-$, $k \geq 2$. Then

$$\mathbb{R}^n = \Omega^- \sqcup \mathcal{S} \sqcup \Omega^+.$$

$$\text{Define} \quad d = \mathrm{dist}(\cdot, \Omega^-) - \mathrm{dist}(\cdot, \Omega^+).$$

Consider the sublevel set filtration $X_\bullet$ where

$$X_t = \{x \in \mathbb{R}^3 \mid d(x) \leq t\}.$$

Compute the persistence diagrams

$$\mathrm{PH}(d) : \forall s \leq t, \quad H(X_s) \to H(X_t).$$

General aims

Are SDPH diagrams **well-defined**?

How to **interpret** SDPH diagrams?

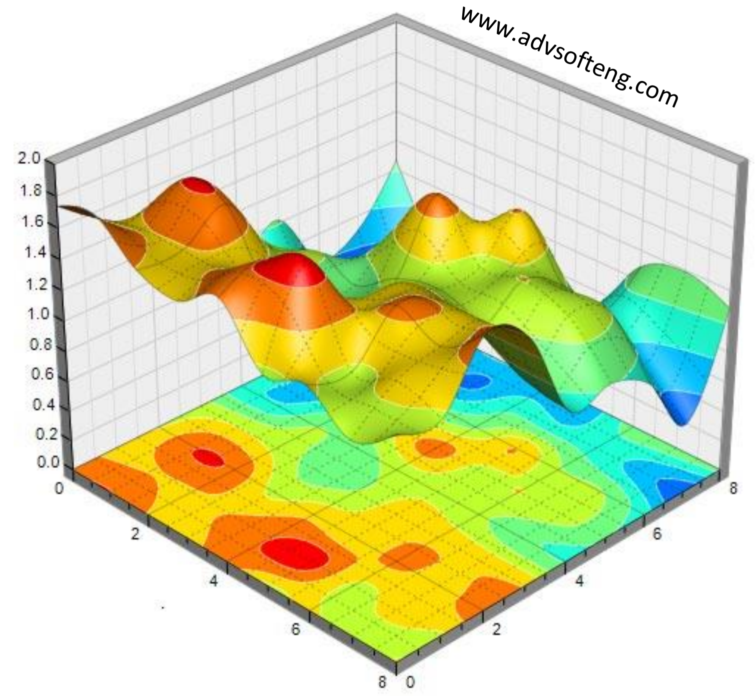
What do they **quantify** in shapes?

notion of **critical points**

Smooth Morse theory and PH

Morse theory studies **non-degenerate critical points** of smooth functions, at which

$$f \underset{\text{diffeo}}{\sim} \text{cst} - \sum_{i=1}^{\lambda} x_i^2 + \sum_{i=\lambda+1}^{n} x_i^2 .$$

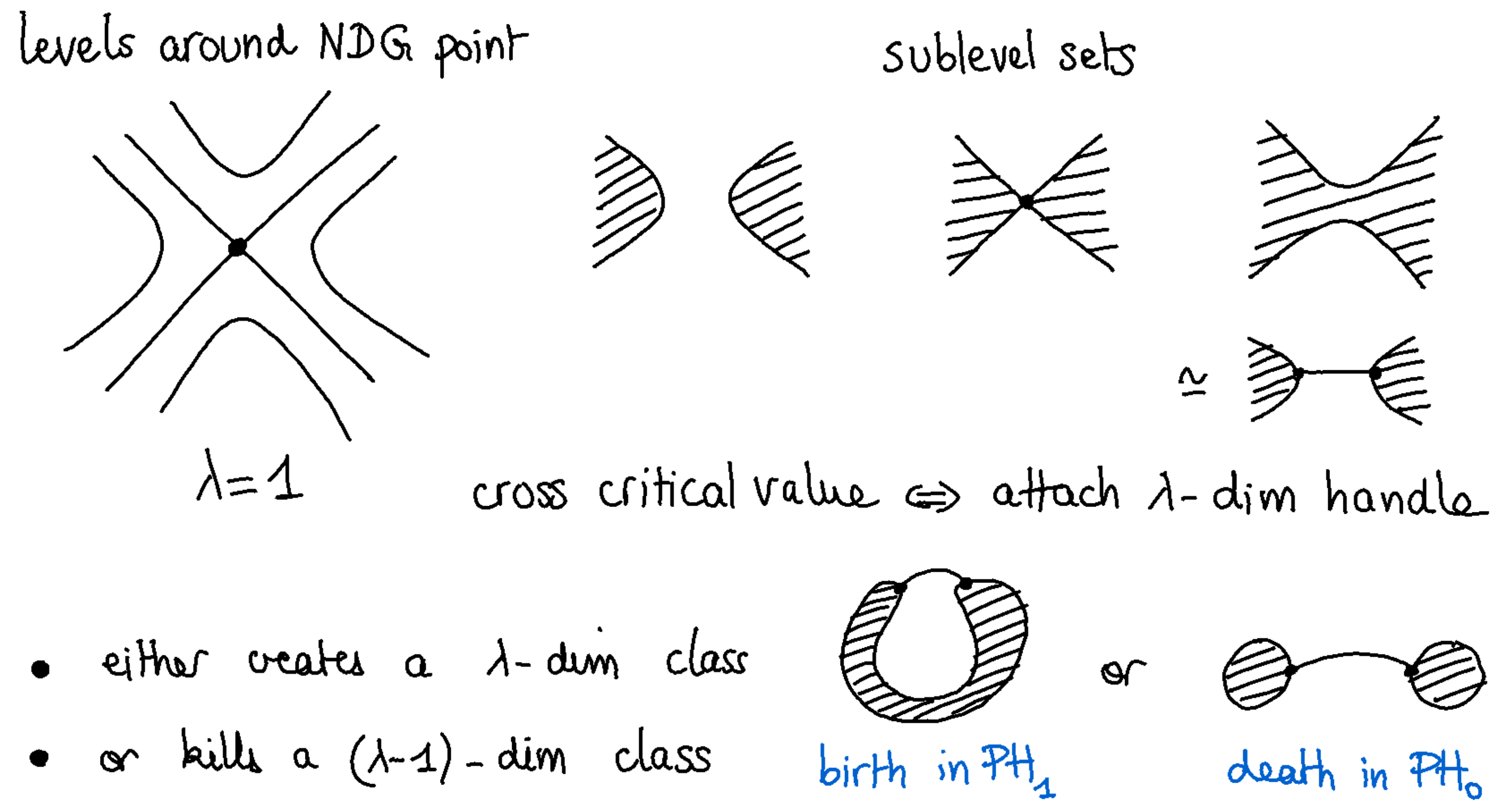


local min
index 0

saddle point
index 1

local max
index 2

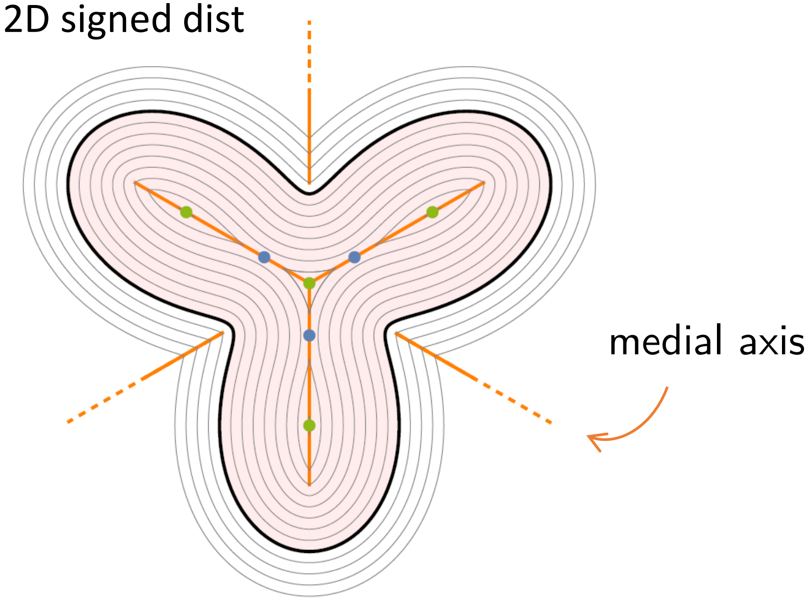
Morse theory relates a smooth proper Morse function f to $\mathrm{PH}(f)$ through the **isotopy lemma** and **handle attachment lemma**. Typically, births and deaths in $\mathrm{PH}_k(f)$ pair **critical points** with indices $(k, k+1)$.



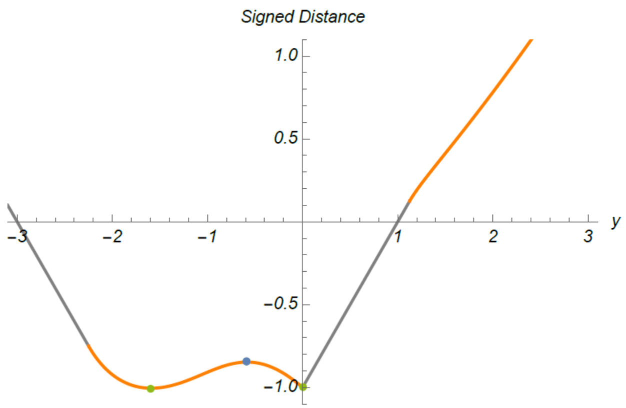
Problem

However, distance functions generated by smooth boundaries $\mathcal{S}$ **are not smooth**, especially on the medial axis $\mathcal{M}_{\mathcal{S}}$.

