SDSS: A Self-Supervised Spheroid Segmentation Method

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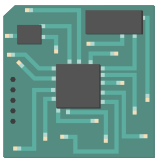
Introduction

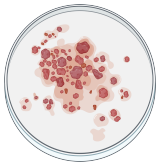
Cell Cultures

- Vital to industrial and academics applications.
- Key part in drug discovery and development:
  - Pre-Clinical.
  - Clinical.

Drug Discovery

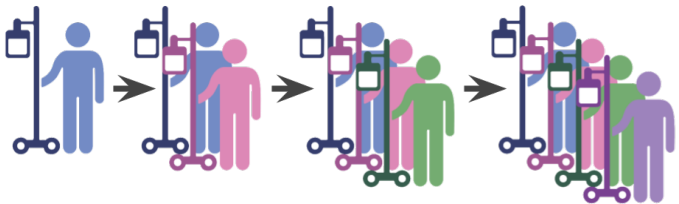


(a) in silico



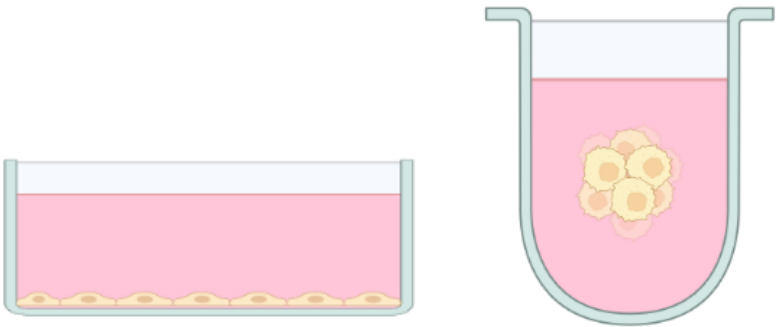
(b) in vitro

(c) in vivo



(d) Clinical Trials

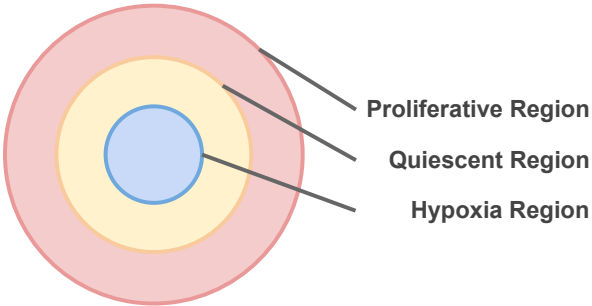
2D vs 3D



(a) 2D culture

(b) 3D culture

Spheroid Regions



Research Questions

1. Shape-aware loss function affects segmentation?
2. Is the U-net encoder a better generator backbone for spheroid segmentation?
3. Can we evaluate spheroids with destroyed proliferative zones?
4. Is scale important in spheroid segmentation?
5. Can a single GAN differentiate all three spheroid zones?

Objectives

Global Objectives

1. Create the spheroid image dataset (SDSS).
2. A self-supervised semantic segmentation method.

Specific Objectives

1. Literature review.
2. Setup dataset.
3. Select metric.
4. Develop method.
5. Evaluate Loss functions.
6. Select GAN backbones.
7. Process results.

Expected Challenges

- Access to data.
- Lack of protocols.
- Heterogeneous evaluation metrics.
- GANs convergence.
- Annotate images.
- Train with few samples.

Expected Contributions

- New public dataset.
- New self-supervised segmentation method.
- Segmentation as an analysis tool.
- Qualitative study.
- Competitive results.

Related Literature

Related Literature

Authors	Method	Metric	Dataset
Lacalle et al.	DeepLabV3+	0.97 Jaccard	Public
Wen et al.	3D U-Net	0.97 Accuracy	Private
Vaidyanathan et al.	Custom	0.95 Dice	Private
García-Domínguez et al.	U^2-Net	0.95 Jaccard	Lacalle's
Chen et al.	PSP-U-Net	0.95 Dice	Private
Ahmad et al.	U-Net*	0.86 Dice	Private
Sadanandan et al.	GAN	0.77 maF	Private
Grexa et al.	Mask R-CNN	0.76 AP	Request
Aida et al.	CGAN	0.10 Dice	Private
Choudhry et al.	Handcrafted	0.99 R^2	Private
Wenzel et al.	MetaXpress	-	Private

Literature Limitations

- Lack of public spheroid datasets.
- Handcrafted features.

