Learning the latent spaces dedicated to the segmentation of medical imaging

Application to cardiac imaging

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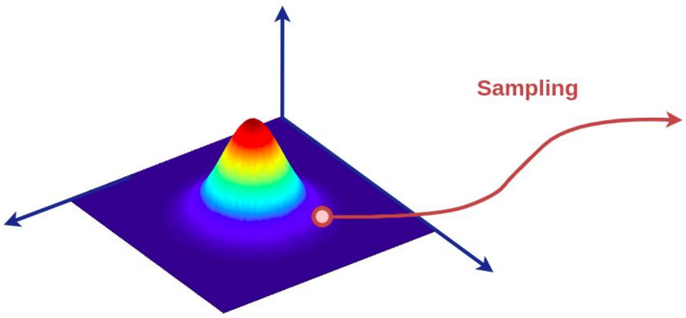
What is the interest of generative models ?

- **How to generate synthetic faces ?**

By modeling the corresponding distribution $p_{\theta}(\cdot)$!

What are the interest of generative models ?

- **How to model complex distributions ?**



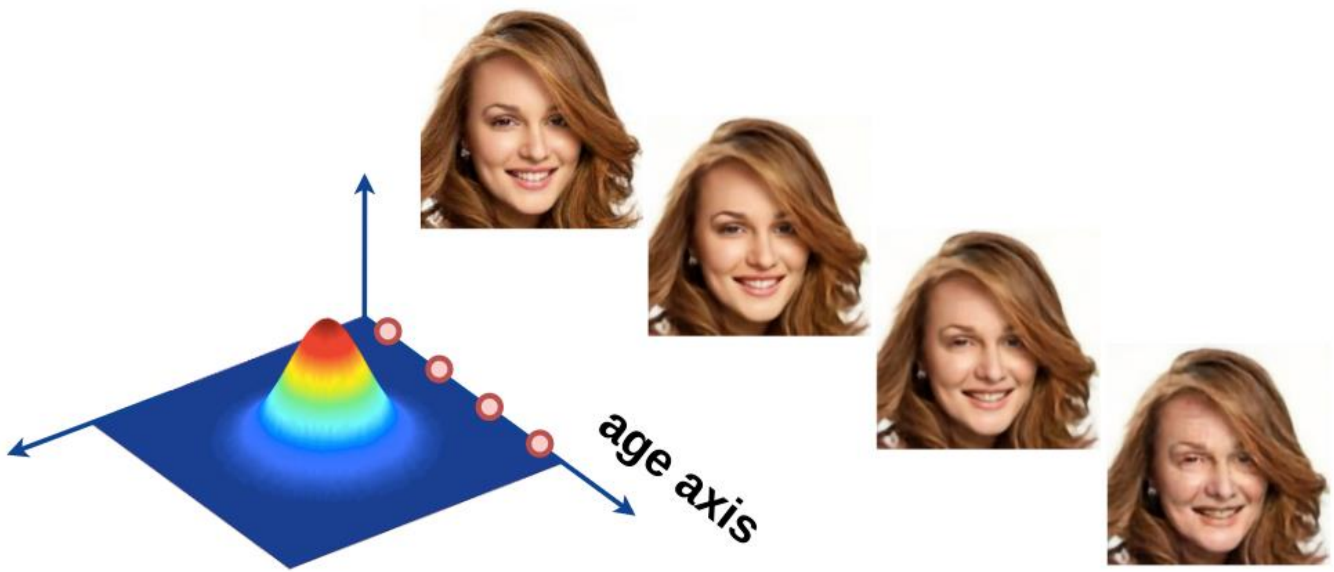
Latent space $z_i \in \mathbb{R}^K$

Face distribution

What are the interest of generative models ?

- **What for ?**

One obsession is to master the latent space !!!



Latent space $z_i \in \mathbb{R}^K$

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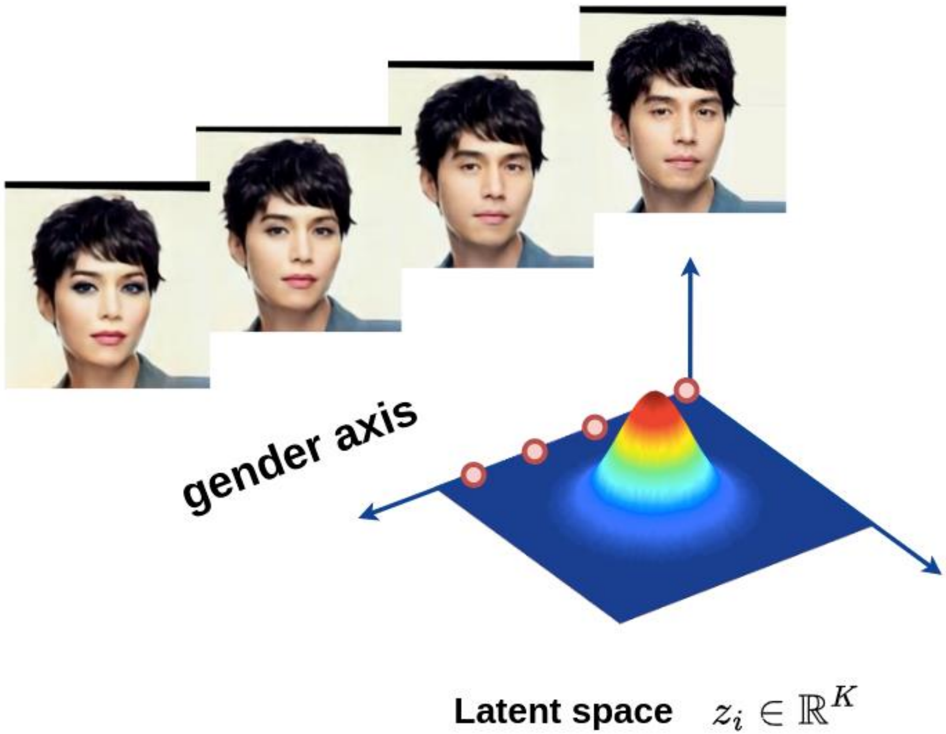
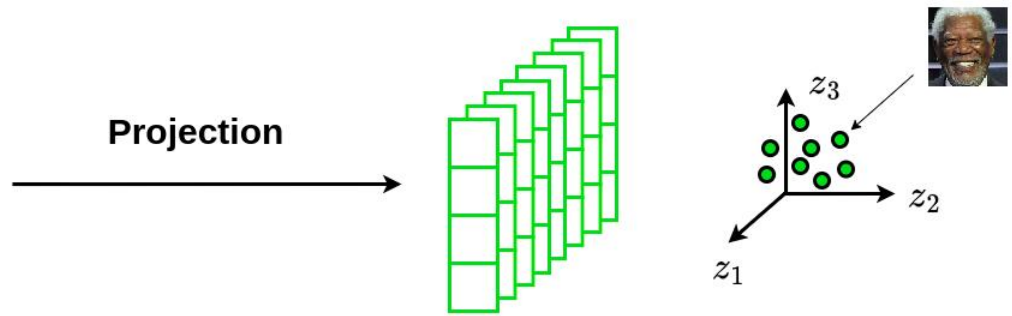


Auto-encoders

How to learn a distribution ?

- Projection into a simpler, lower-dimensional representation space

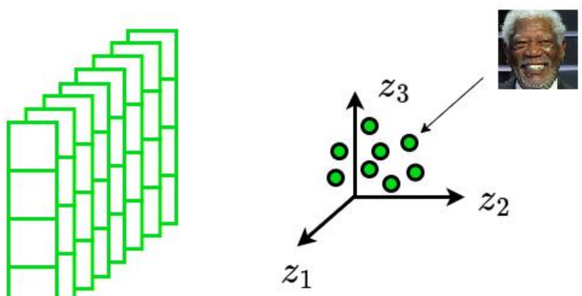
Input space $x_i \in \mathbb{R}^{N \times M}$



Latent space $z_i \in \mathbb{R}^K$

How to learn a complex distribution ?