2D signed dist



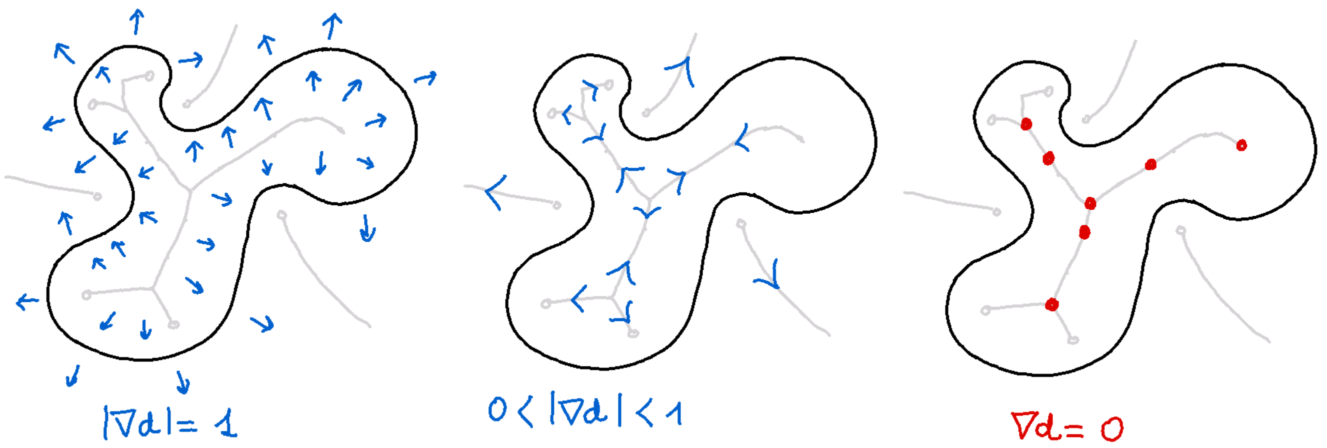
nonsmooth profile on vertical axis



Contribution: Morse theory for (signed) distance functions

Critical points

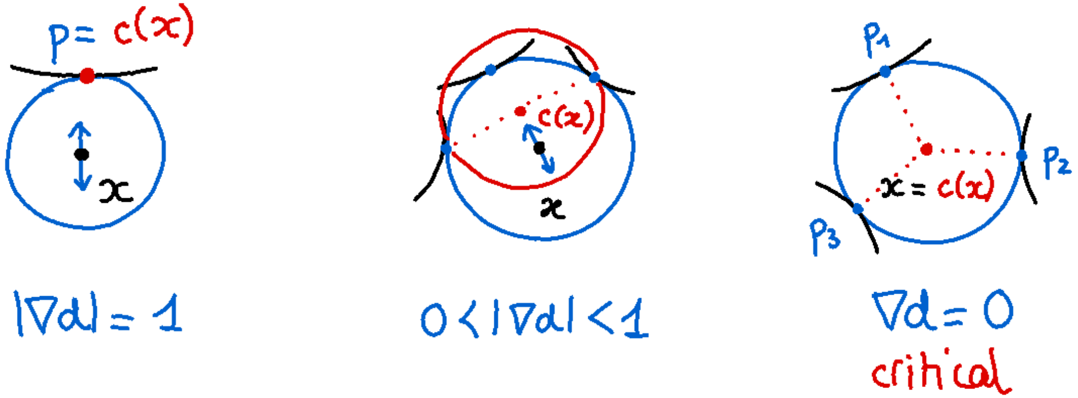
Nonetheless, **critical points** can be defined for distance fields too (Grove & Shiohama, 1977; Cheeger, 1991; Grove, 1993; Lieutier, 2003), as points where an **extended gradient field** vanishes.



Definition

A point $x \in \mathbb{R}^n \setminus \mathcal{S}$ is critical for the signed distance d if $\nabla d(x) = 0$. Equivalently,

- $x = c(x)$, or
- $x \in \mathrm{Conv}(\{p_1, \ldots, p_k\})$



Contributions: generalized Morse lemmas

Theorem (Isotopy lemma for signed distance)

Let $a < b$ in $\mathbb{R}$. Suppose that $d^{-1}[a, b]$ contains no critical point of d (it is compact). Then $d^{-1}(-\infty, a]$ is a deformation retract of $d^{-1}(-\infty, b]$, and therefore they are homotopy-equivalent.

Apply (Grove, 1993, Proposition 1.8)

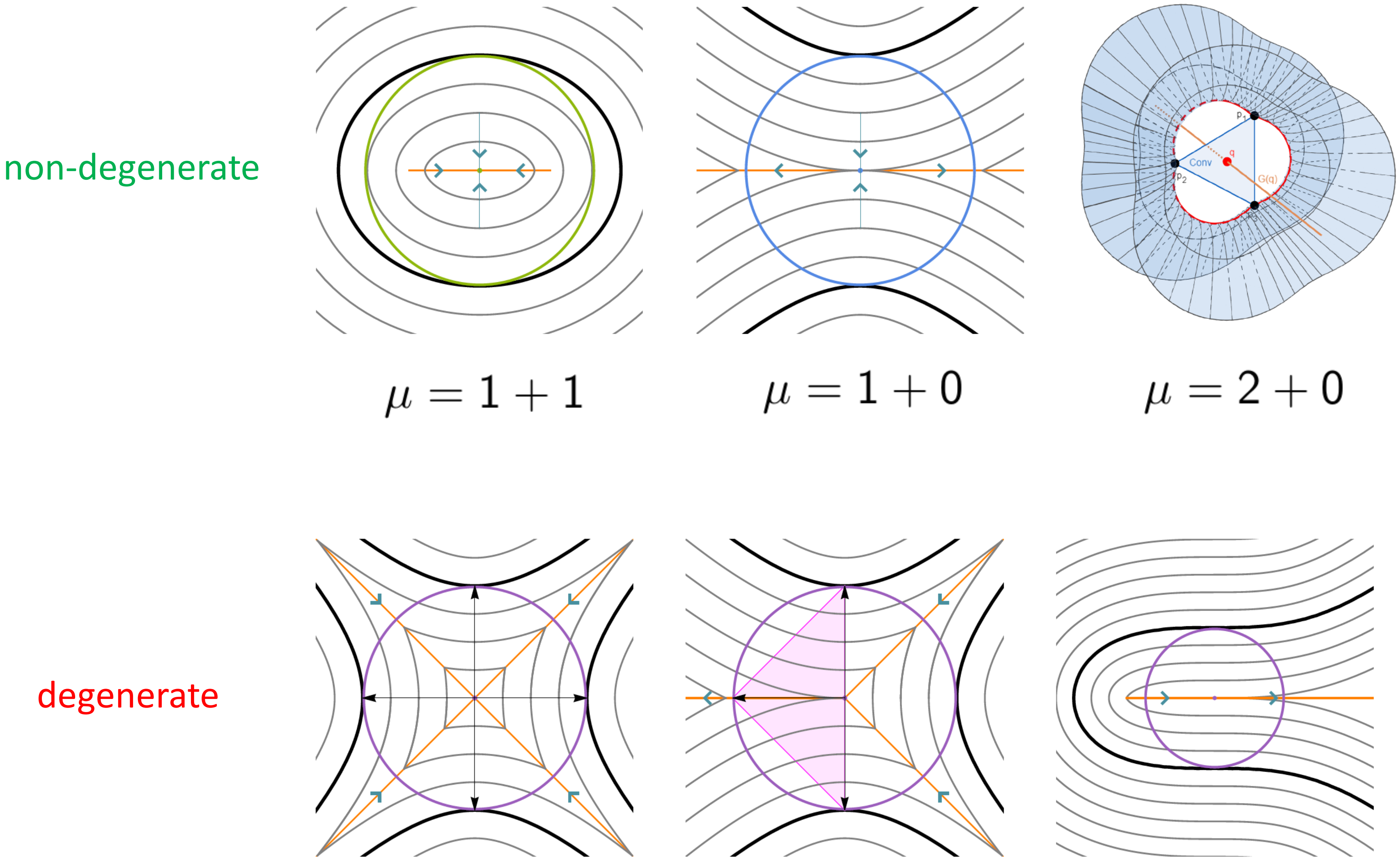
Theorem (Handle attachment lemma for signed distance)

At a Min-type NDG critical point $x \in \mathbb{R}^n \setminus \mathcal{S}$ with index λ and value $d(x) = c$, if the interlevel set $d^{-1}[c - \epsilon, c + \epsilon]$ contains no other critical point for some $\epsilon > 0$, then

$$d^{-1}(-\infty, c + \epsilon] \simeq d^{-1}(-\infty, c - \epsilon] \cup e^{\lambda}.$$

C^k Min-type theory (Gershkovich & Rubinstein, 1997) defines NDG points and gives topological normal form for distance functions **under suitable geometric conditions**

Smooth Morse theory can be **generalized to Topological Morse theory**


non-degenerate
$\mu = 1 + 1$
$\mu = 1 + 0$
$\mu = 2 + 0$
degenerate

Contributions: genericity and classification

Theorem (Genericity)

For generic embeddings of a C^k-smooth ($k \geq 3$) closed orientable surface into $\mathbb{R}^3$, the induced signed distance d admits only a finite number of critical points, that are all non-degenerate.

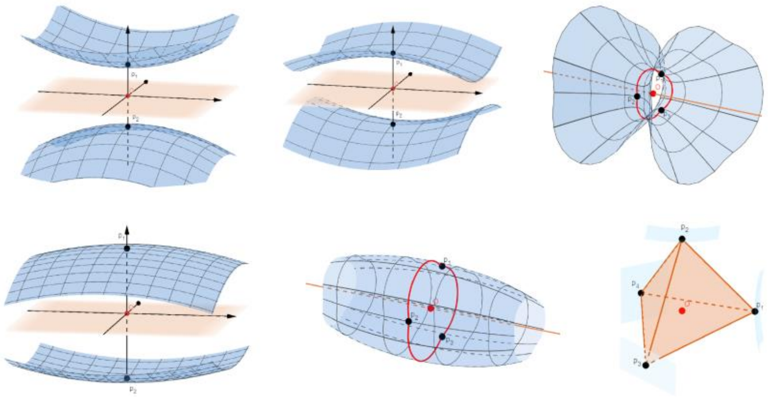
use transversality theory...

Corollary (SDPH)

For generic 3D shapes, the SDPH module PH_k can be decomposed into a finite sum of $\{[b_i, d_i)\}$ intervals pairing NDG points with indices $(k, k+1)$.

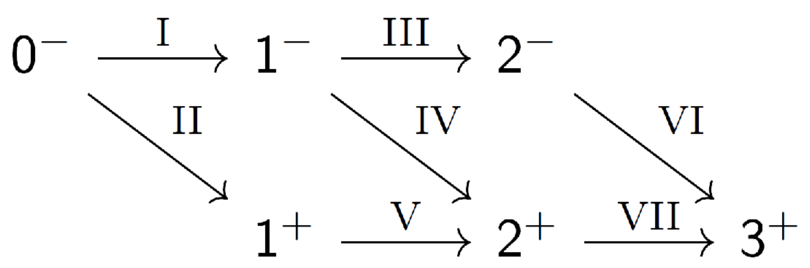
	$\lambda = 0$	$\lambda = 1$	$\lambda = 2$	$\lambda = 3$
$d < 0$	**type** 0^- 3 subtypes	**type** 1^- 2 subtypes	**type** 2^- 1 subtype	—
$d > 0$	—	**type** 1^+ 1 subtype	**type** 2^+ 2 subtypes	**type** 3^+ 3 subtypes