Datasets

Available Datasets

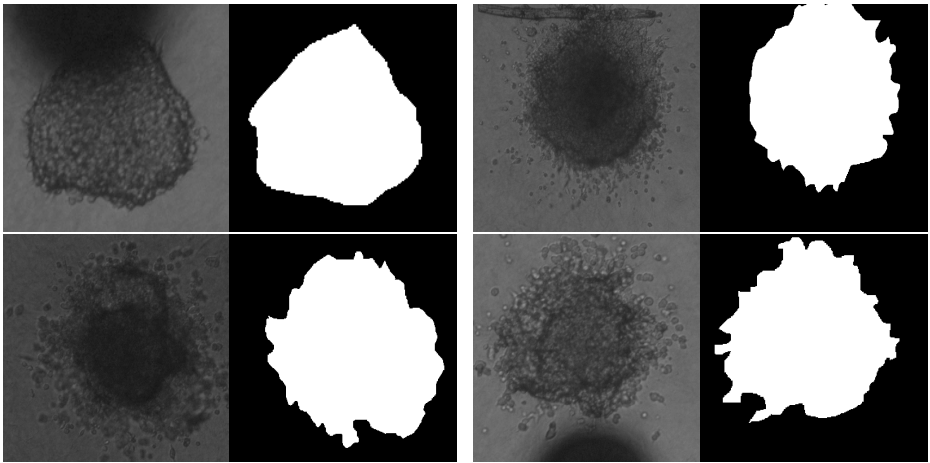
- Majority of related works acquired their own images.
- The work of Lacalle et al.

Name	BL5S	BN2S	BN10S	FL5C	FL5S	FN2S
Method	Brif	Brif	Brif	Fluo	Fluo	Fluo
Images	50	154	105	19	50	34
Magnification	5x	2x	10x	5x	5x	2x
Culture	Susp	Susp	Susp	Colla	Susp	Susp

Lacalle et al. annotations

- Annotated via ImageJ software.
- ImageJ only saves the vertices.
- Python script to generate mask images.

Samples from Lacalle et al.



Proposed Datasets

- OncoBiomarkers Research Laboratory at UNICAMP;
- Two images per spheroid;

Spheroid Acquisition

titlepage

mainpoint

blank

vertical

horizontal

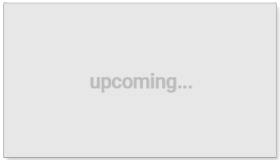
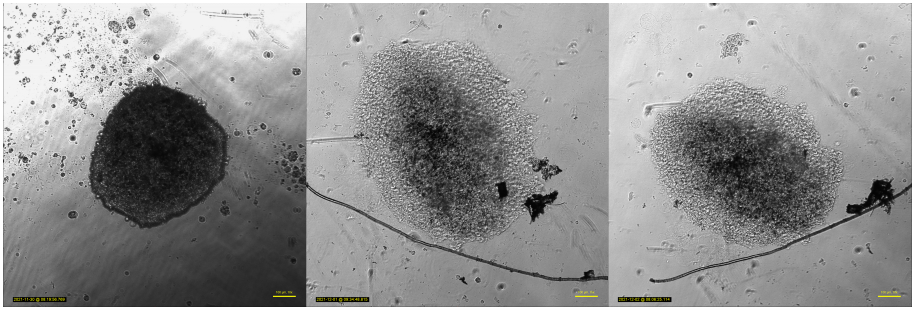


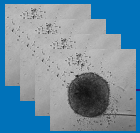
Image Acquisition

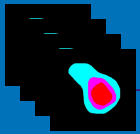


(a) 48h (b) 72h (c) 96h

Method

Overview





Resize

Image Augmentation

1. Affine Transform
2. Flip Horizontal
3. Flip Vertical
4. Random Brightness Contrast
5. Random Crop
6. Random Rotation
7. Scaling