- **How to have a relevant representation space ?**



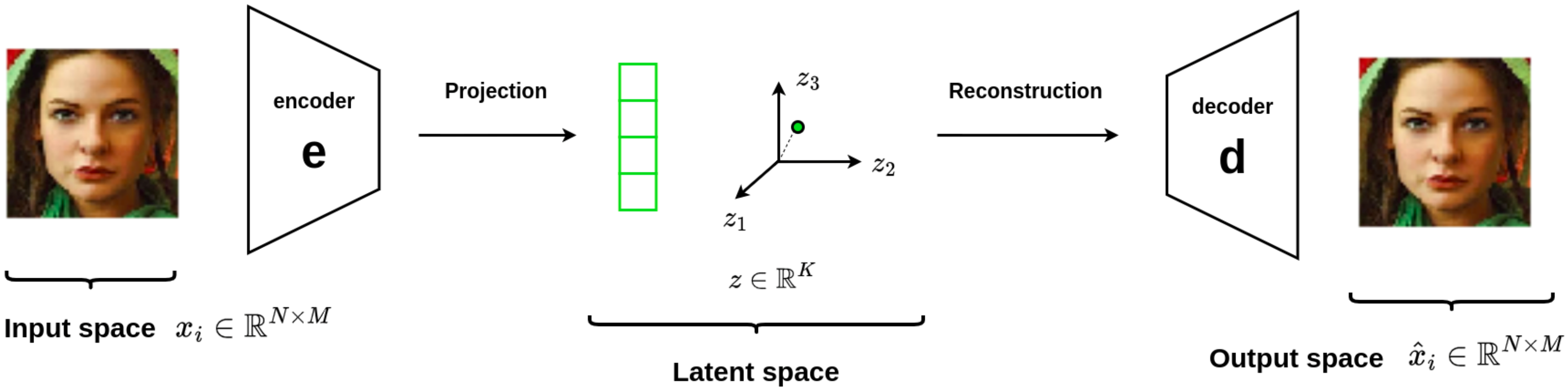
$\xrightarrow{\textbf{Reconstruction}}$

Latent space $z_i \in \mathbb{R}^K$

Output space $\hat{x}_i \in \mathbb{R}^{N \times M}$

Auto-encoder framework

- **Standard architecture**

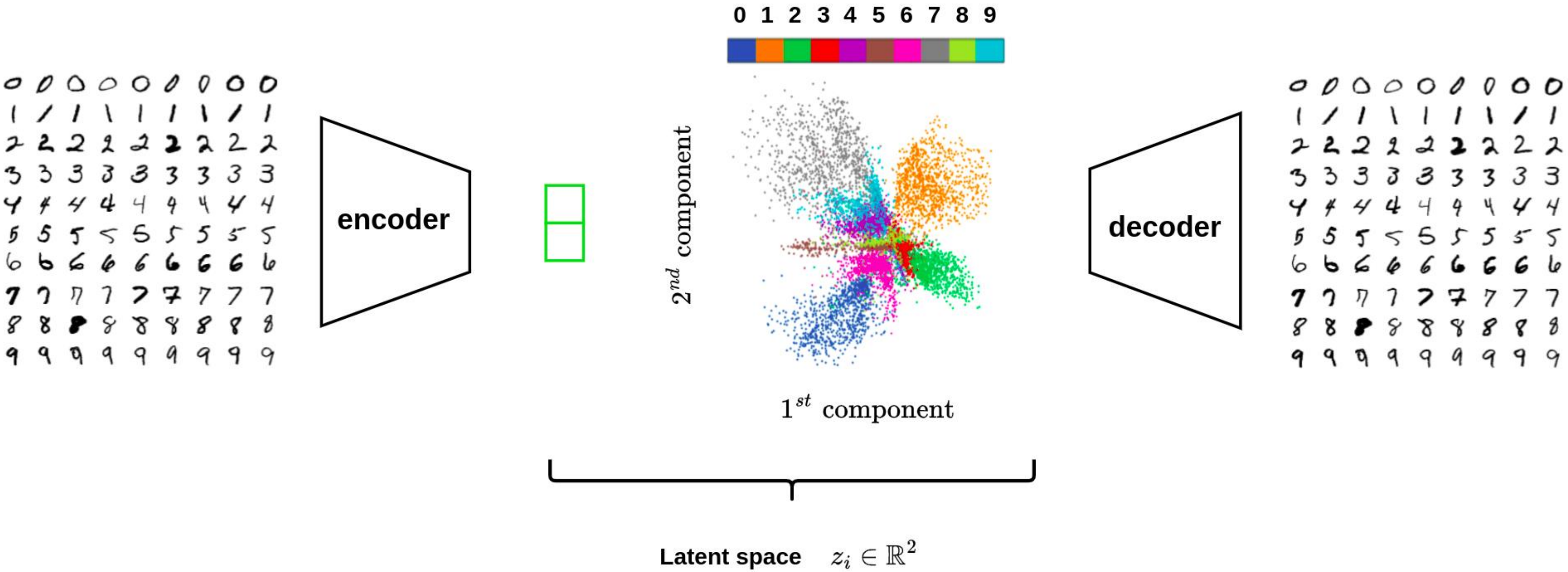


- **Deep learning loss function**

$$\text{loss} = \|x - \hat{x}\|^2$$

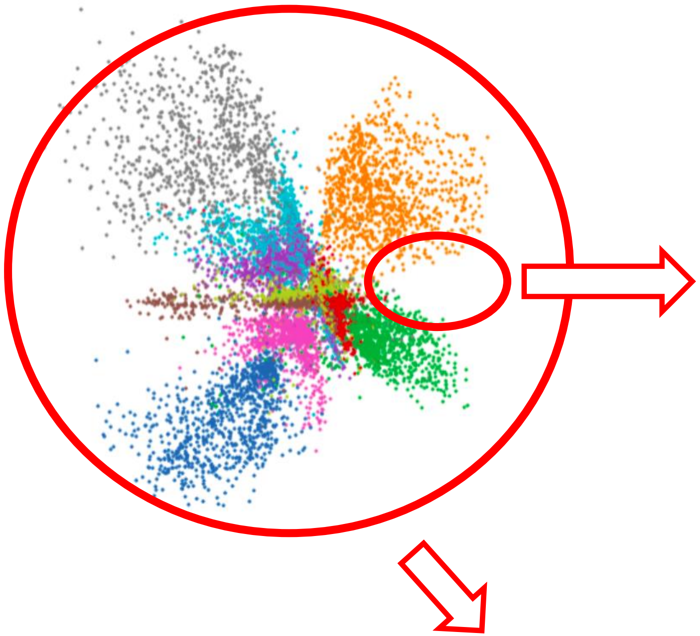
Interest of auto-encoders

- **Generative model**



Limitations

- **Needs to better control the structure of the latent space**

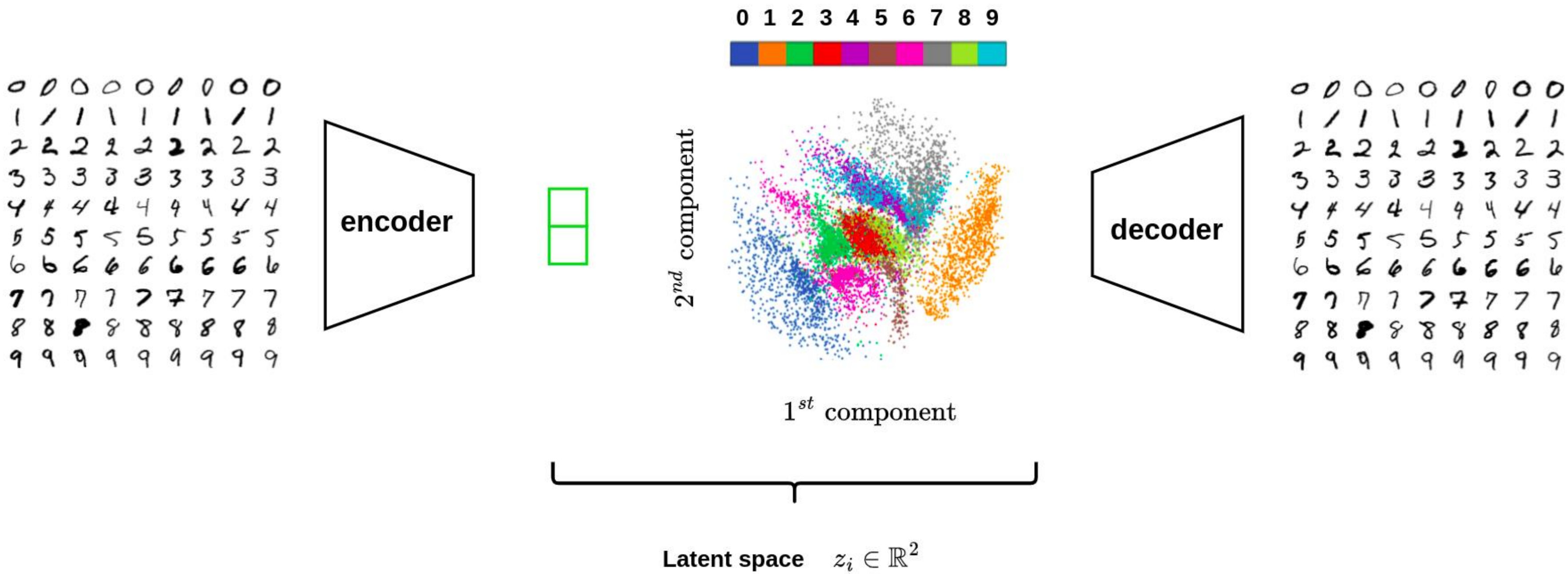


Lack of local continuity

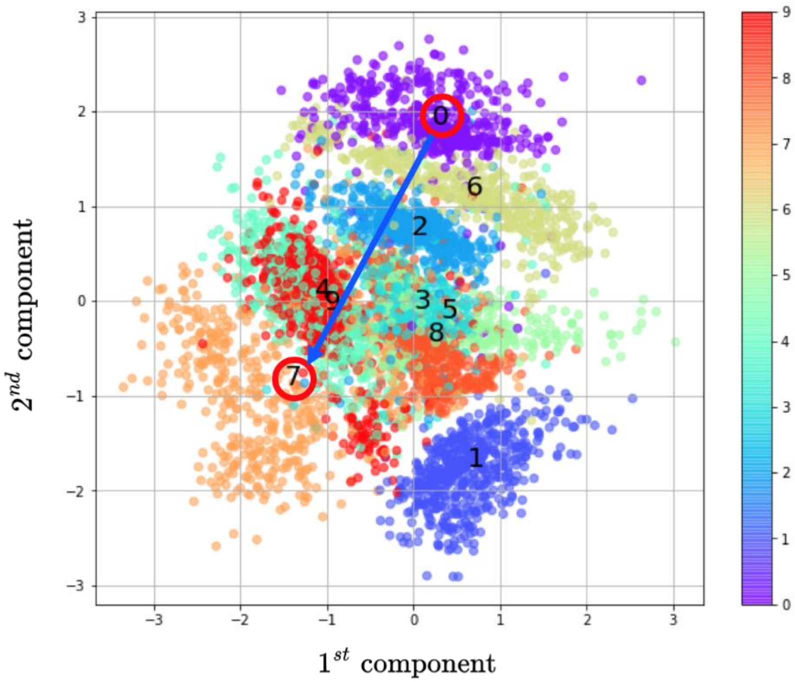
Lack of global completeness

Interest of auto-encoders

- **Generative model with better properties thanks to *variational framework***



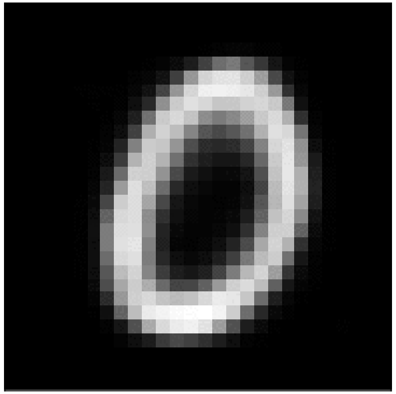
- **Generative model with variational framework**



Linear interpolation into the latent space

$$t \cdot z_0 + (1-t) \cdot z_7, \qquad 0 \leq t \leq 1$$

t=0 %



Variational autoencoders

All the mathematical details are given there !

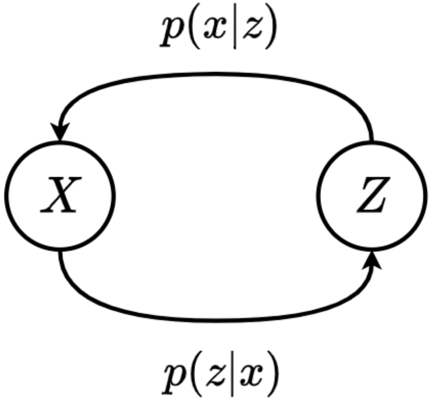
https://creatis-myriad.github.io/tutorials/2022-09-12-tutorial-vae.html

Key concepts

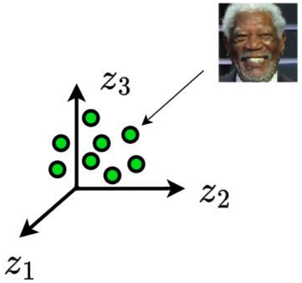
- **Enforcing a structured latent space**
  - → **Through a probabilistic framework**
  - → **By imposing continuity**
  - → **By imposing completeness**

▶ Mathematical formulation

Observation variables



Hidden variables



Approximation of $p(z|x)$ through a variational inference technique

Probabilistic framework

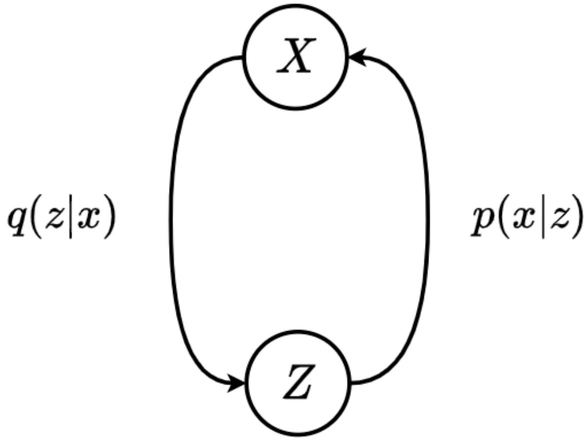
- **Hypotheses**

  - → $q(z|x)$ **is modeled by an axis-aligned Gaussian distribution**

  - → $q(z|x) = \mathcal{N}\left(\mu_x, \sigma_x\right) = \mathcal{N}\left(g(x), diag(h(x))\right)$

$$\boxed{(g^*, h^*) = \underset{(g,h)}{\arg\min}\ D_{KL}\left(q(z|x) \parallel p(z|x)\right)}$$

$D_{KL}\left(\cdot \parallel \cdot\right)$ *Kullback-Liebler divergence function*



Probabilistic framework

- **Optimization process**

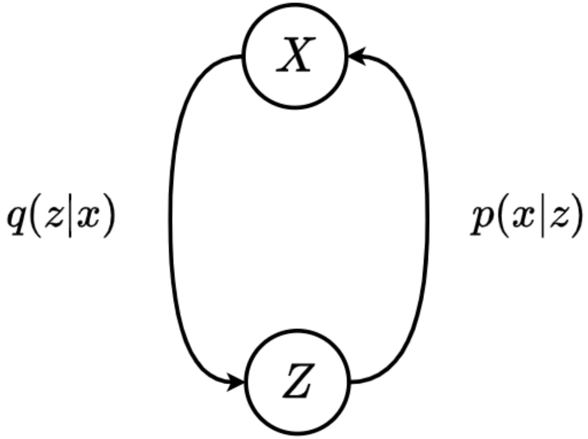
  → **Maximization of the Evidence Lower Bound (ELBO)**

$$\mathcal{L} = \mathbb{E}_{z\sim q_x}\left[log\left(p(x|z)\right)\right] - D_{KL}\left(q(z|x) \parallel p(z)\right)$$

  → **By exploiting gaussian assumption**

$$p(x|z) = \mathcal{N}\left(f(z), cI\right)$$

$$\mathcal{L} \propto \mathbb{E}_{z\sim q_x}\left[-\alpha\|x - f(z)\|^2\right] - D_{KL}\left(q(z|x) \parallel p(z)\right)$$



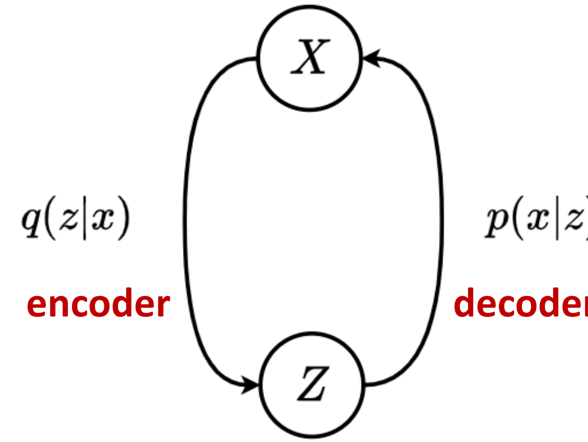
Probabilistic framework

- **Optimization process**

$$(f^*, g^*, h^*) = \underset{(f,g,h)}{\arg\min} \left(\mathbb{E}_{z \sim q_x} \left[\alpha \|x - f(z)\|^2 \right] + D_{KL} \left(q(z|x) \parallel p(z) \right) \right)$$

- **Deep learning loss function**

$$\text{loss} = \alpha \|x - f(z)\|^2 + D_{KL} \left(\mathcal{N} \left(g(x), diag \left(h(x) \right) \right), \mathcal{N}(0, I) \right)$$



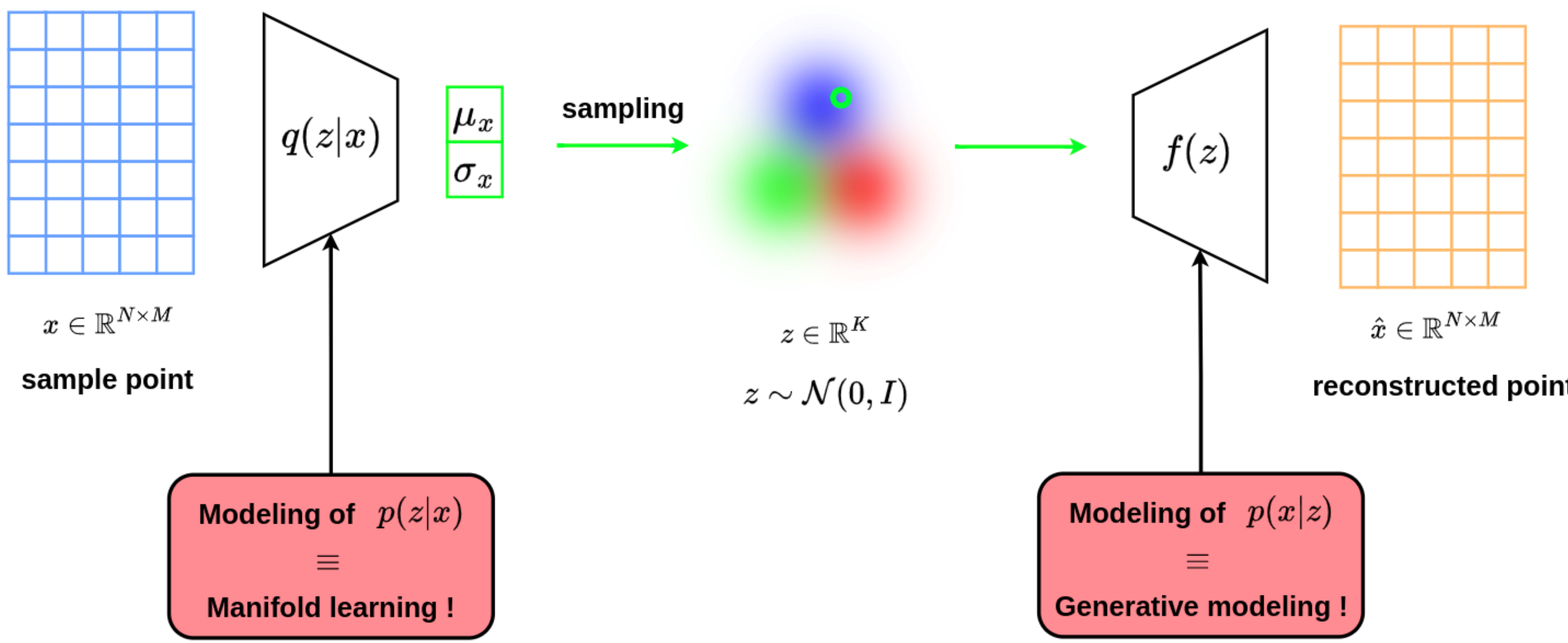
→ $g(\cdot)$ **and** $h(\cdot)$ **are modeled through an encoder**

→ $f(\cdot)$ **is modeled through a decoder**

Probabilistic framework

- **Loss interpretation**

$$\text{loss} = D_{KL}\left(\mathcal{N}\left(g(x), diag\left(h(x)\right)\right), \mathcal{N}\left(0, I\right)\right) + \alpha\|x - f(z)\|^2$$