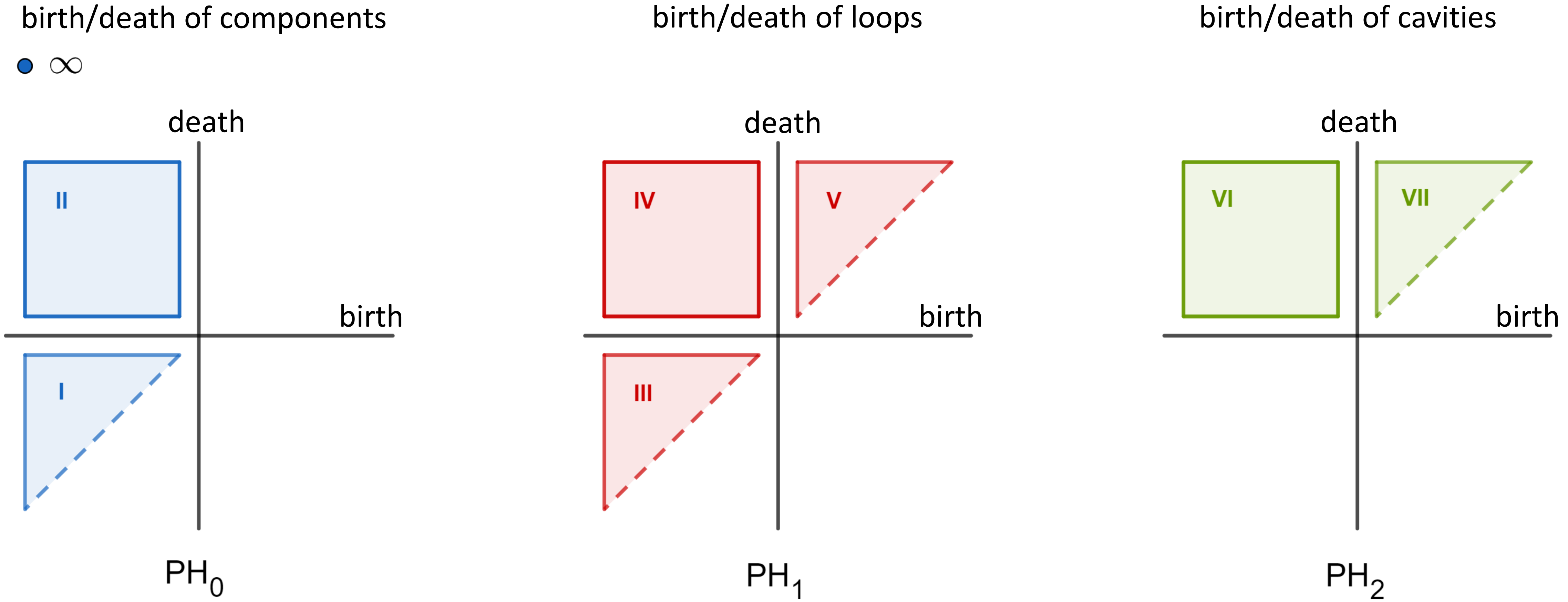
Table: **Classification of NDG critical points of d in dimension 3.**



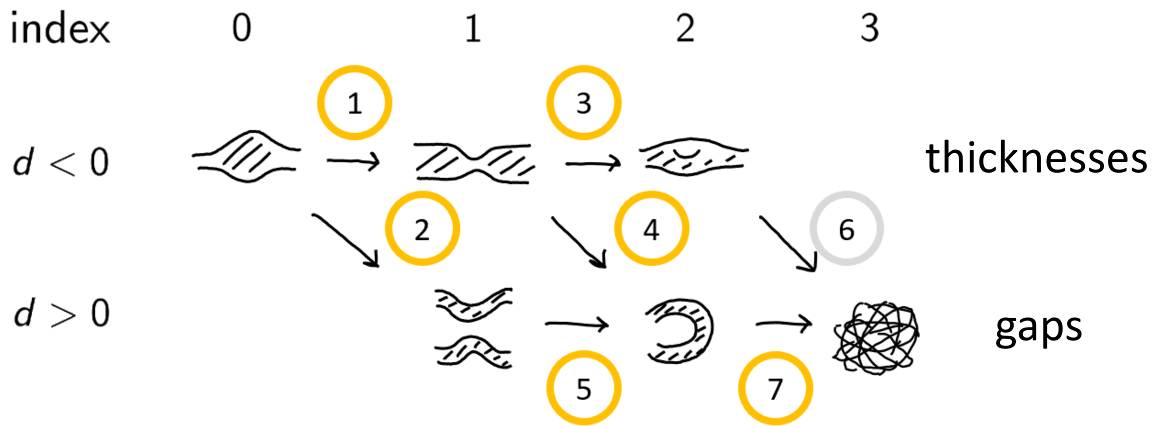
(subtypes)

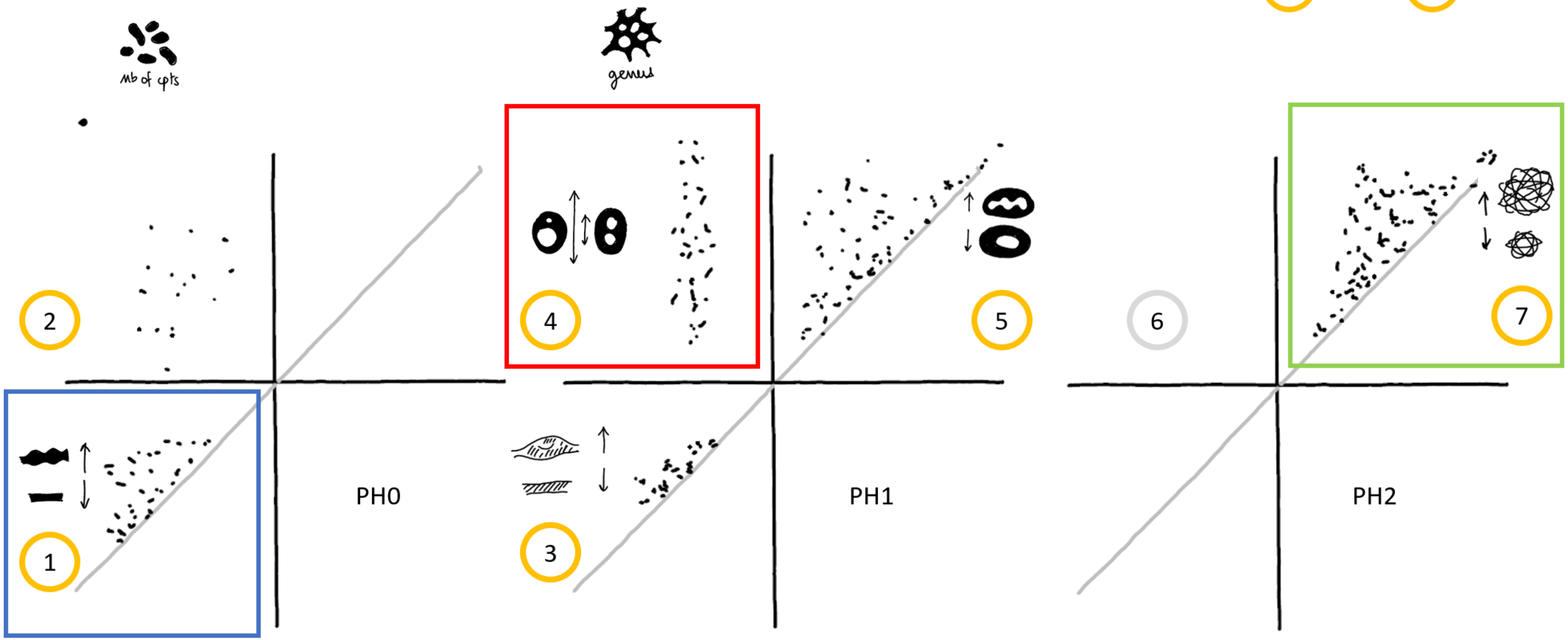
SDPH diagrams in theory





SDPH diagrams in practice





Take-home message

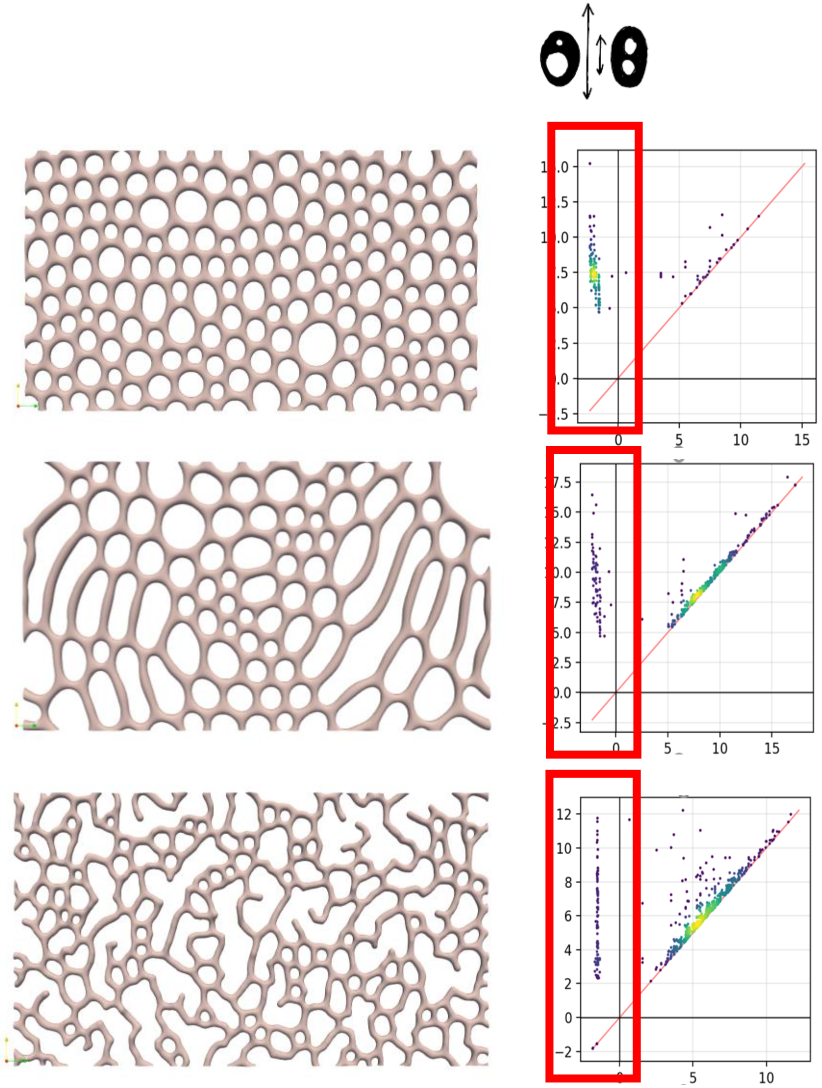
Persistent homology describes shapes by **pairing critical points**.