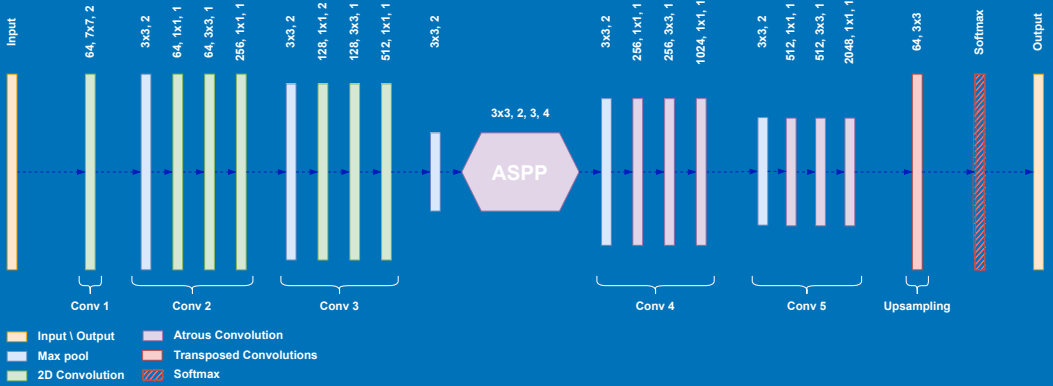
Loss Function

Segmentator

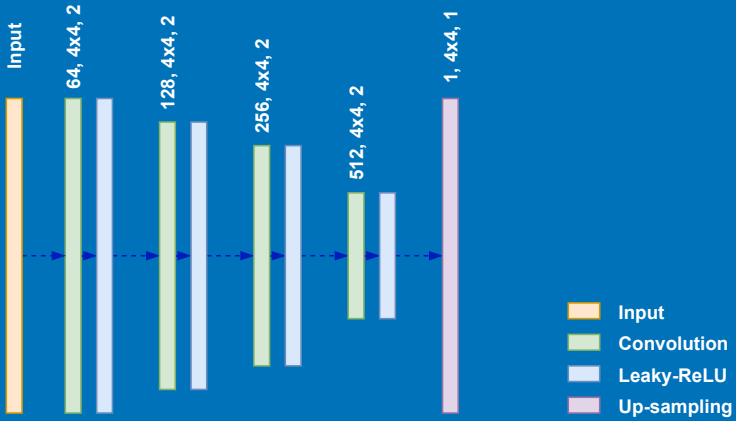
Discriminator

Data Augmentation

Generator Architecture



Discriminator Architecture



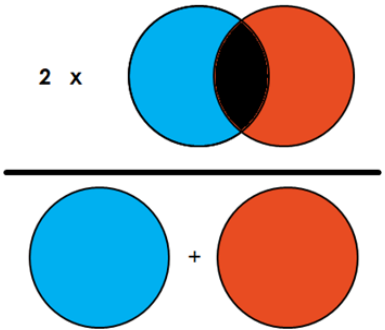
Loss Functions

Generator Loss

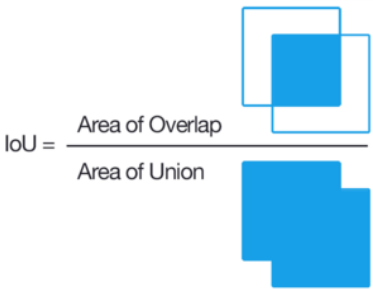
$$\mathcal{L}_{seg} = \mathcal{L}_{ce} + \lambda_{adv}\mathcal{L}_{adv} + \lambda_{semi}\mathcal{L}_{semi} \tag{1}$$