Probabilistic framework

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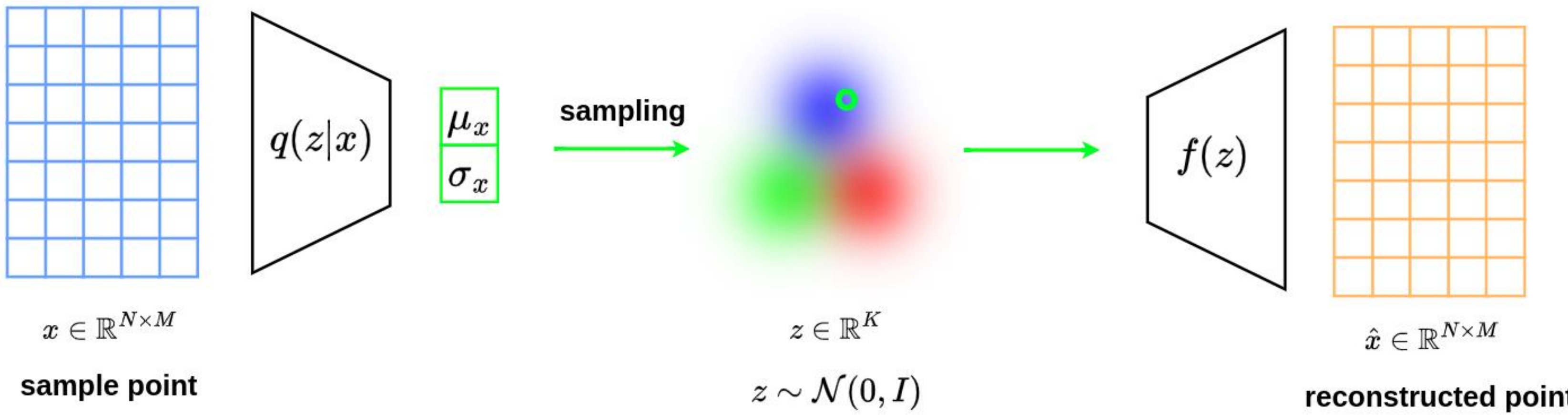


→ $\mathcal{N}\left(g(x), h(x)\right)$ **imposes local** ***continuity***

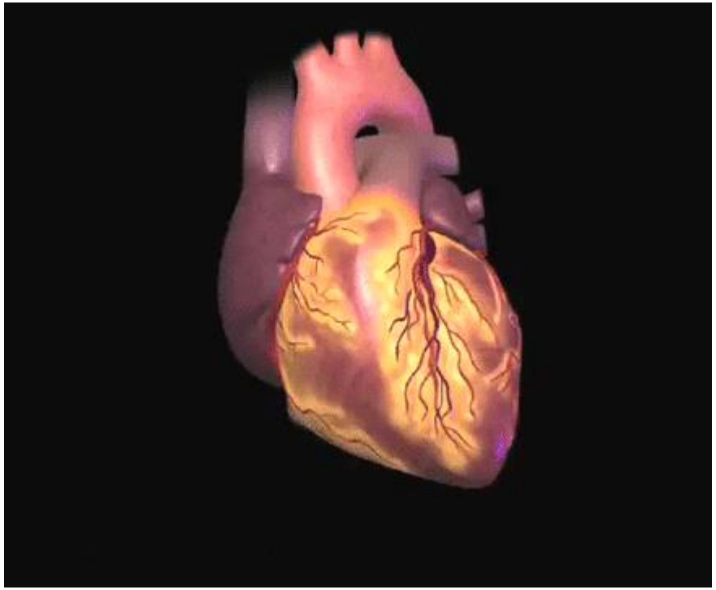
→ $\mathcal{N}\left(\cdot, \mathcal{N}(0, I)\right)$ **imposes global** ***completeness***

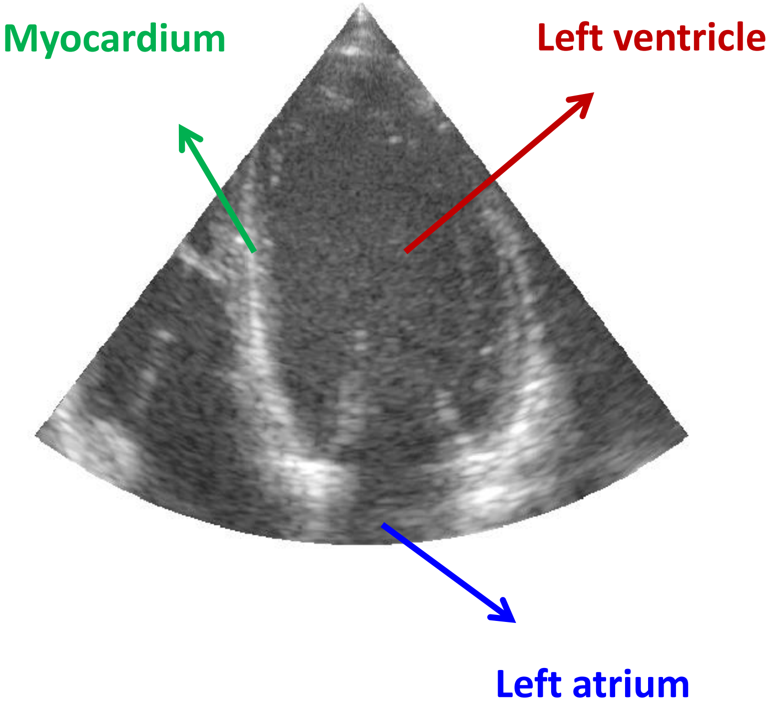
Practical applications

The obsession is to master the latent space !!!

Needs for accurate and robust segmentation of cardiac structures

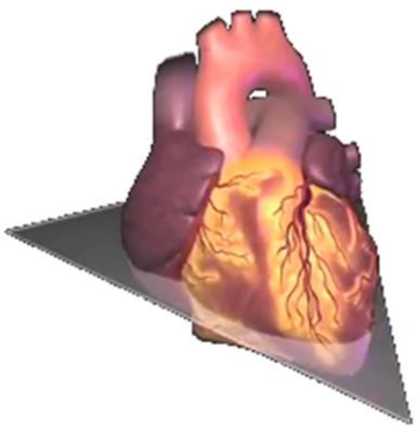
- **Quantification of clinical indices from echocardiographic images**



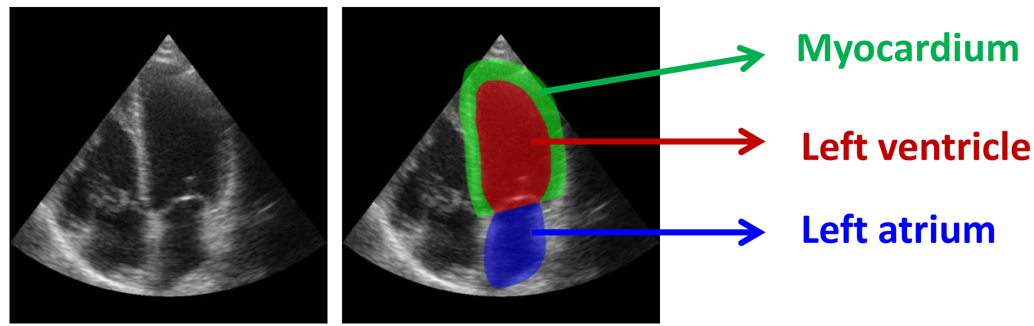


Needs for accurate and robust segmentation of cardiac structures

▶ Anatomical clinical indices



Apical views

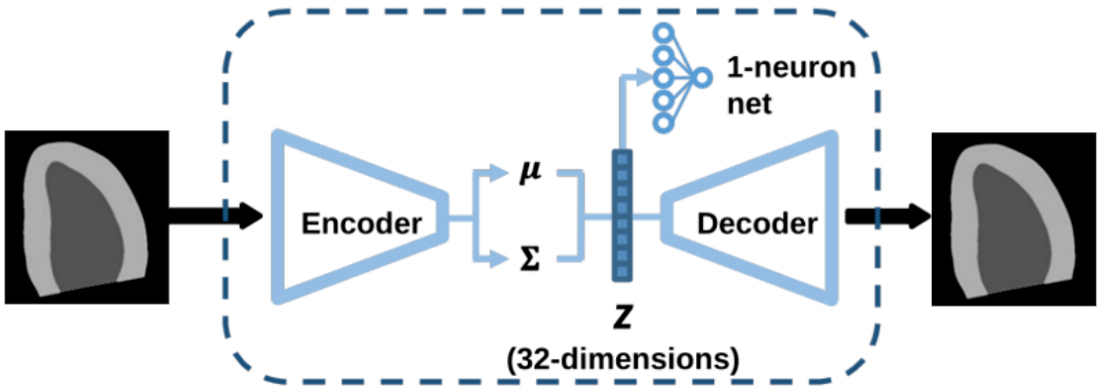


- ➔ **Left ventricle volumes**
- ➔ **Left ventricle ejection fraction**

How to guarantee the anatomical coherence ?

- **Constrained Variational Auto Encoder**
  - **Approximation of a latent space with local linear properties**

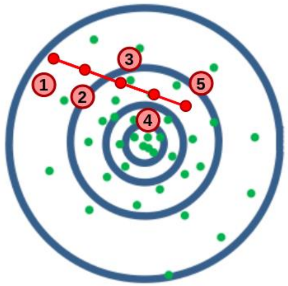
Use of a 1-neuron net to reinforce the linearity of the latent space

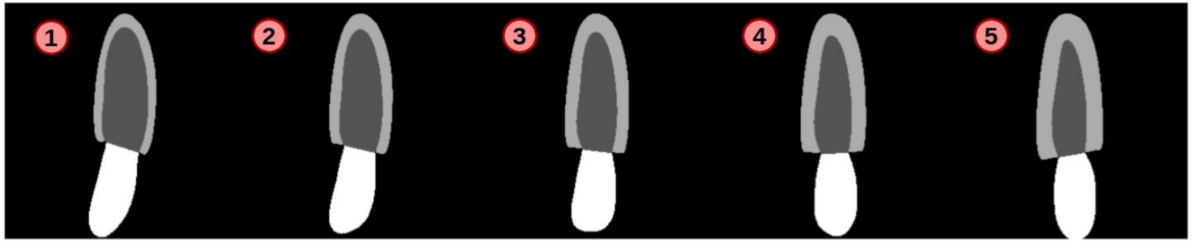


▶ Constrained Variational Auto Encoder

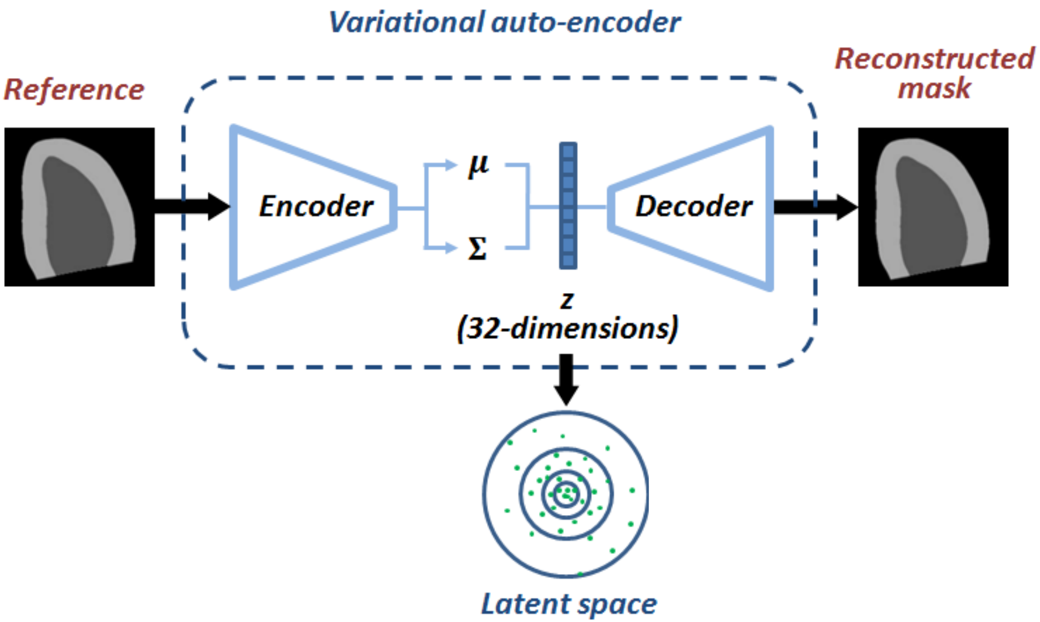
- **Approximation of a latent space with local linear properties**
  - ➔ **Linear interpolation in the latent space makes sense**

Constrained latent space





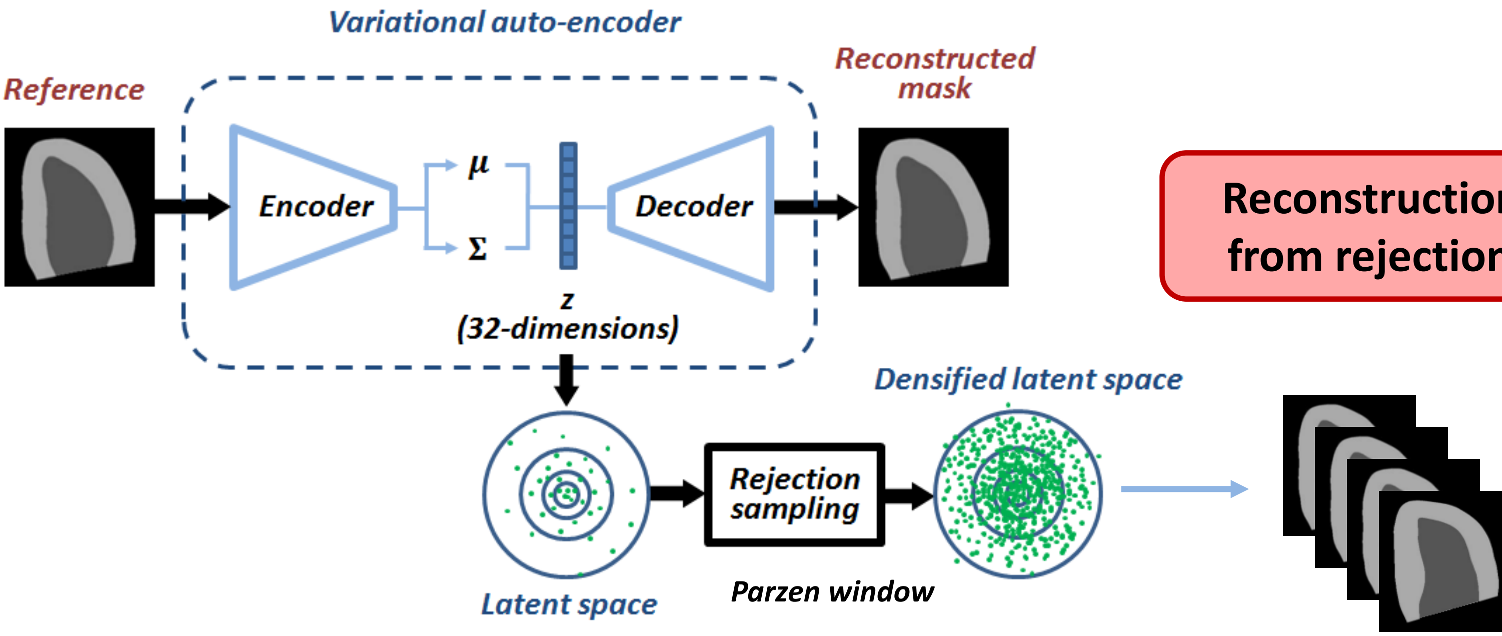
Cardiac segmentation with strong anatomical guarantees [Painchaud, IEEE TMI, 2020]