- one (b,d) point in SDPH diagram = two critical points in the shape
- a critical point is either a creator / destroyer of a topological feature

- each critical point carries a value: a **critical size**
- no need to measure thicknesses and interspaces by hand! no annotation!
- long-lived features are more significant

--> SDPH diagrams quantify the **texture of shapes**

Examples

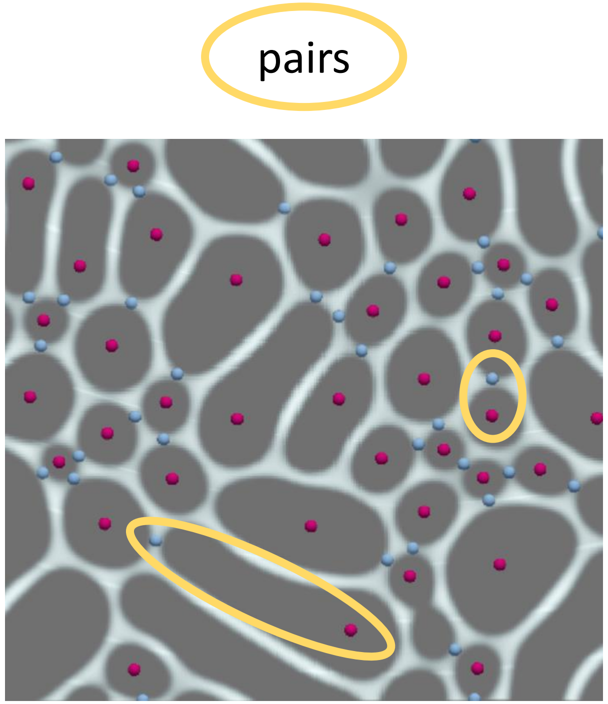


PH1

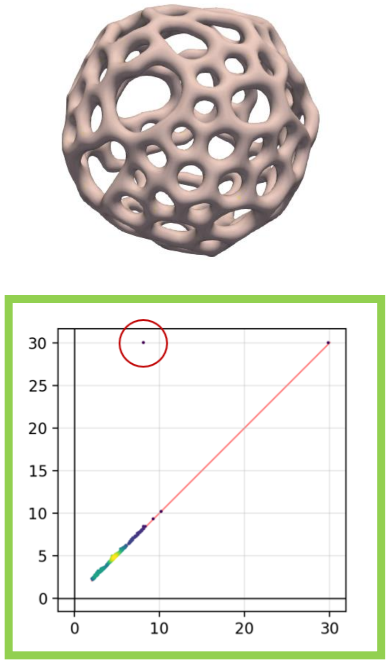
PH1

PH1

Increasing loop heterogeneity induces larger spread in PH1 NW.



Creator-destroyer critical points (blue-red).

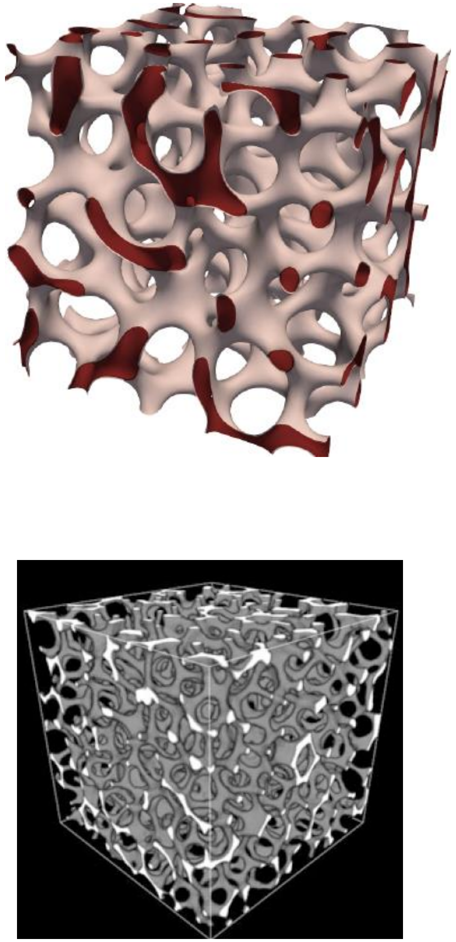


PH2

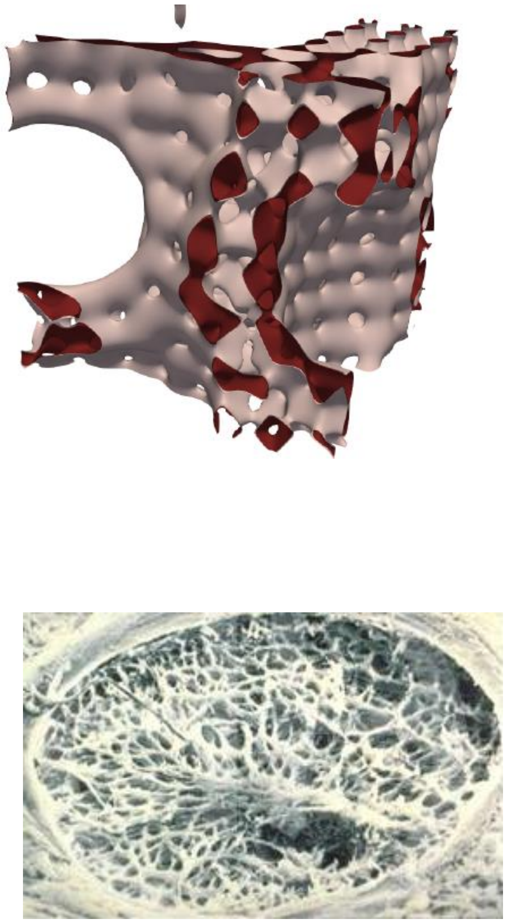
PH2 NE measures bubble interspaces.

By pairing (creator – destroyer) critical points, SDPH quantifies the **texture of shapes.**

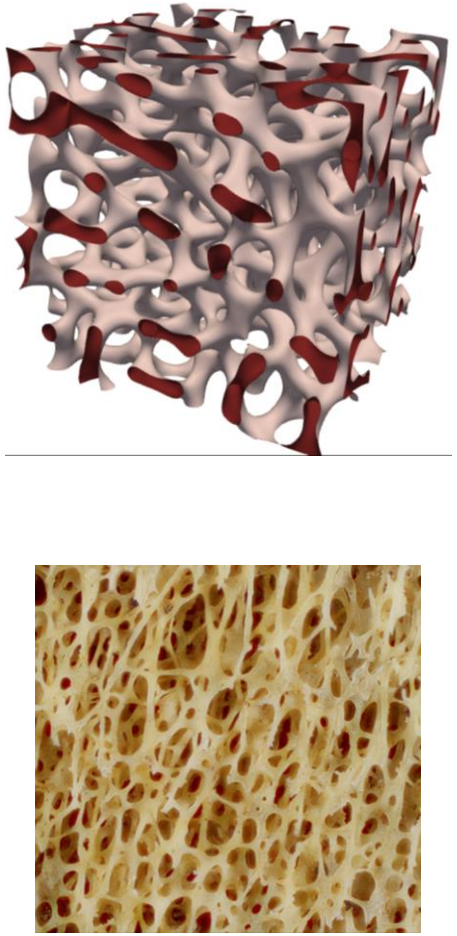
III. Applications to biology and materials science