Evaluation Metrics

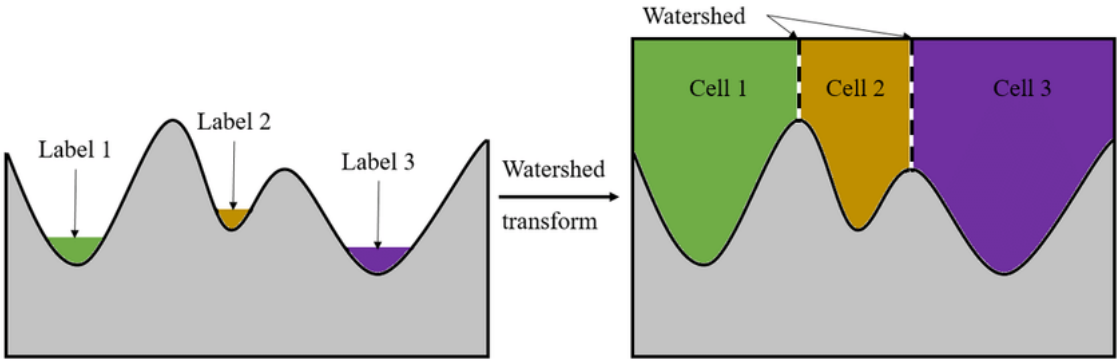
Dice Coefficient



Jaccard Index



Watershed


Label 1
Label 2
Label 3
Watershed
transform
Watershed
Cell 1
Cell 2
Cell 3

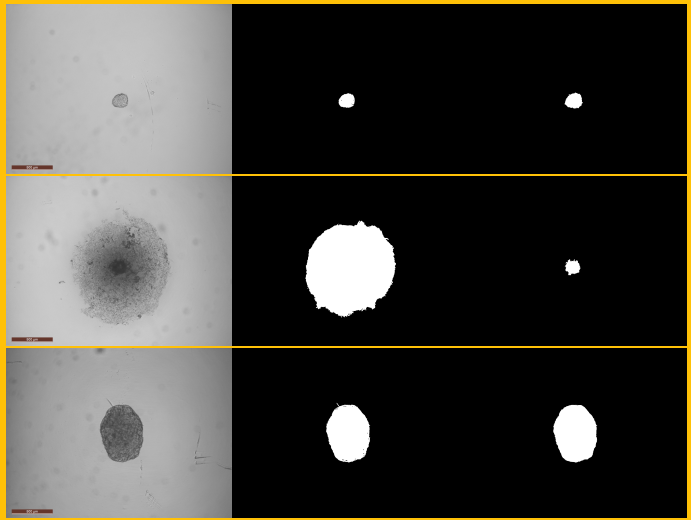
Preliminary Results

Comparative Table

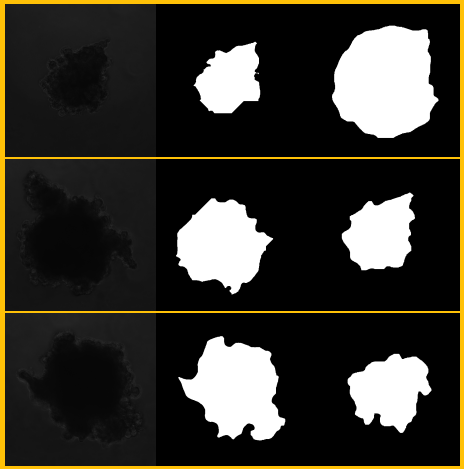
Metric used: Mean Jaccard.

Method	BL5S	BN10S	BN2S	FL5C	FL5S	FN2S	Ours
Watershed	0.73	0.64	0.45	0.63	0.44	0.41	-
U-Net	0.75*	-	-	0.93	-	-	-