Efficient encoding of anatomical shapes in a latent space

Cardiac segmentation with strong anatomical guarantees

[Painchaud, IEEE TMI, 2020]

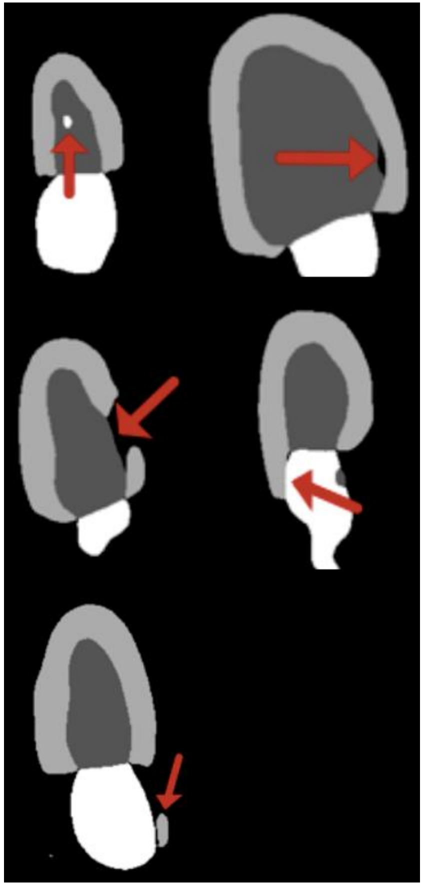


Reconstruction of masks from rejection sampling

Densified latent space with 5 million points

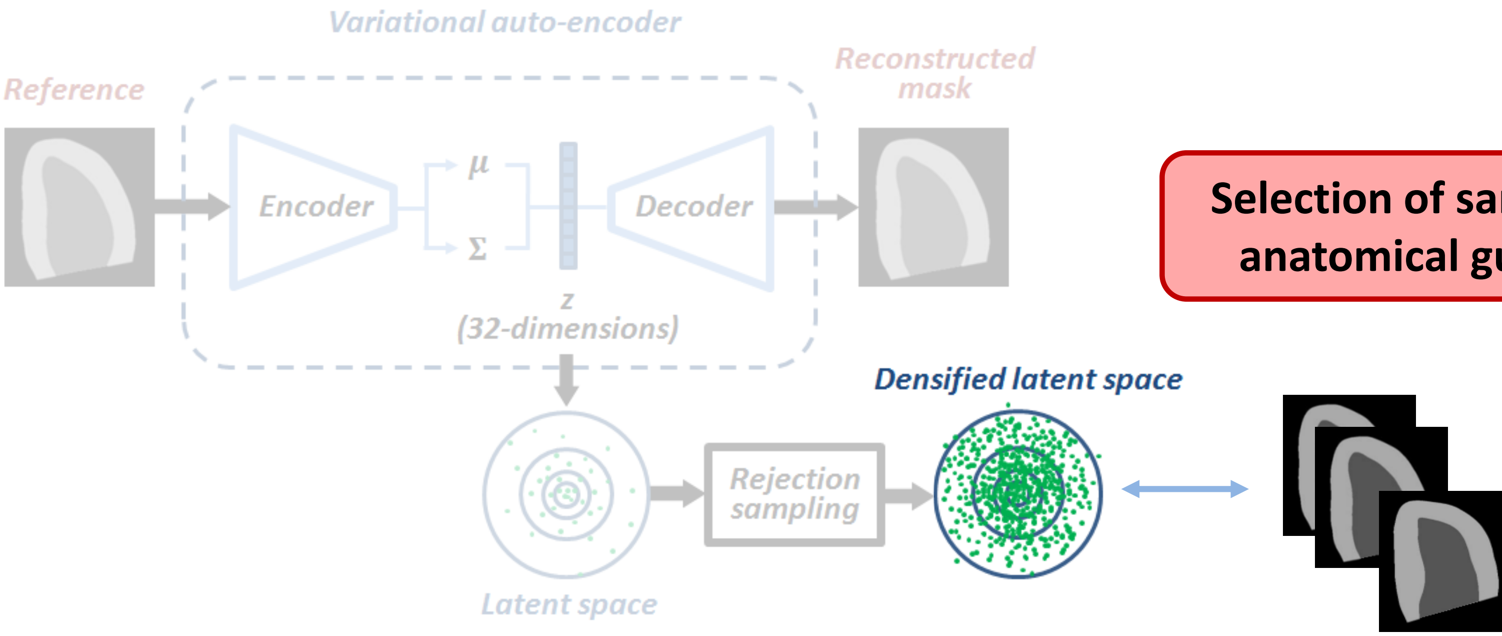
Cardiac segmentation with strong anatomical guarantees *[Painchaud, IEEE TMI, 2020]*

- **Definition of 12 anatomical metrics**
  - **(3 criteria) hole(s) in the LV, RV or LA**
  - **(2 criteria) hole(s) between LV and MYO or between LV and LA**
  - **(3 criteria) presence of more than one LV, MYO or LA**
  - **(2 criteria) size of the area by which the LV touches the background or the MYO touches the LA**
  - **(1 criterion) ratio between the minimal and maximal thickness of the MYO**
  - **(1 criterion) ratio between the width of the LV and the average thickness of the MYO**



Cardiac segmentation with strong anatomical guarantees

[Painchaud, IEEE TMI, 2020]



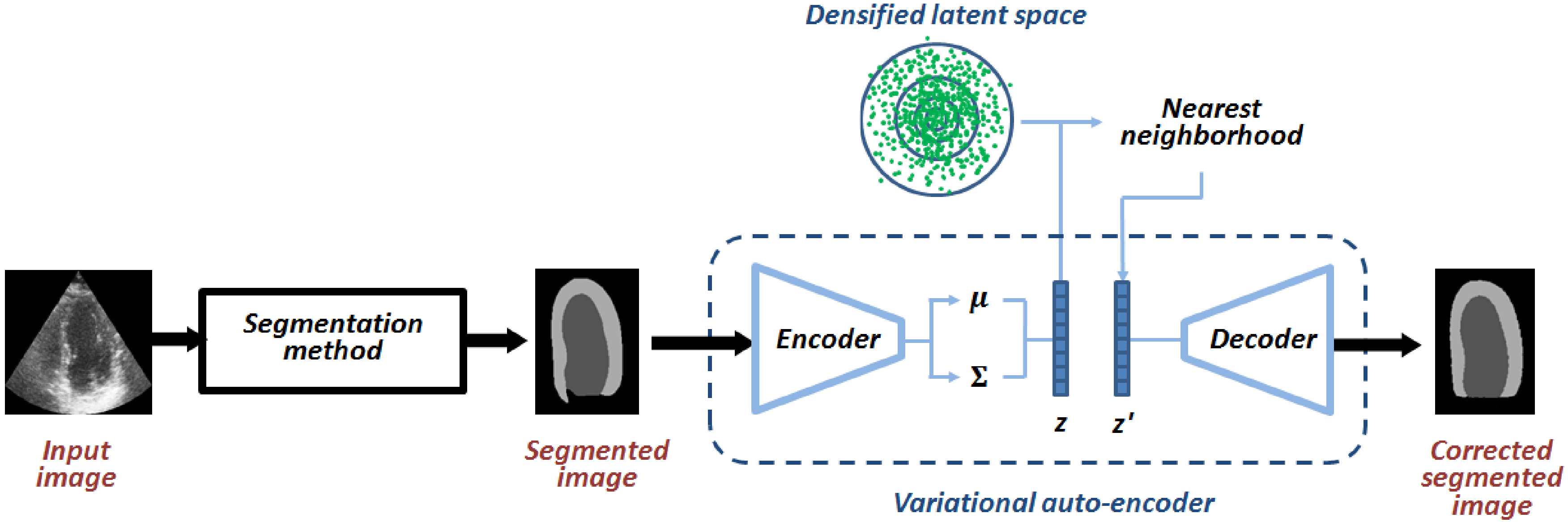
Selection of samples with anatomical guarantees

Densified latent space with 4 million points

Cardiac segmentation with strong anatomical guarantees [Painchaud, IEEE TMI, 2020]

Correction of segmentation to guarantee the plausibility of anatomical shapes

Almost same accuracy as the original methods but with correct anatomical shapes

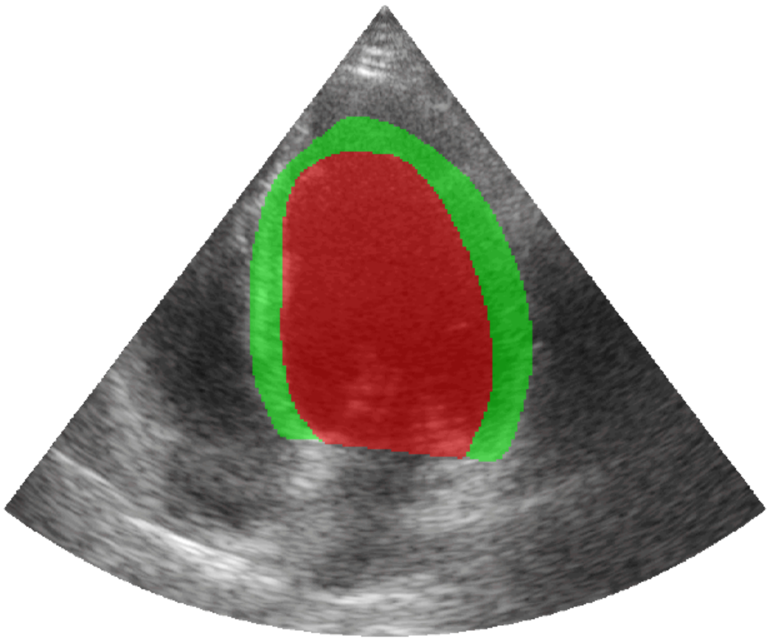


How to guarantee temporal consistency ?

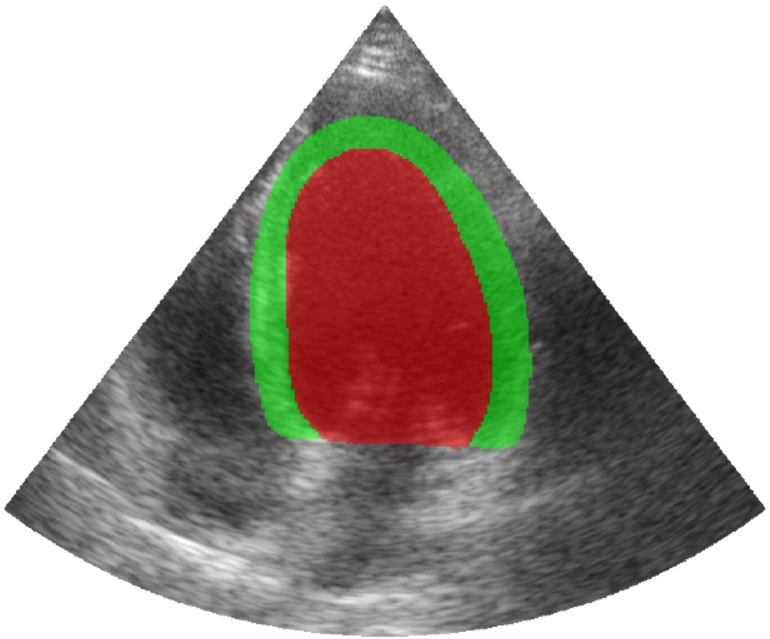
 [Painchaud, IEEE TMI, 2022]

- **Quantification of clinical indices from echocardiographic images**

What we have with a 2D U-Net

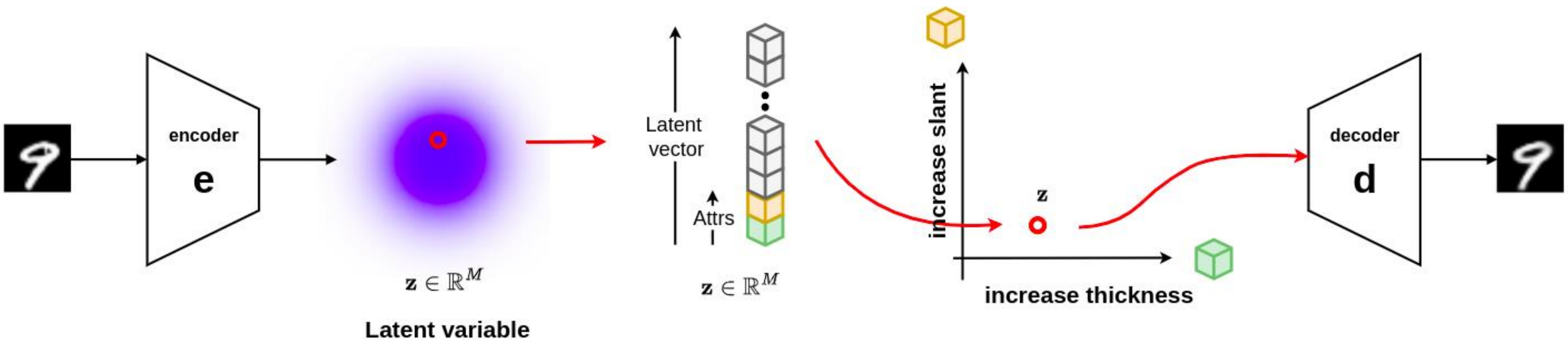


What we want

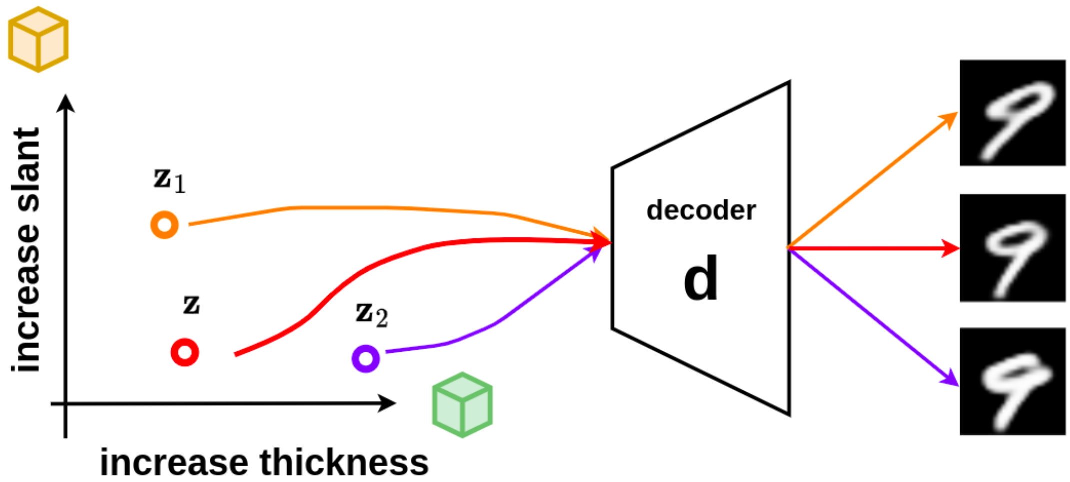


- **AR-VAE: attribute-based regularization of VAE latent space**
  [Pati, Neural Comp. Appli., 2021]