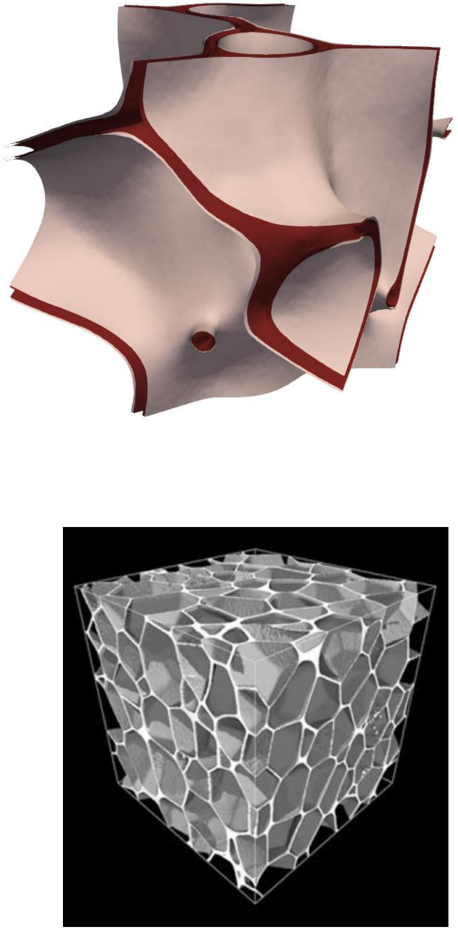
μCT image of open aluminium foam



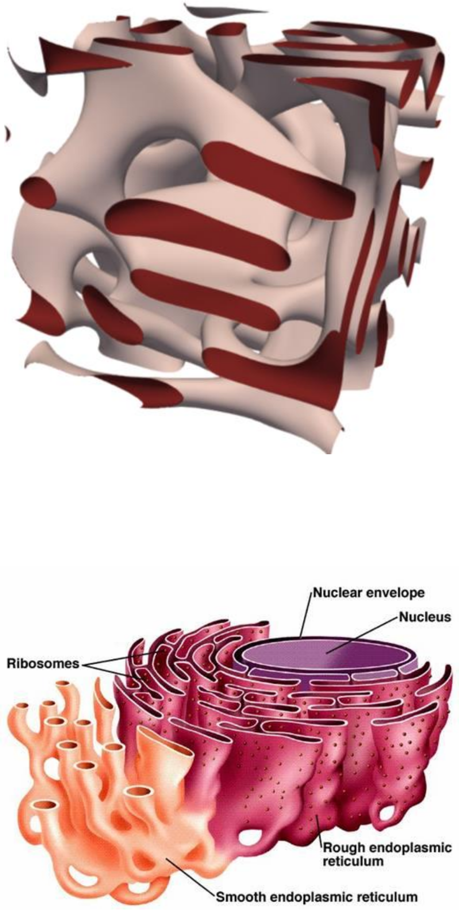
lamina cribrosa behind the eye



trabecular bone

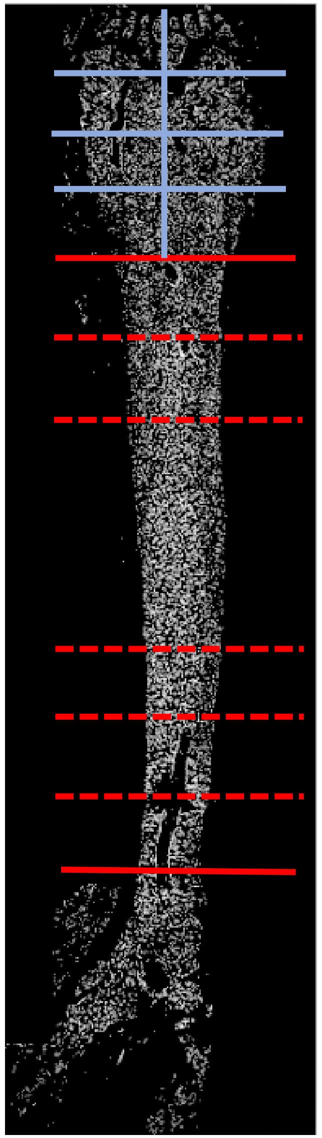


μCT image of closed polymer foam

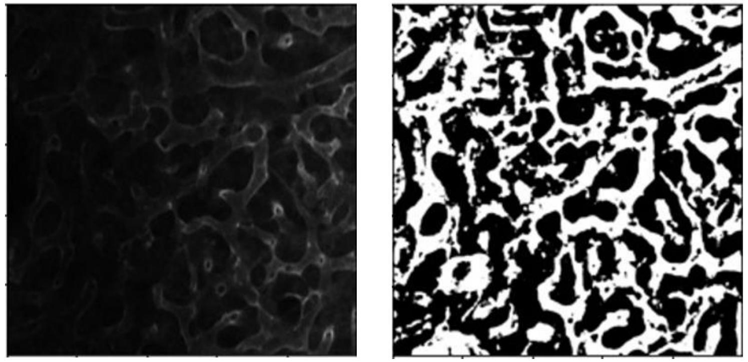


endoplasmic reticulum

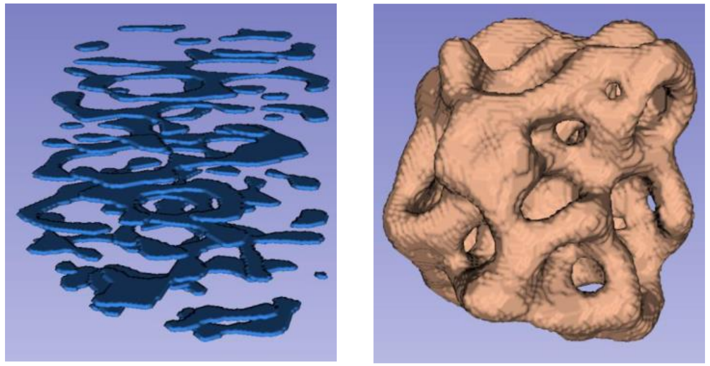
3D data (slices)
300 GB



Application: leukaemia in bone marrow vessels

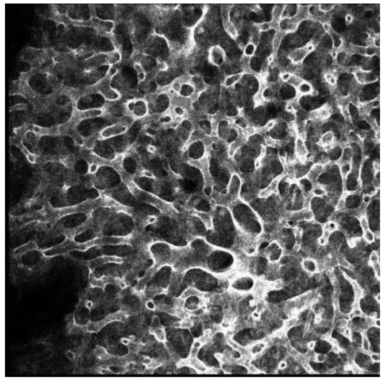


Niblack local thresholding

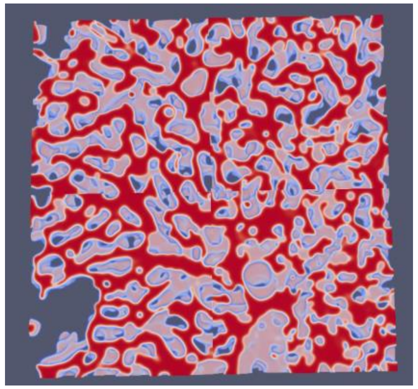


Willmore 3D reconstruction

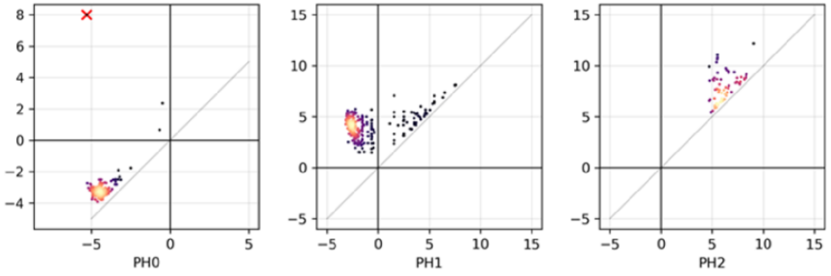
E = Reg + Fid