  - **Generation of structured latent space**
    - ➔ **Specific continuous-valued attributes forced to be encoded along specific dimensions**
    - ➔ $\boldsymbol{Loss = VAE\ loss + Attribute\ Regularisation\ Loss}$



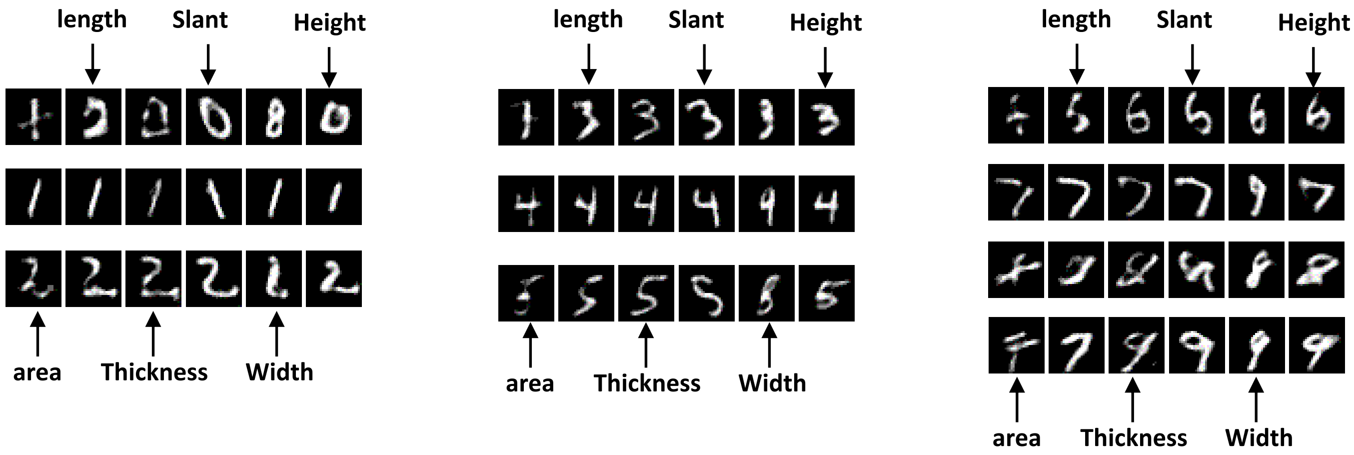
- **AR-VAE: attribute-based regularization of VAE latent space**
  [Pati, Neural Comp. Appli., 2021]
  - **Sampling of the structured latent space**



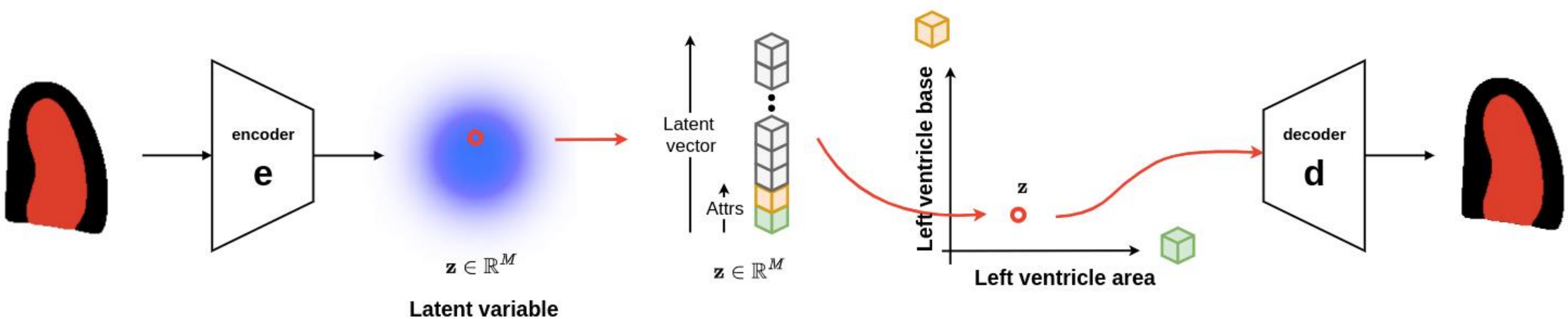
AR-VAE: attribute-based regularization of VAE latent space

[Pati, Neural Comp. Appli., 2021]

- **Sampling of the structured latent space**
  - ➔ **Specific attribute (from left to right): area, length, thickness, slant, width, height**
  - ➔ **Each column corresponds to traversal along a regularized dimension**

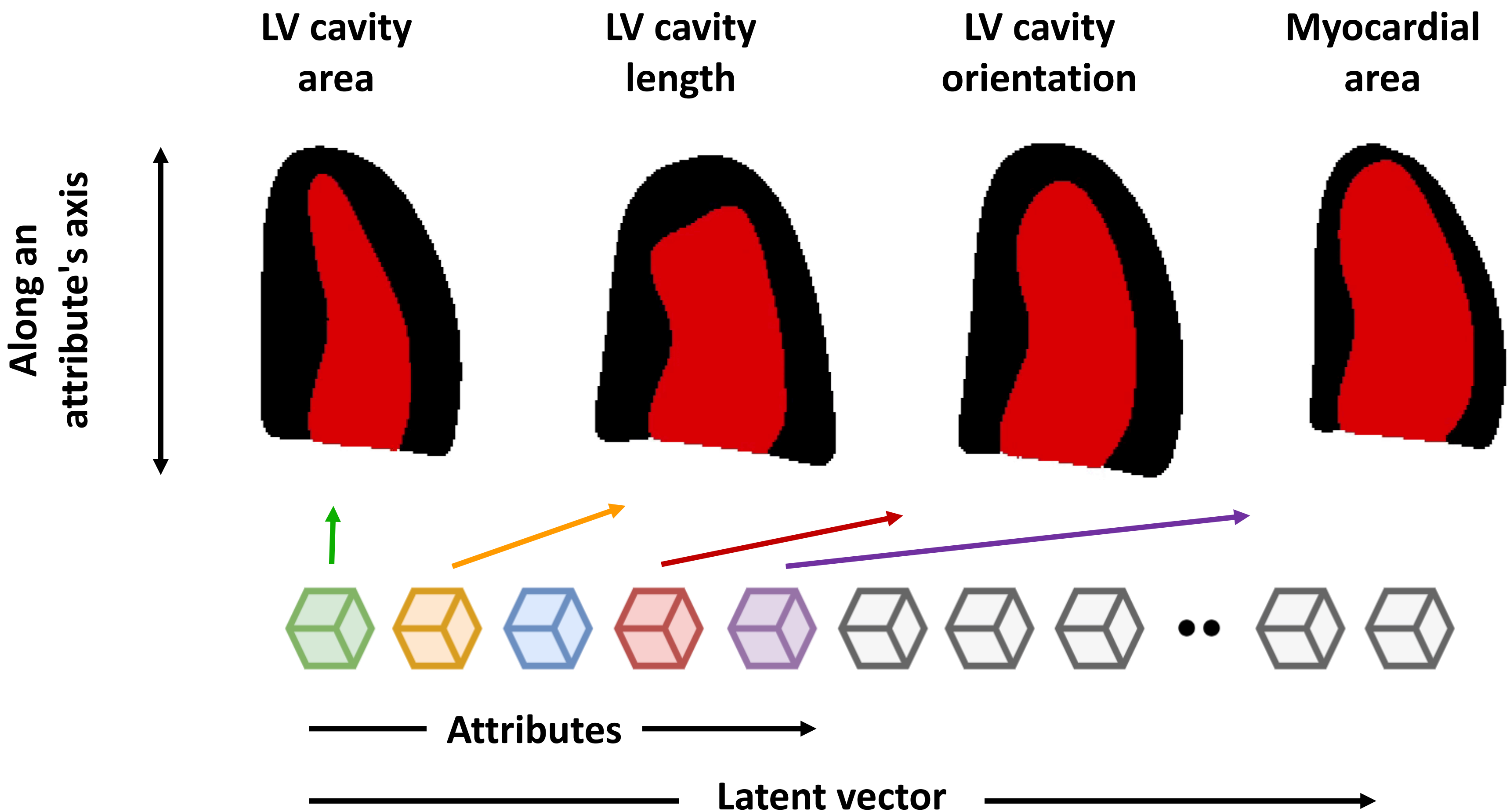


- Application to the description of the cardiac shapes
  - Generation of structured latent space according to the following attributes
    - → Left ventricle (LV) cavity: area, length, basal width, orientation
    - → Myocardial area
    - → Epicardial center



Cardiac segmentation with temporal consistency

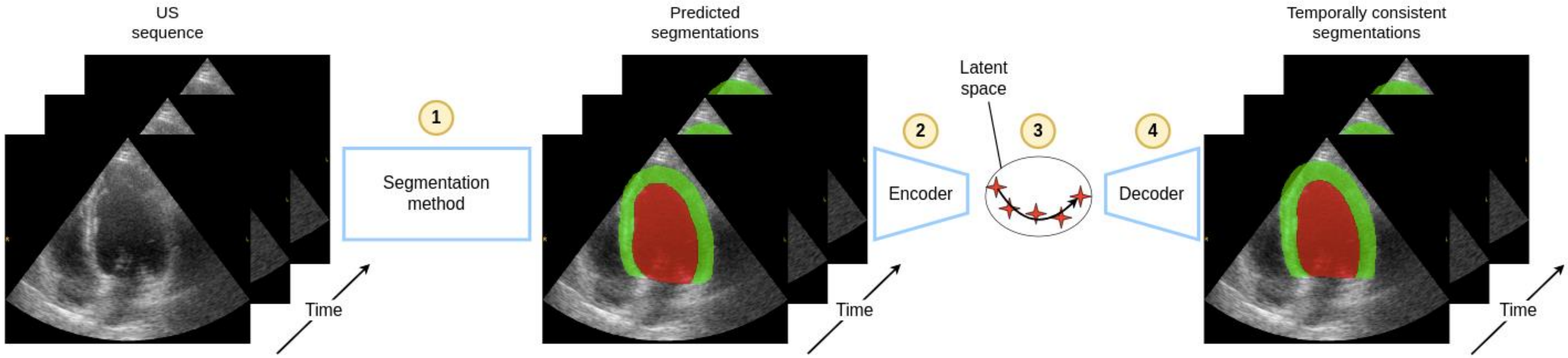
[Painchaud, IEEE TMI, 2022]



Cardiac segmentation with temporal consistency

[Painchaud, IEEE TMI, 2022]