original data

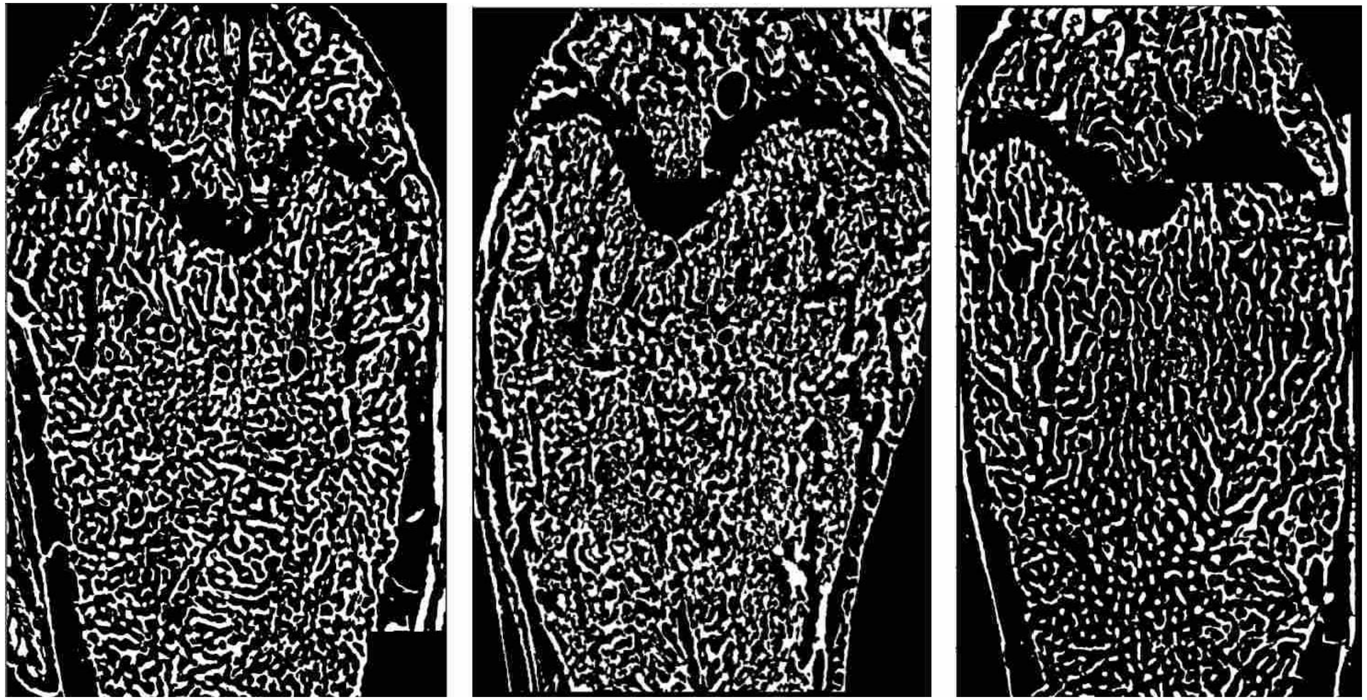


3D segmented data



SDPH diagrams

Vessels at three stages



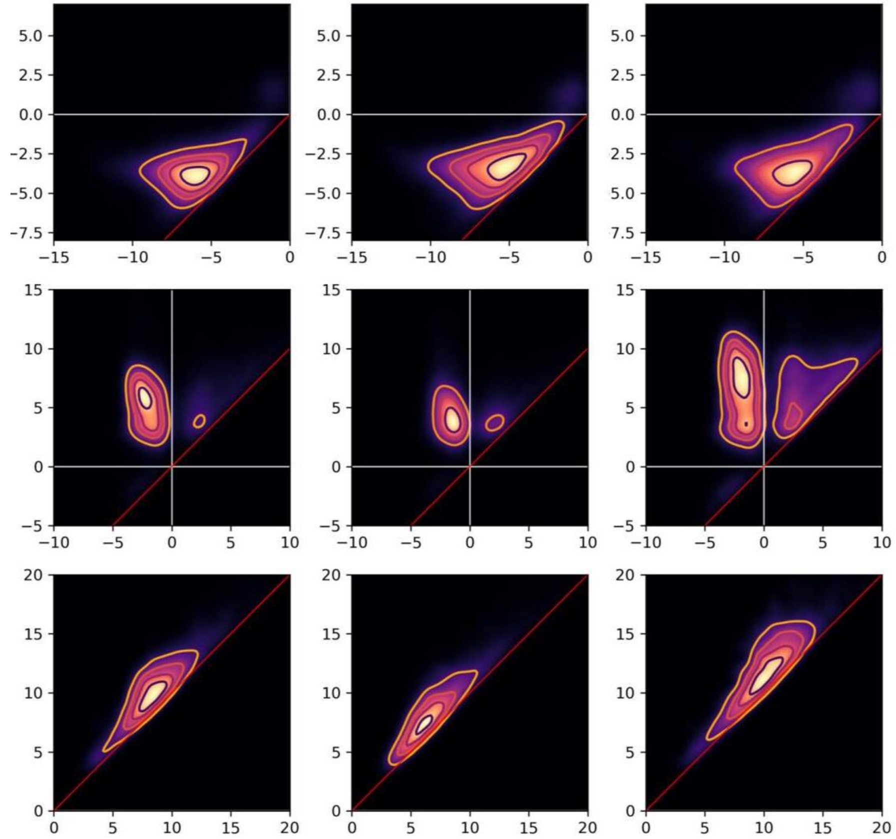
CTRL | Early | Late

CTRL at 0% | U937 at 10% | P2 at 59%

PH0

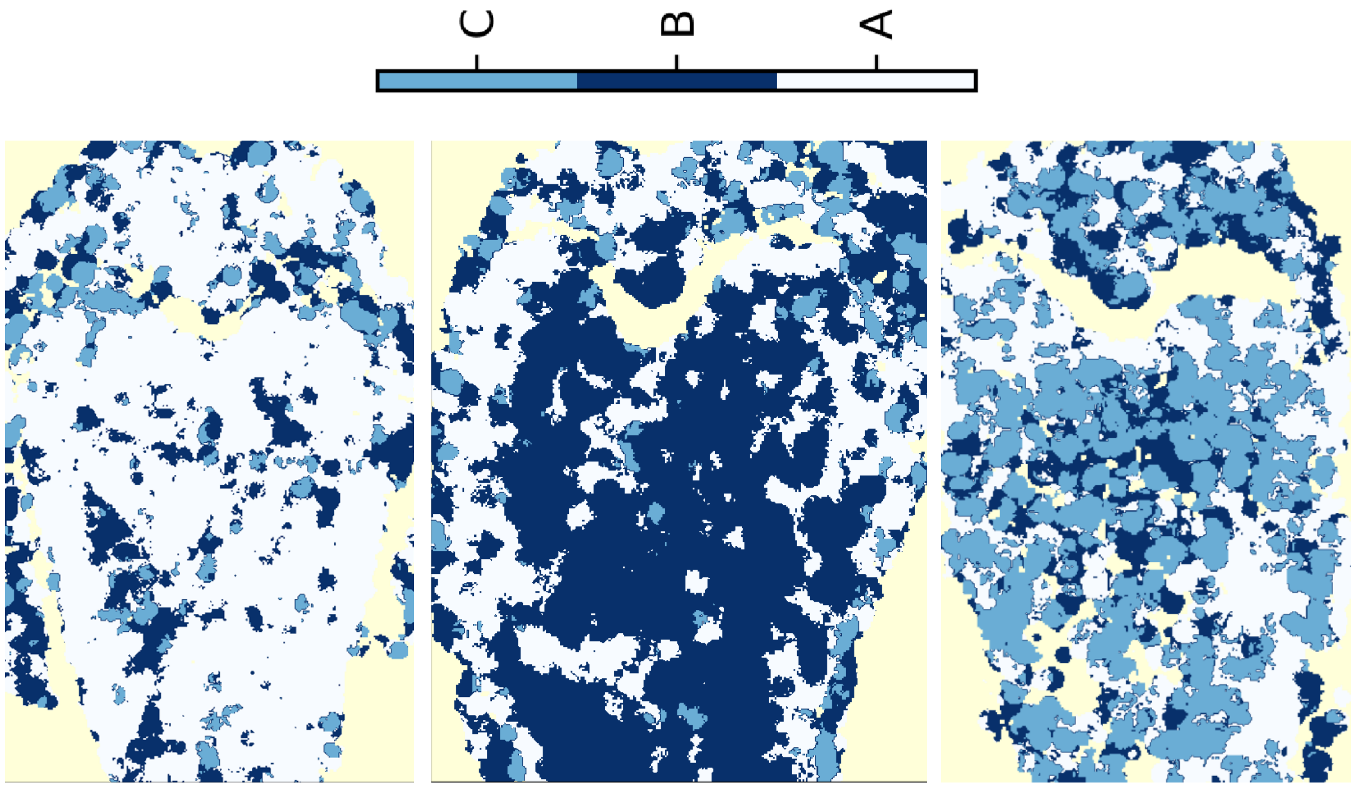
PH1

PH2

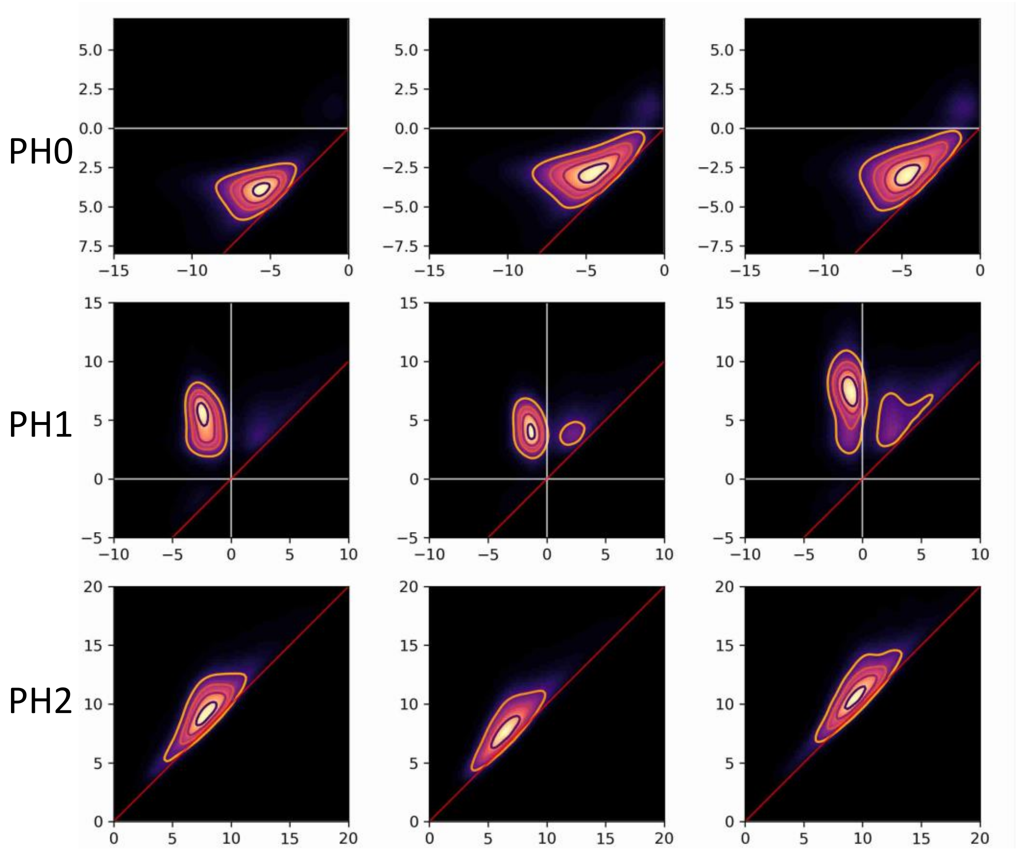


CTRL at 0% | U937 at 10% | P2 at 59%

Spatial texture decomposition



CTRL	Early	Late
CTRL at 0%	U937 at 10%	P2 at 59%

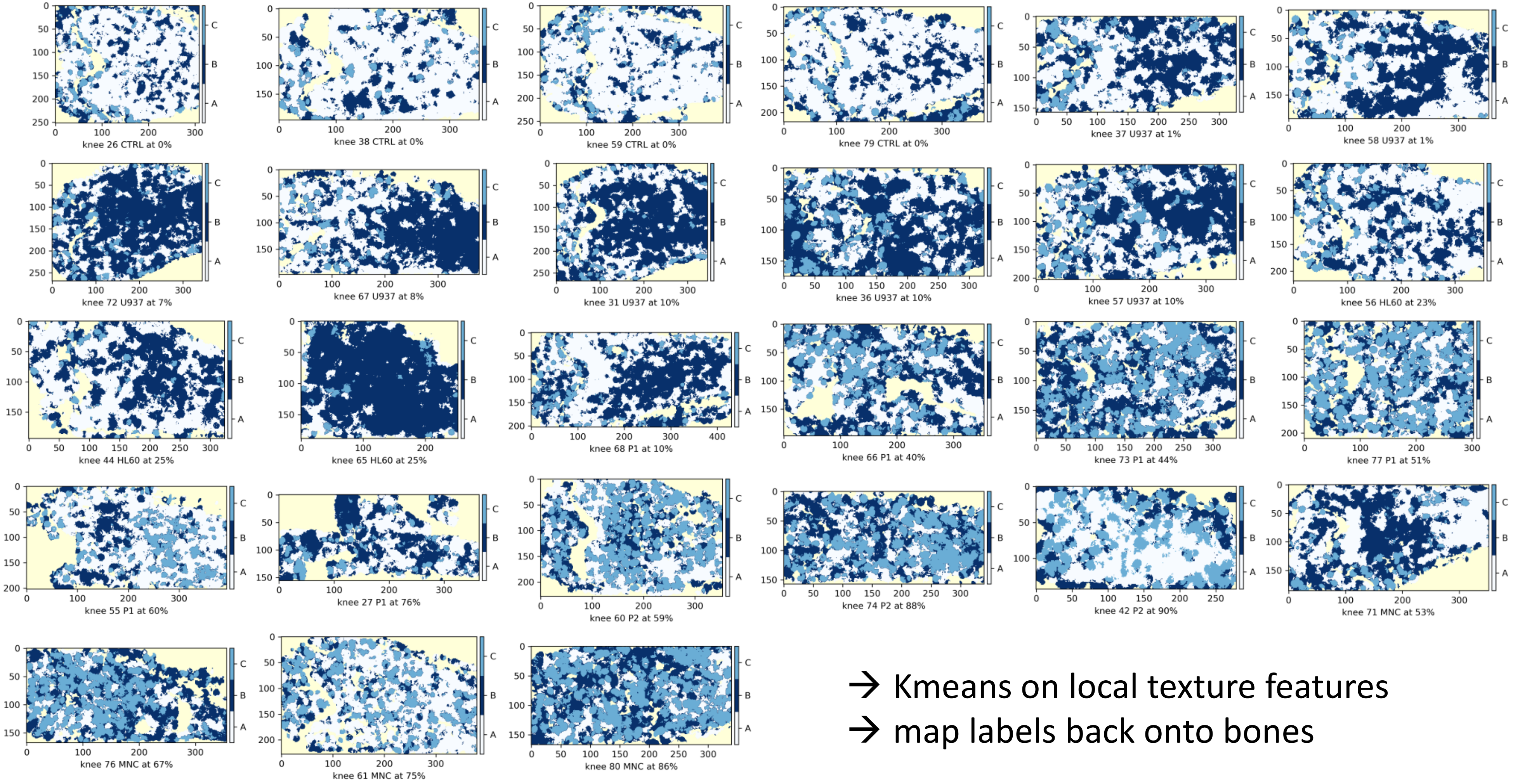


Texture A	Texture B	Texture C

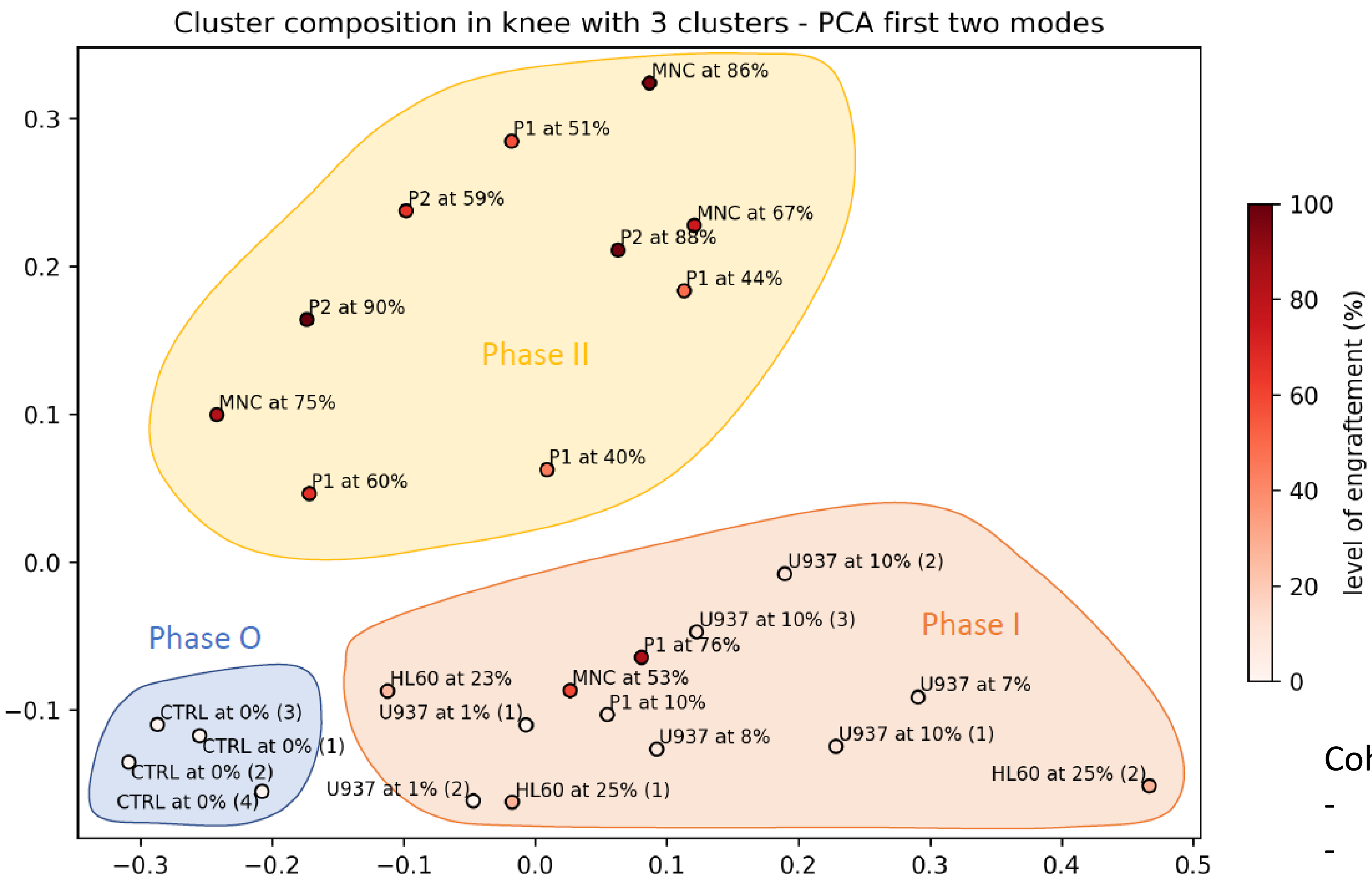
B v.s. A
- angiogenesis
- thin vessels
- small loops
- dense network

C v.s. A
- thin vessels
- heterogeneous loop sizes
- sparser network

Spatial texture decomposition



→ Kmeans on local texture features
→ map labels back onto bones

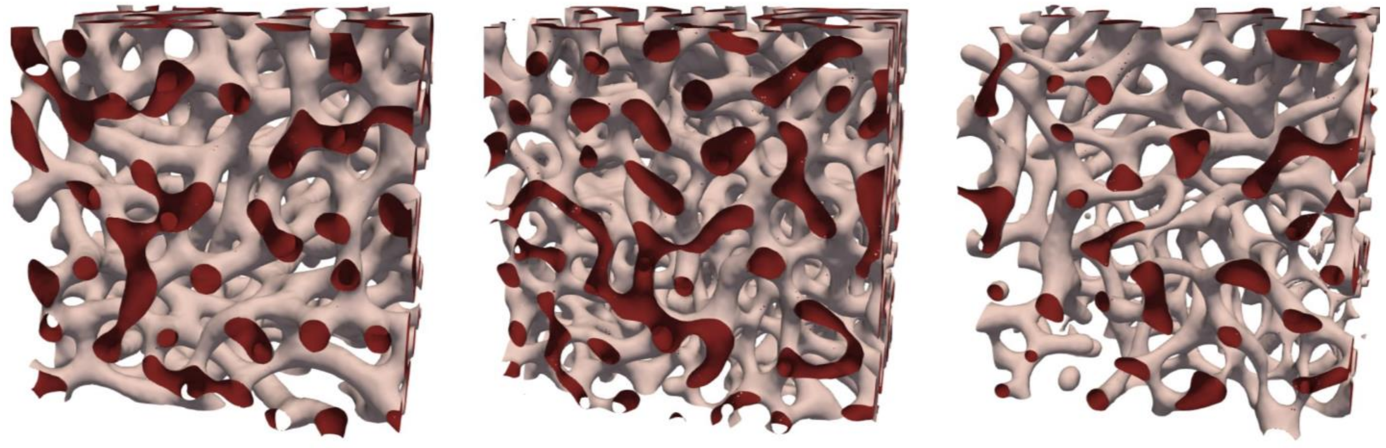


Cohort:

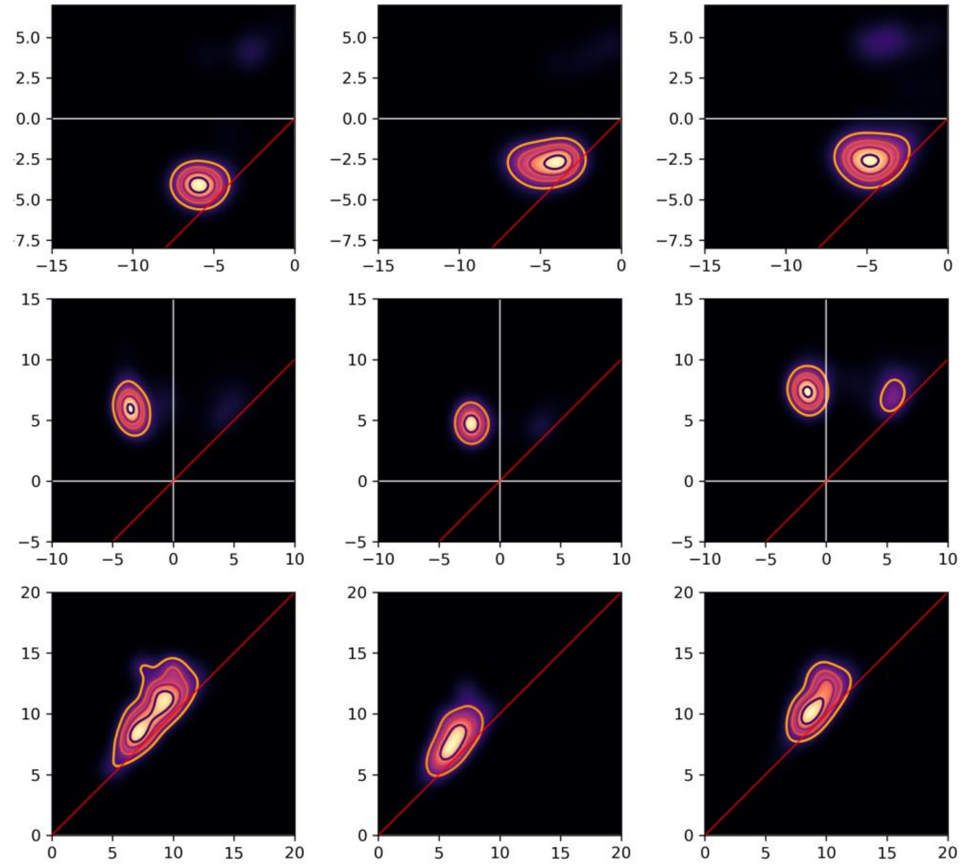
- 4 CTRL (0%)
- 4 MNC (53%-86%)
- 7 U937 (1%-10%)
- 3 HL60 (23%-25%)
- 6 P1 (10%-76%)
- 3 P2 (59%-90%)

Evolution in three phases : Phases O, I, II
Dominant Textures A, B, C

Emulating real textures with curvatubes



Emulated A | Emulated B | Emulated C



Emulated A | Emulated B | Emulated C

Bayesian Optimization w.r.t. SDPH diagrams

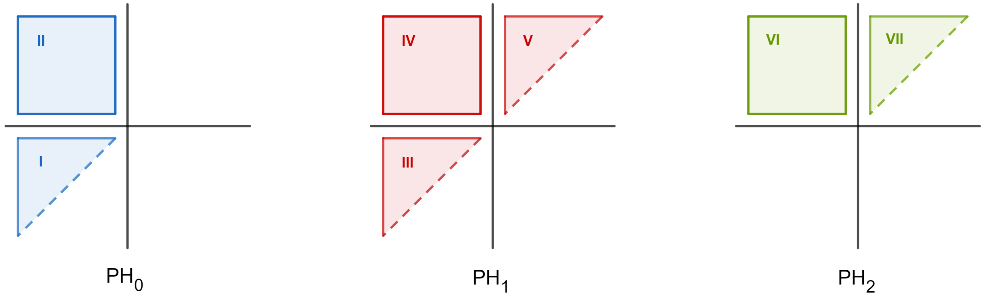
Non-linear impact of AML

Conclusion: what is *texture* in shapes?

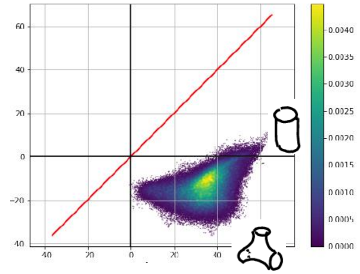
texture = curvatubes parameters

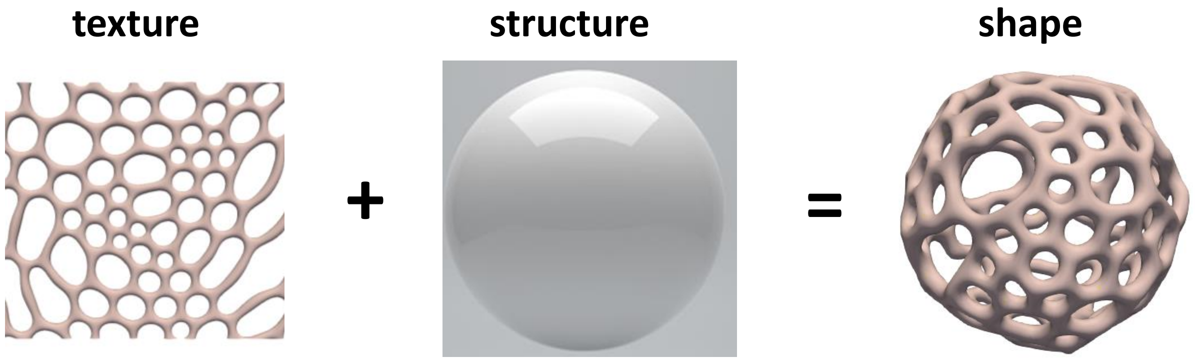
$$\mathbf{F}(\mathcal{S}) = \int_{\mathcal{S}} \left(a_{2,0}\ \kappa_1^2 + a_{1,1}\ \kappa_1\kappa_2 + a_{0,2}\ \kappa_2^2 + a_{1,0}\ \kappa_1 + a_{0,1}\ \kappa_2 + a_{0,0}\right)\ dA$$

= SDPH diagrams



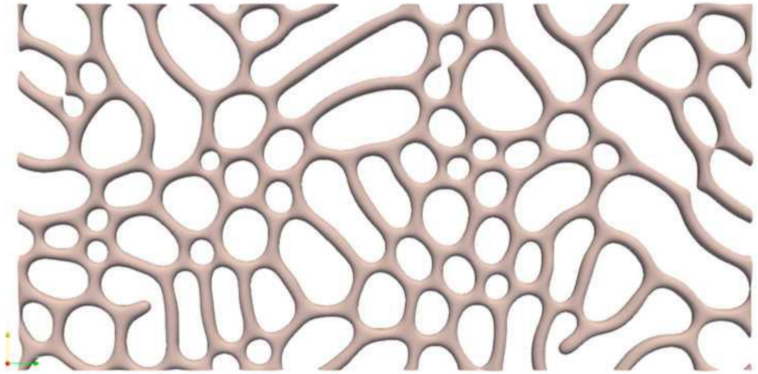
= curvature diagram





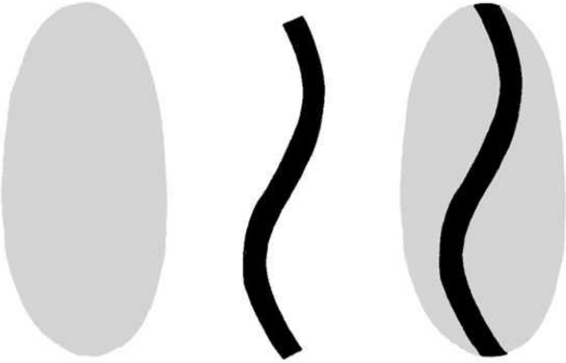
Curvatubes **synthesizes** shape textures
SDPH **quantifies** them