▶ Proposed temporal pipeline



Cardiac segmentation with temporal consistency

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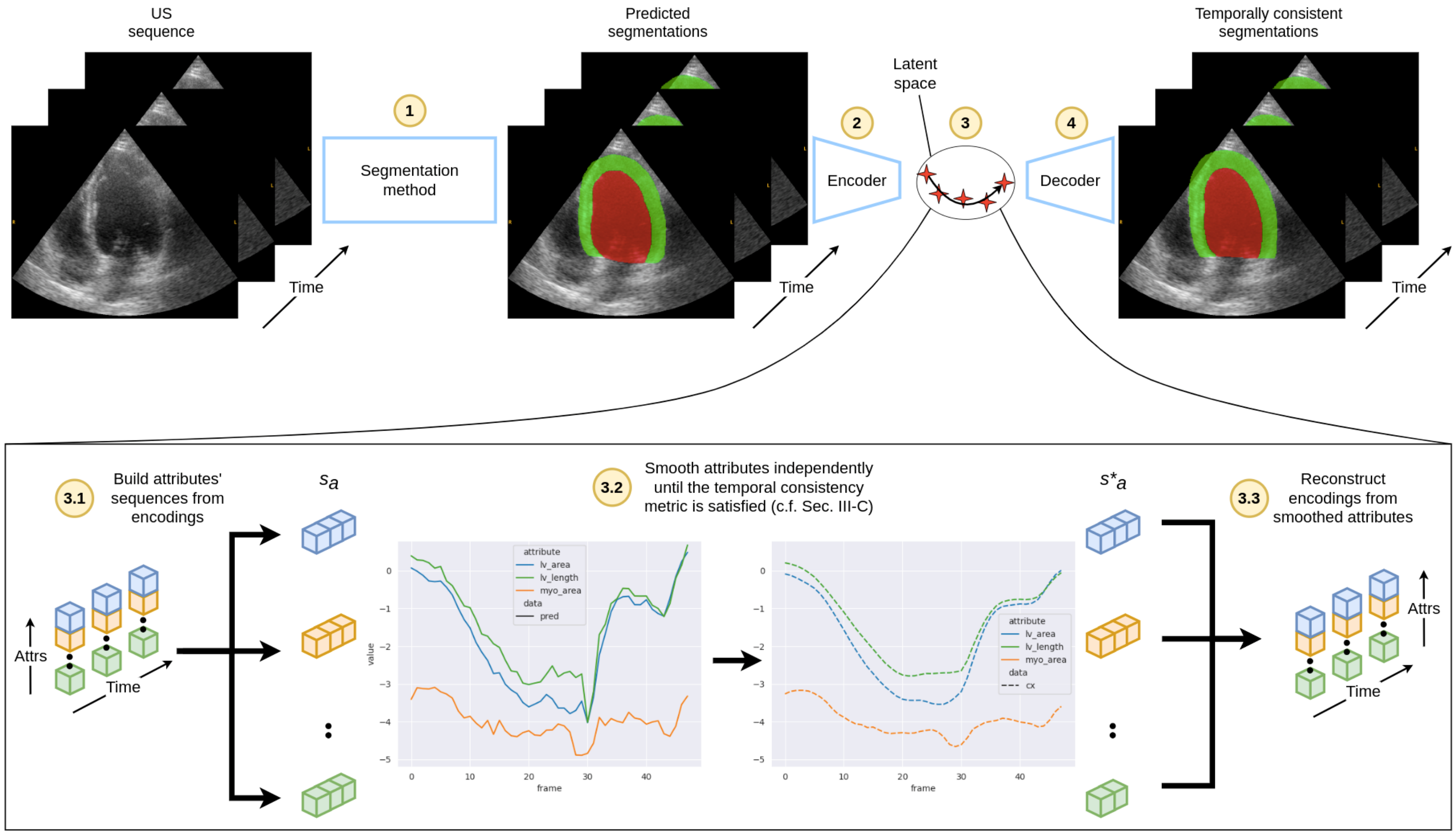
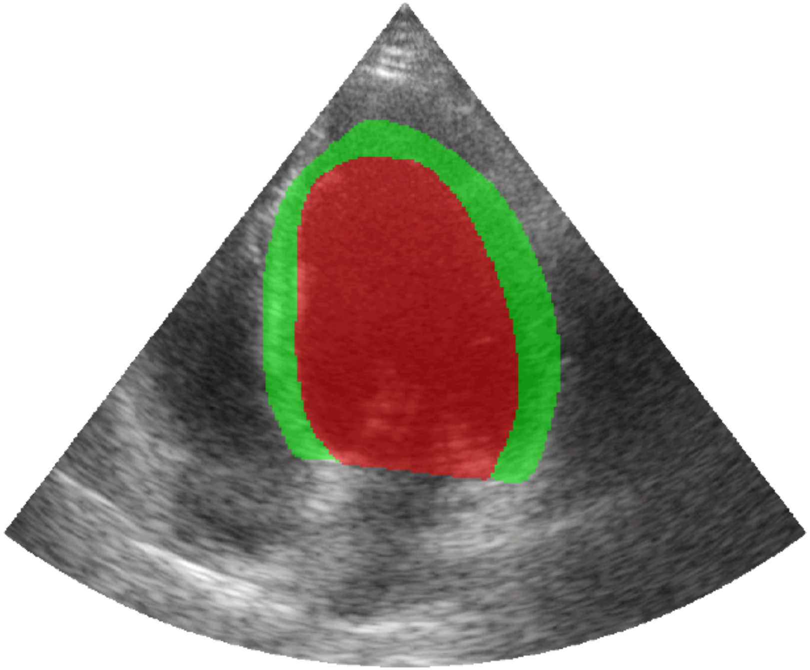
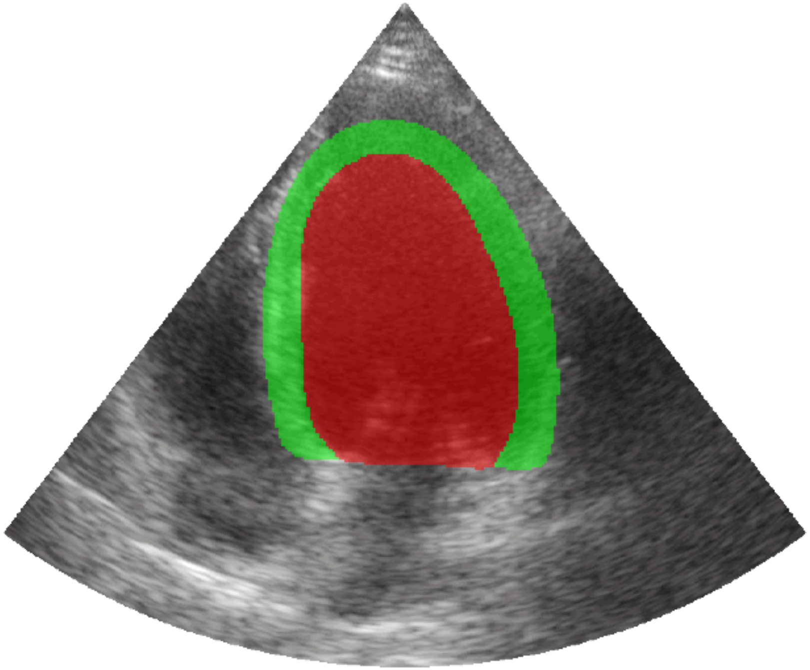


- **Some post-processing examples**

Original U-Net

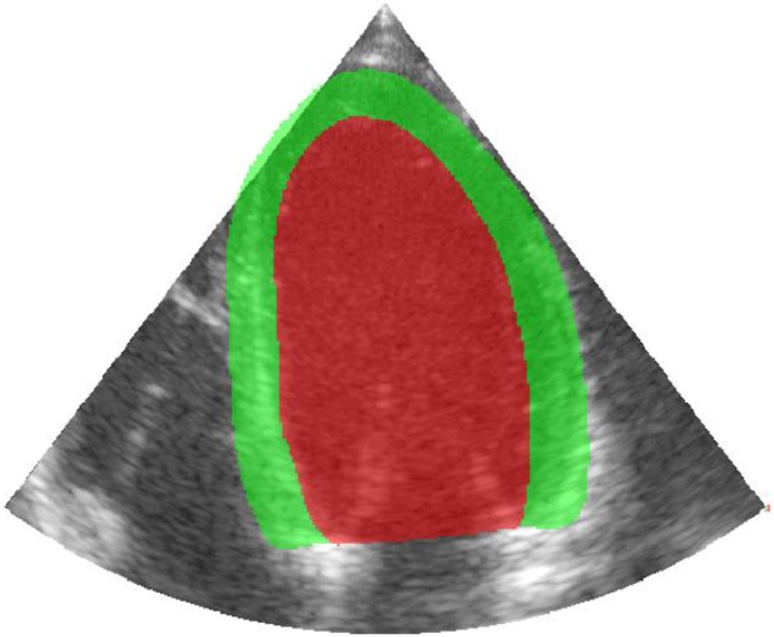


Post-processed U-Net

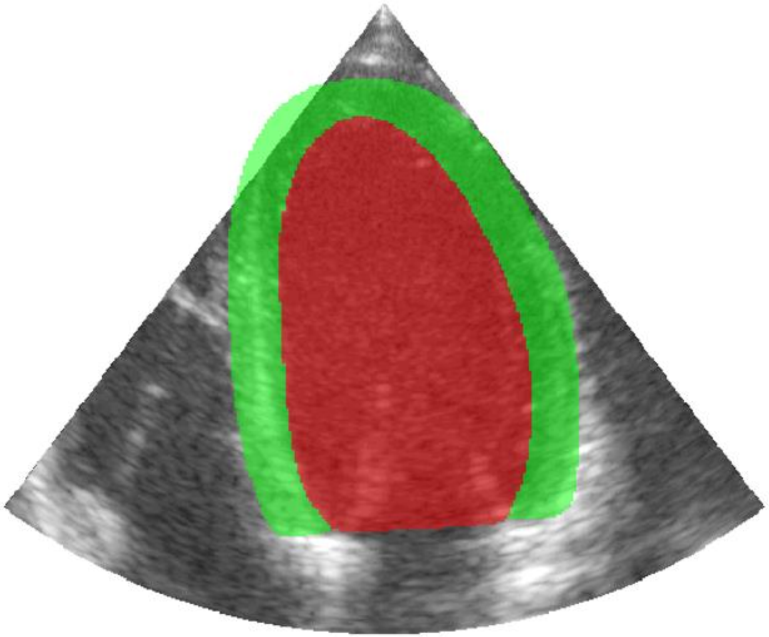


- Some post-processing examples

Original U-Net



Post-processed U-Net

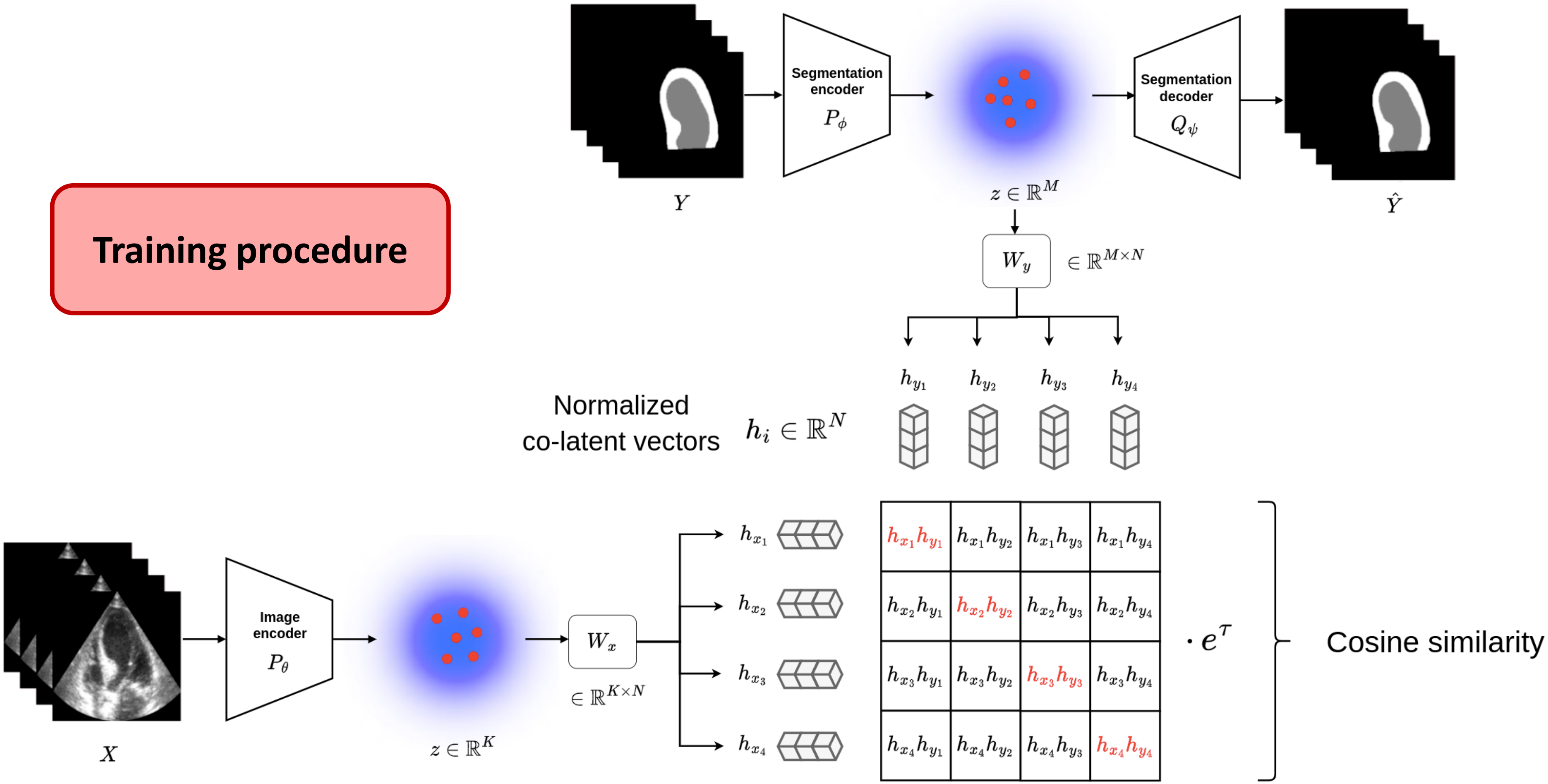


Uncertainty estimation for cardiac image segmentation

Uncertainty estimation for image segmentation

[MICCAI, 2022]

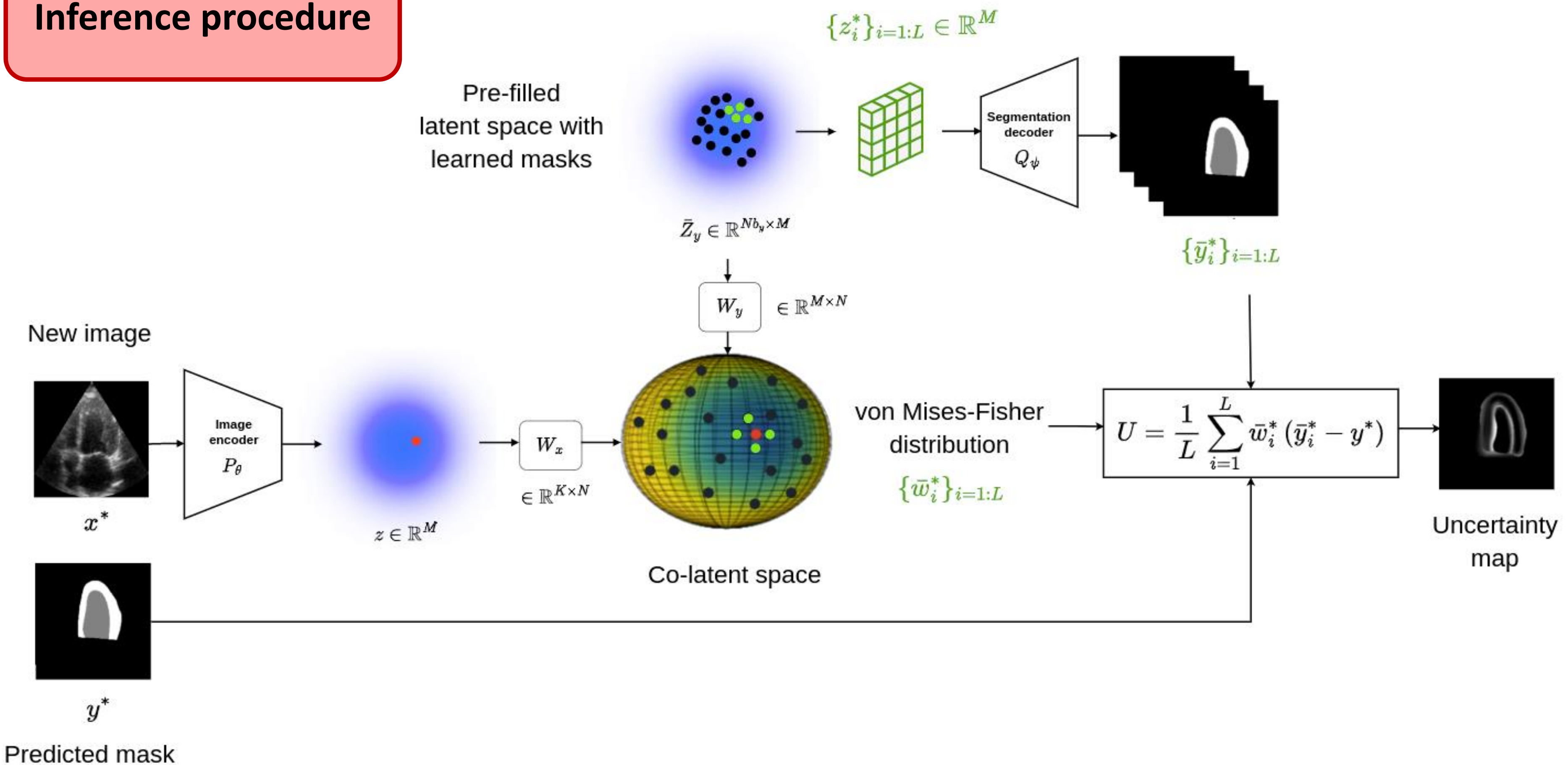
Training procedure



Uncertainty estimation for image segmentation

[MICCAI, 2022]