Other project: 3D bioprinting vessels



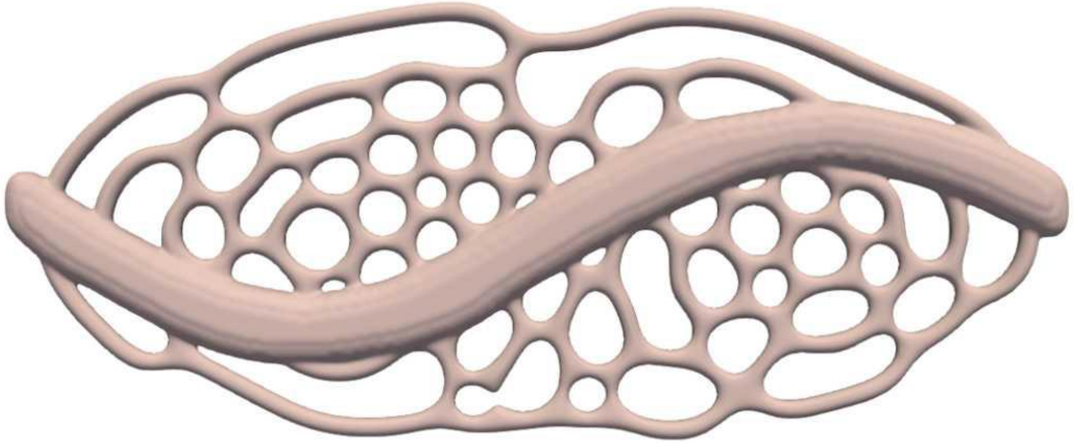
texture

+

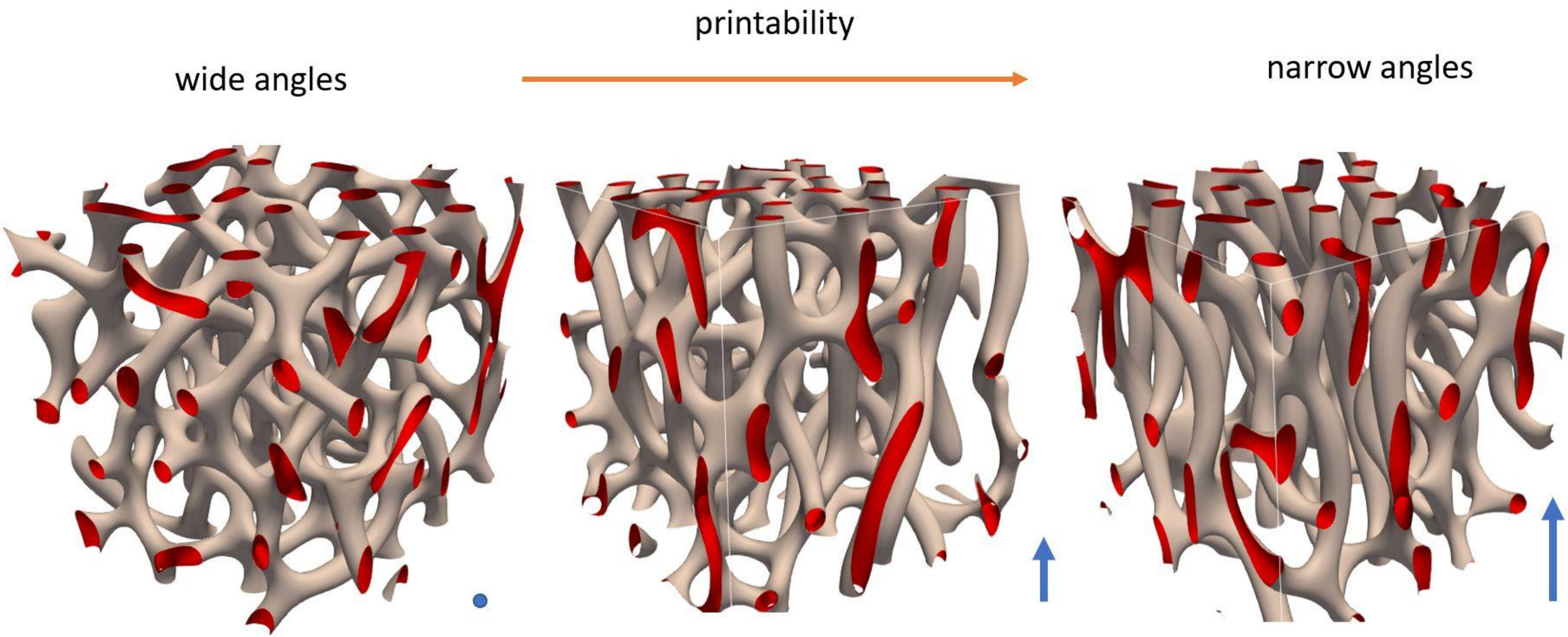


structure

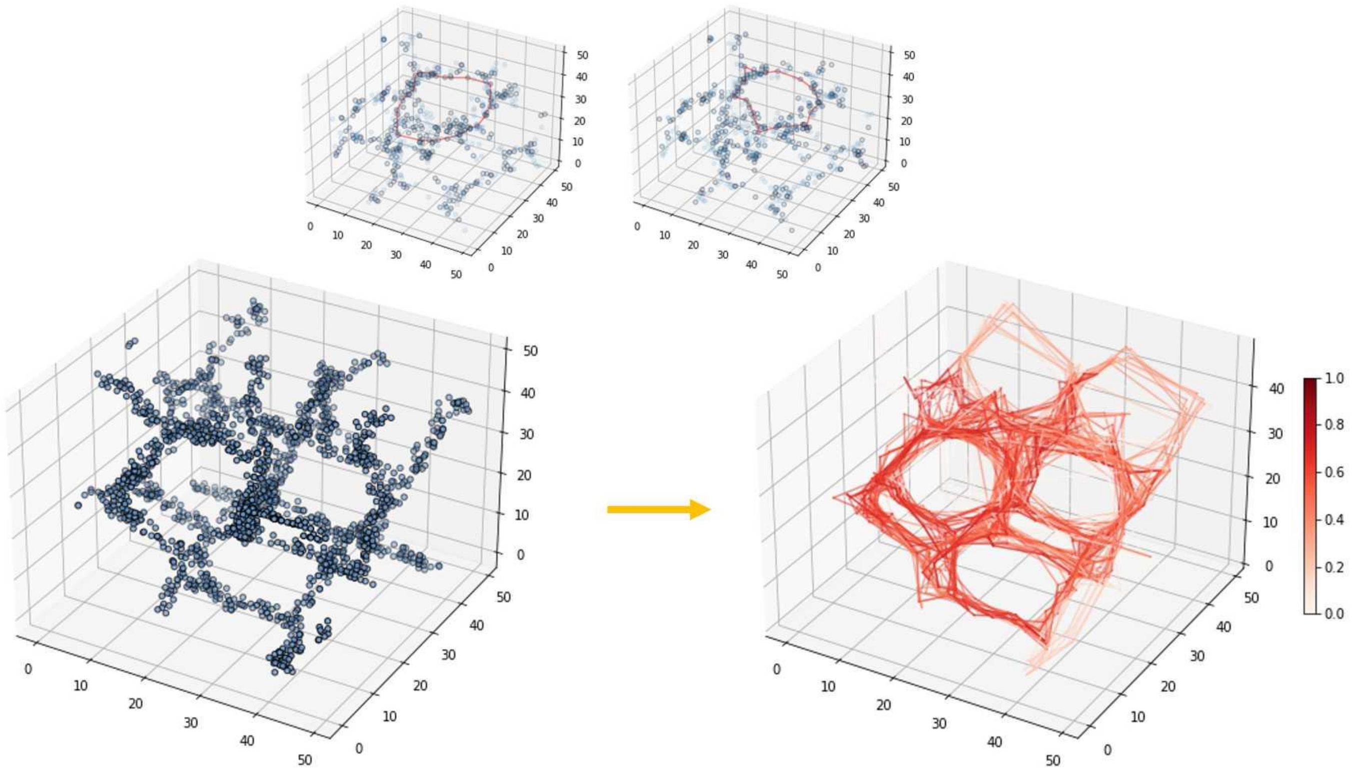
=



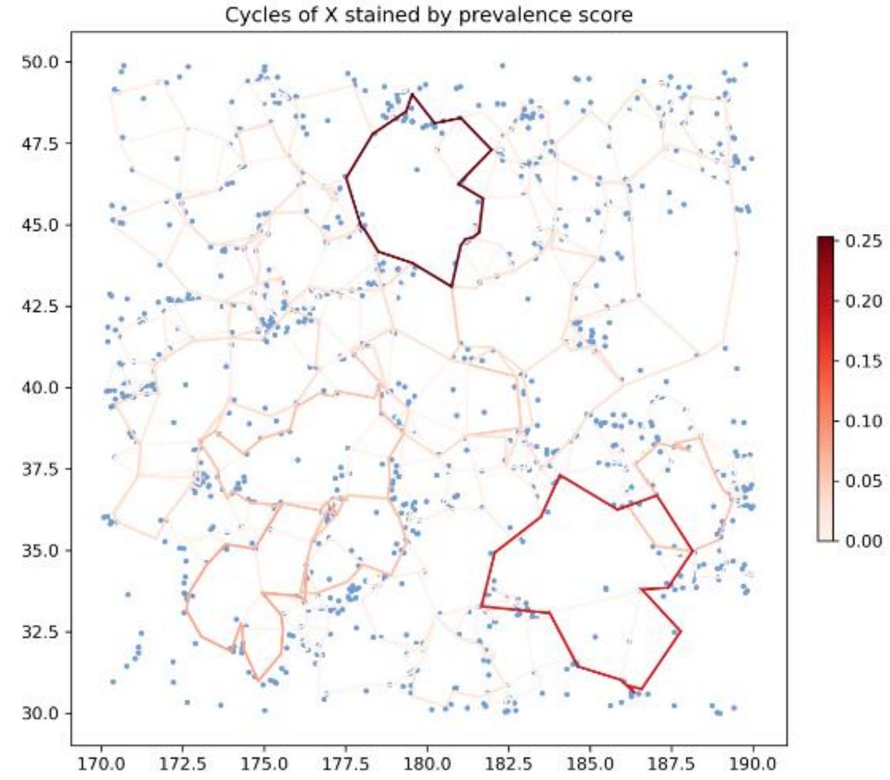
Syed Mian,
Jenny Huang,
Fatihah Mohamad Nor,
Dominique Bonnet,
Christina Dix,
Albane Imbert


printability
wide angles
narrow angles

Other project: Finding “true cycles” in data



network data



cosmic web data

Fast Topological Signal Identification and Persistent Cohomological Cycle Matching, Ines Garcia-Redondo, Anthea Monod, Anna Song (arXiv 2022)

Thank you!

Questions?