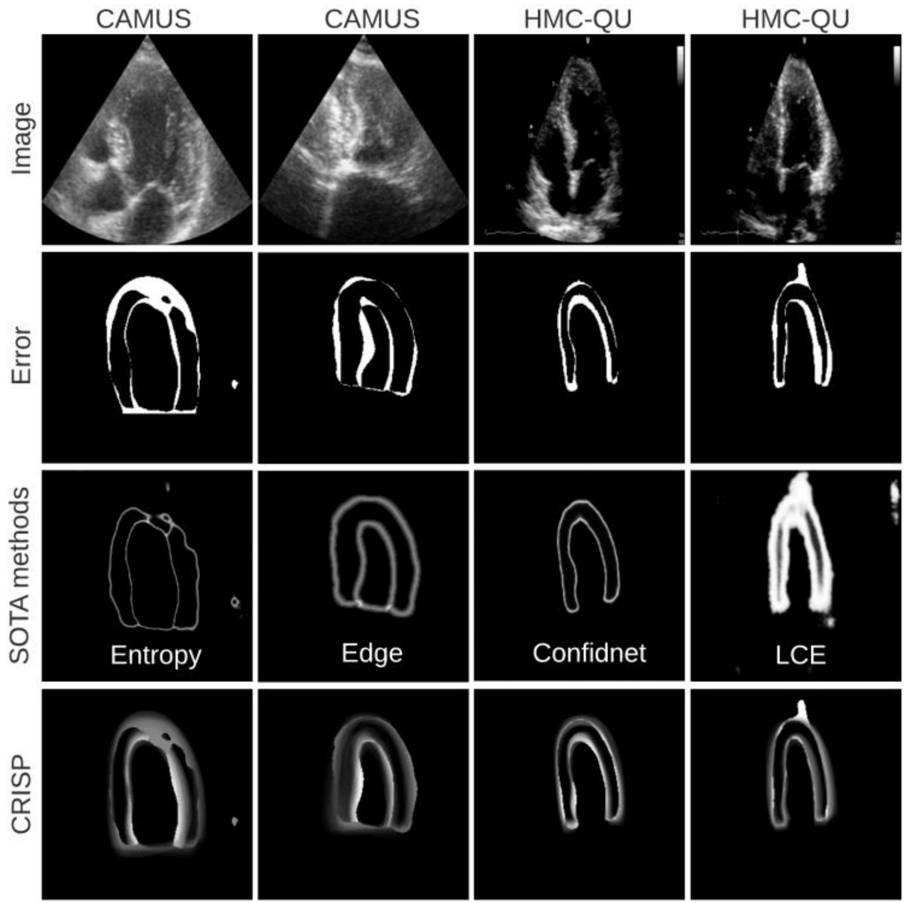
Inference procedure



Uncertainty estimation for image segmentation

[MICCAI, 2022]

- **Uncertainty results**



To conclude

To conclude

- VAEs can be used effectively in medical imaging
  - Guarantee anatomical coherence ✓
  - Guarantee temporal consistency ✓
  - Estimation uncertainty for image segmentation ✓
  - Generative interest limited to simple distribution

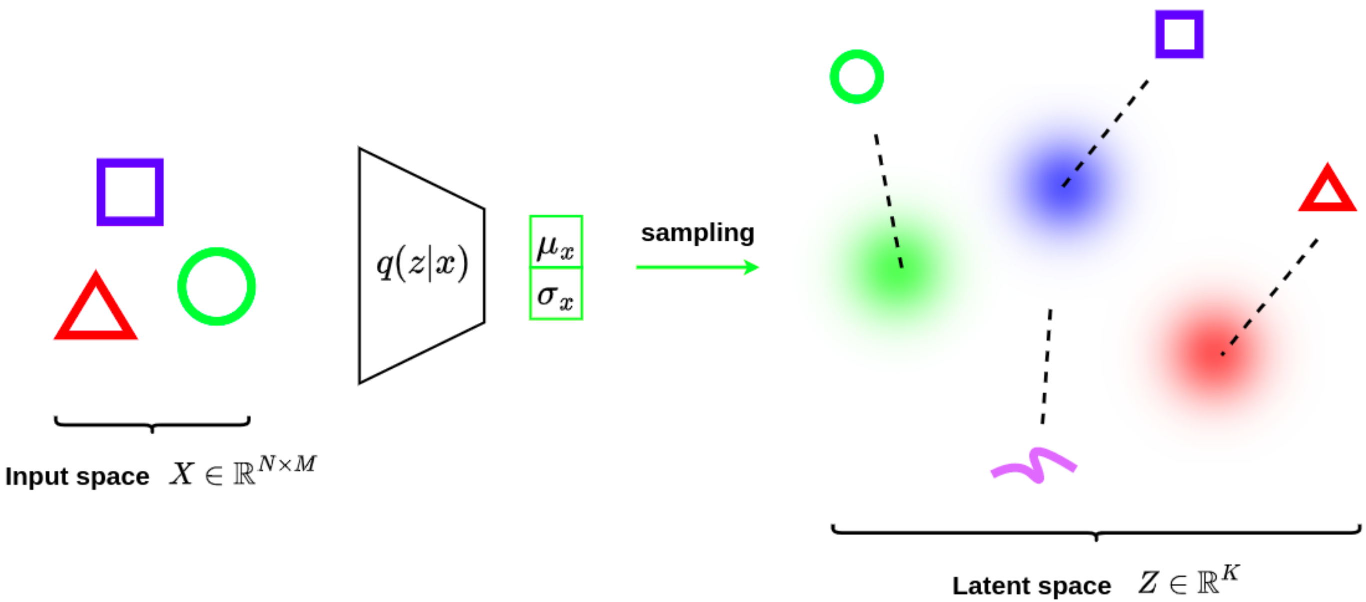
- Useful tool for characterizing populations
  - Need to properly structure the learned latent space
  - Need to work on relatively large cohorts

Appendix

Probabilistic framework

- **Continuity**

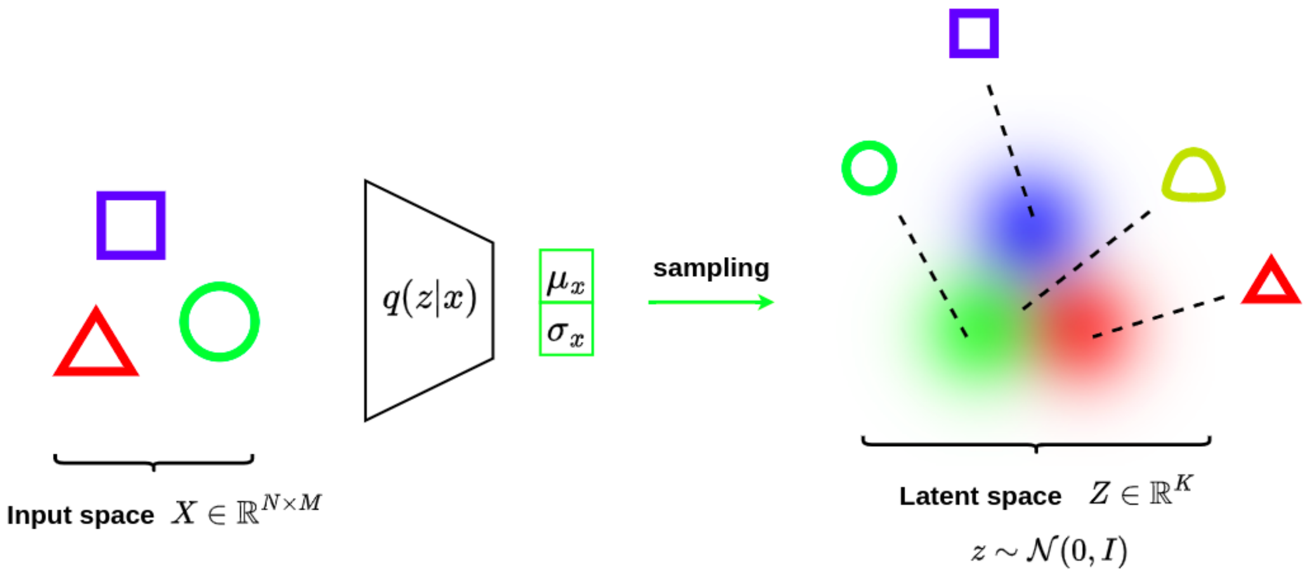
$$\mathcal{N}\left(g(x), h(x)\right)$$



Probabilistic framework

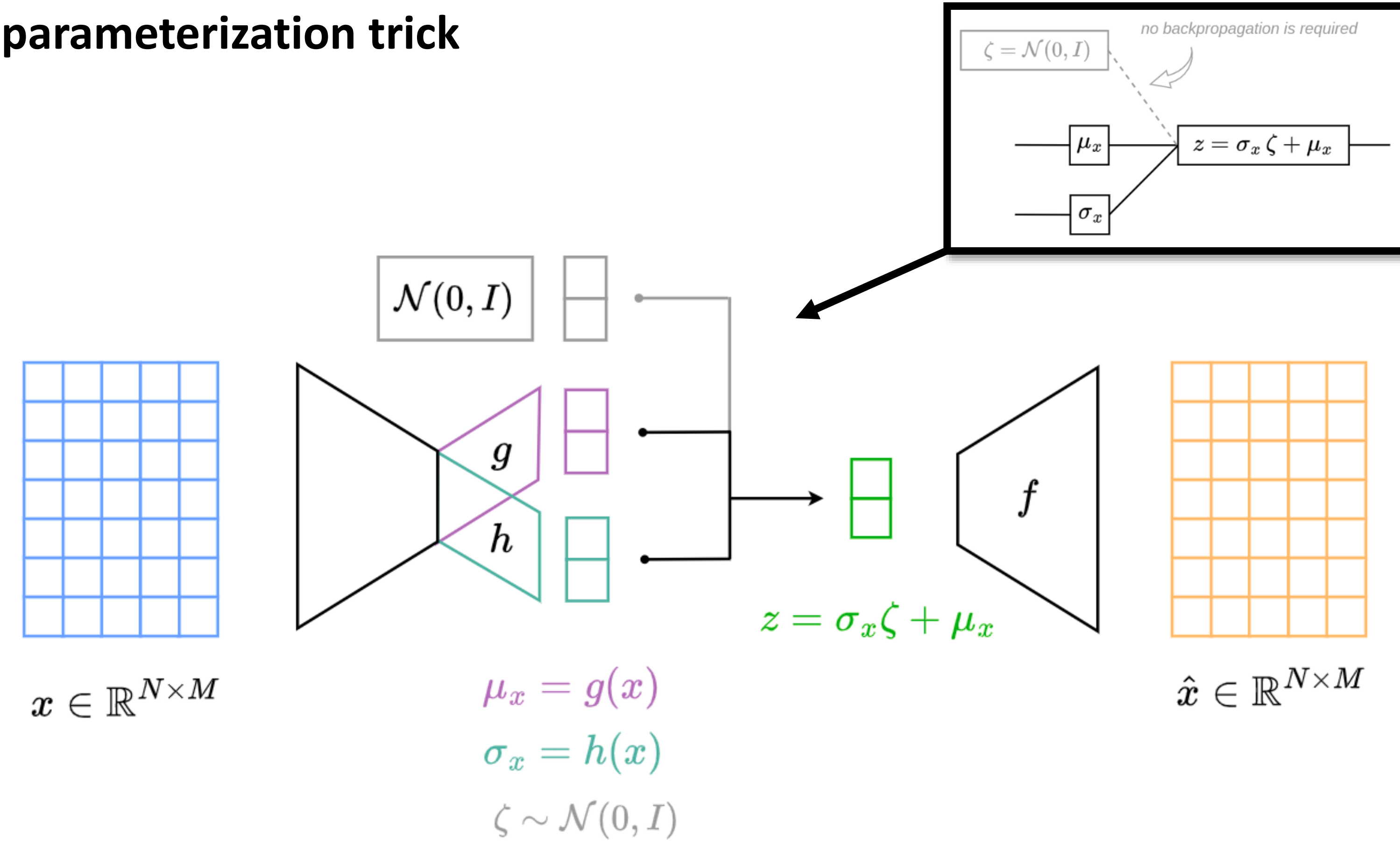
- **Completeness**

$\mathcal{N}\left(\cdot, \mathcal{N}(0, I)\right)$

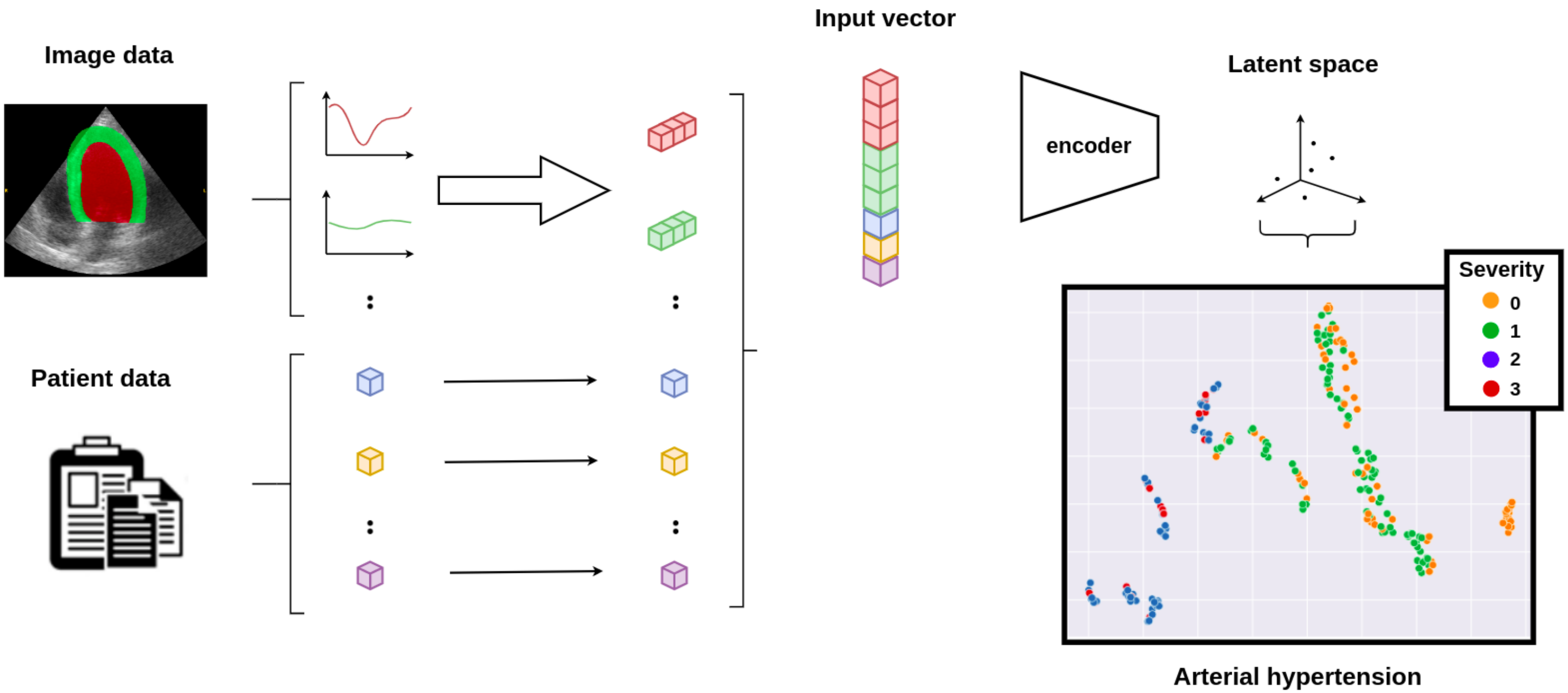


Deep learning implementation

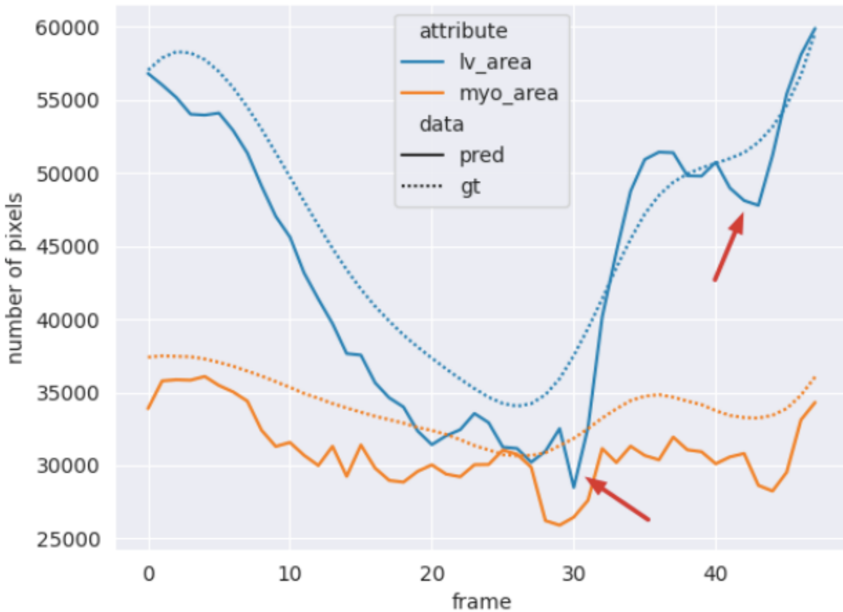
- **Reparameterization trick**



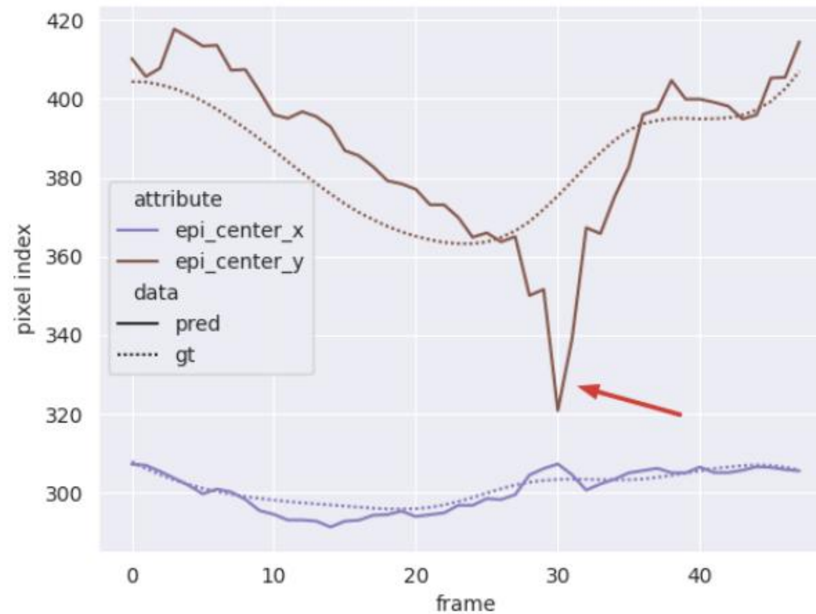
▶ Data representation



Temporal inconsistency detection from the latent space



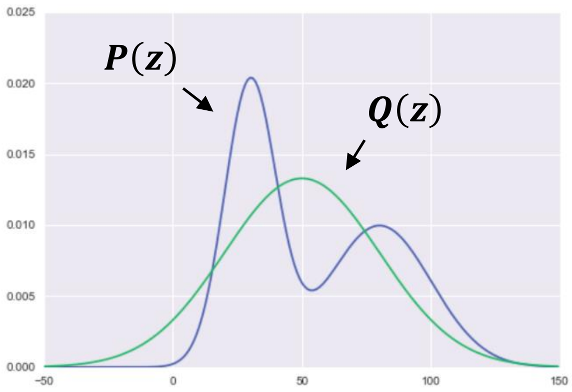
Choppy contraction/dilation of the LV cavity



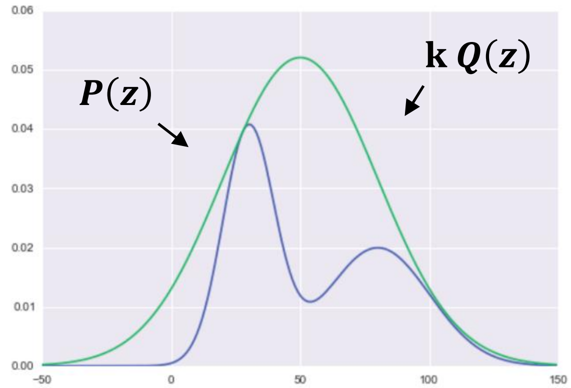
Abrupt vertical shifts of the cardiac shape

Rejection sampling

- Targeted distribution $P(z)$
  - → Parzen window technique
- Proposed distribution $\mathrm{Q}(z)$



- Constrain $\mathrm{kQ(z)} > P(z)$
  - → Automatic choice of k



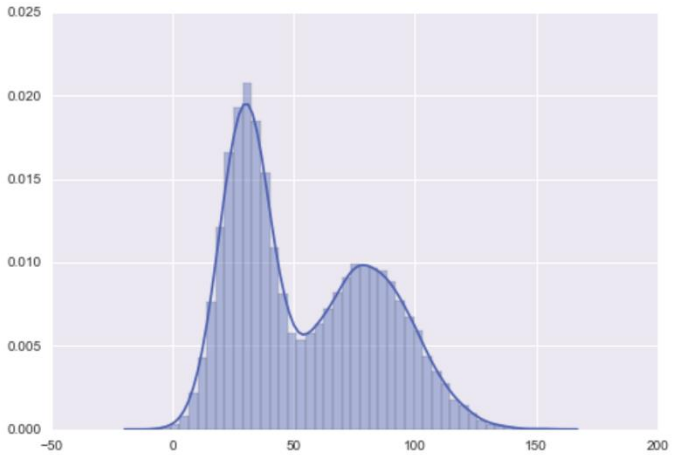
Cardiac segmentation with strong anatomical guarantees *[Painchaud, IEEE TMI, 2020]*

Rejection sampling

- $\mathbf{z} \sim Q(z)$
- $\mathbf{u} \sim Unif(0, kQ(z))$

- **Computation of** $P(z)$
  - ➔ **If** $u \leq P(z)$ **then keep** z
  - ➔ **If** $u > P(z)$ **then reject** z

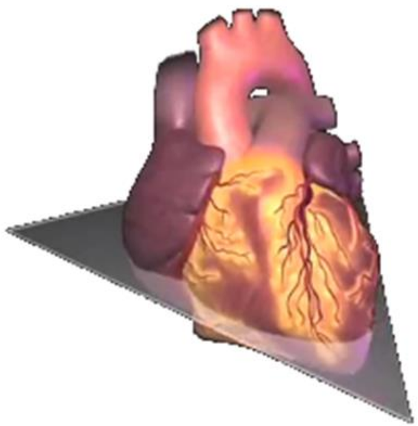
Populated space

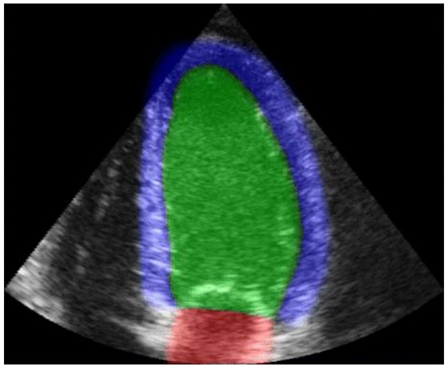


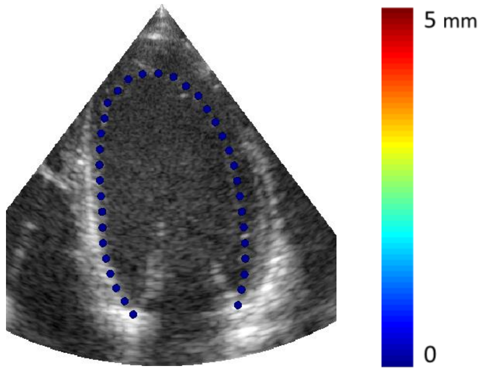
Needs for accurate and robust segmentation of cardiac structures

- **Functional clinical indices**

Apical views

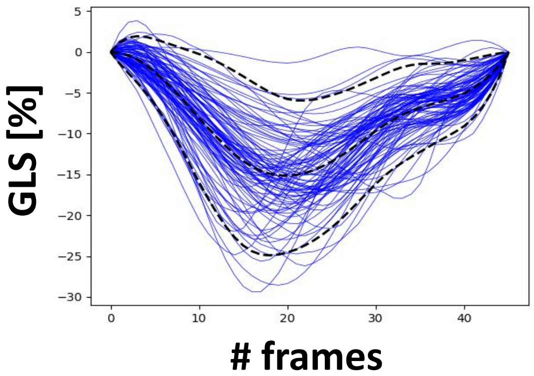






➔ **Volume dynamic of the cavities over the cardiac cycle**

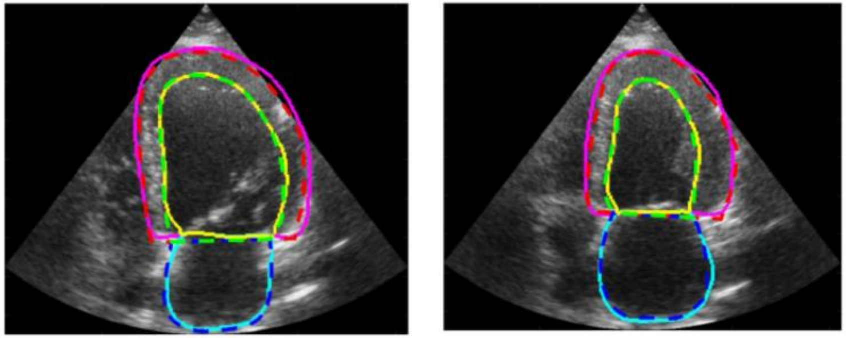
➔ **Global longitudinal strain of the heart muscle**



Quantitative evaluation

- **CAMUS dataset**
  - **500 patients x 2 probe orientation x 2 key frames**
  - **2000 images with reference contours**
  - **Metrics: Dice / Hausdorff dist.**

Example of a segmentation result



Methods	Original	VAE		Nearest Neighbors	
		-	Robust	w/o RS	w/ RS
U-Net [5], [8]	.921 / 6.0	.923 / 5.7	.923 / 5.7	.922 / 5.7	.922 / 5.7
LUNet [14]	.922 / 5.9	.921 / 5.9	.922 / 5.9	.921 / 5.9	.921 / 6.0
ENet [31]	.923 / 5.8	.921 / 5.9	.921 / 5.9	.920 / 5.9	.920 / 5.9
SHG [32]	.915 / 6.2	.915 / 6.2	.916 / 6.2	.915 / 6.2	.915 / 6.2
SRF [33]	.879 / 13.1	.877 / 13.2	.878 / 13.2	.879 / 13.0	.879 / 13.0
BEASM-auto [34], [35]	.868 / 10.5	.868 / 10.5	.867 / 10.5	.868 / 10.5	.868 / 10.5
BEASM-semi [5], [34]	.899 / 7.8	.899 / 7.8	.899 / 7.8	.899 / 7.8	.899 / 7.8

Uncertainty estimation for image segmentation

[MICCAI, 2022]

Quantitative evaluation

- **Corr: Correlation between the sum of the uncertainty values (foreground) and Dice score**
- **MI: Mutual Information between the uncertainty map and the error map**

Training data / Testing data	CAMUS / CAMUS		CAMUS / HMC-QU		Shenzen / JSRT	
Method	Corr. ↑	MI ↑	Corr. ↑	MI ↑	Corr. ↑	MI ↑
Entropy	0.66	0.02	0.34	0.02	**0.89**	0.02
ConfidNet [1]	0.34	0.04	0.36	0.04	0.69	0.01
CRISP	**0.71**	**0.20**	**0.41**	**0.06**	0.83	**0.11**
McDropout [3]	0.67	0.03	0.26	0.02	**0.82**	0.03
CRISP-MC	**0.78**	**0.26**	**0.29**	**0.06**	**0.82**	**0.08**
LCE [2]	0.58	0.44	**0.35**	0.37	**0.87**	0.06
CRISP-LCE	**0.59**	**0.08**	0.34	**0.13**	0.85	**0.11**