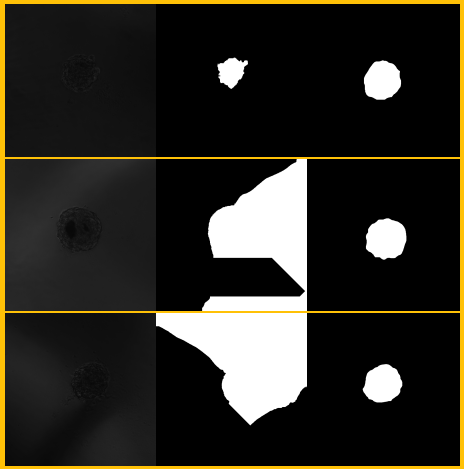
BL5S - 0.73



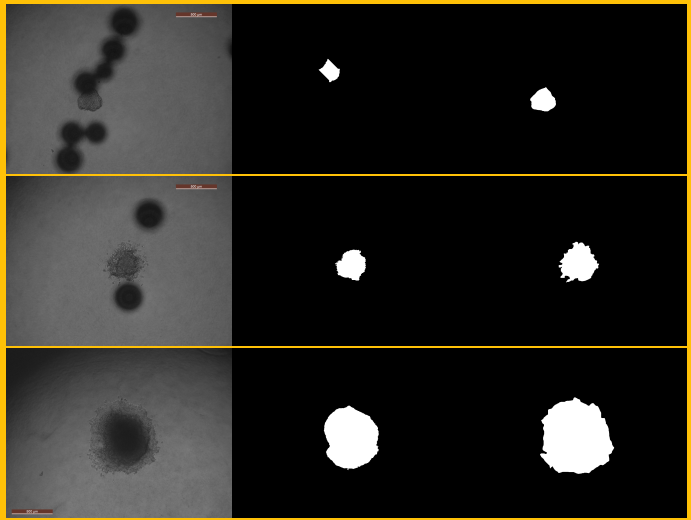
BN10S - 0.64



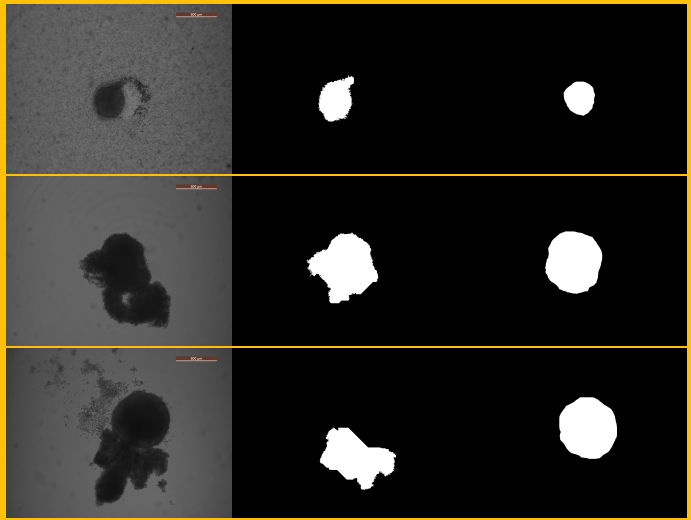
BN2S - 0.45



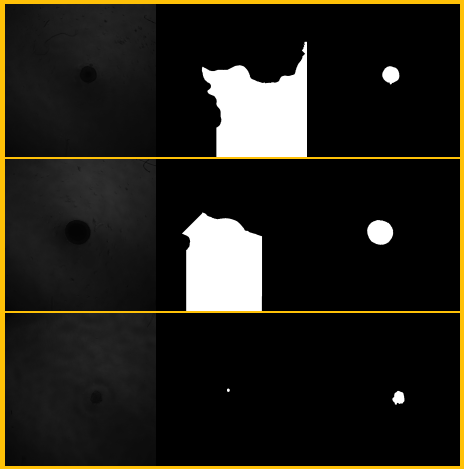
FL5C - 0.63



FL5S - 0.44



FN2S - 0.41

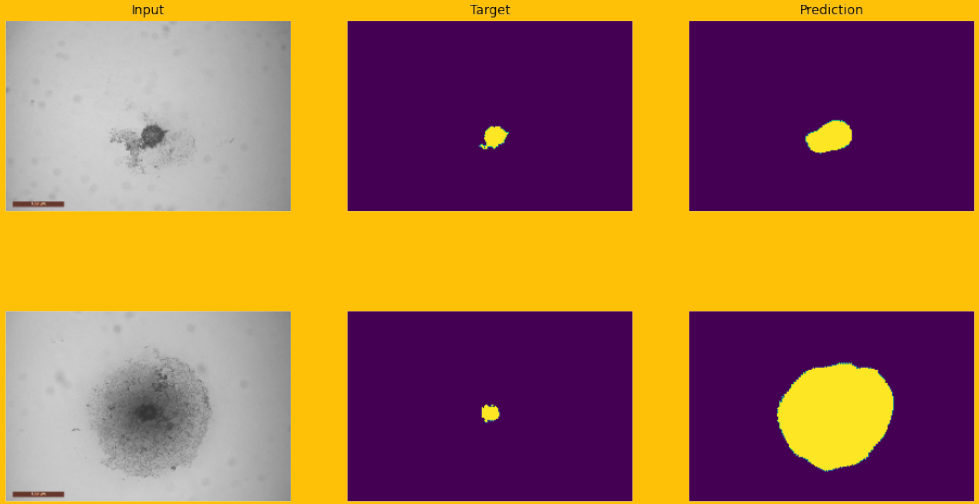


Comparative Table

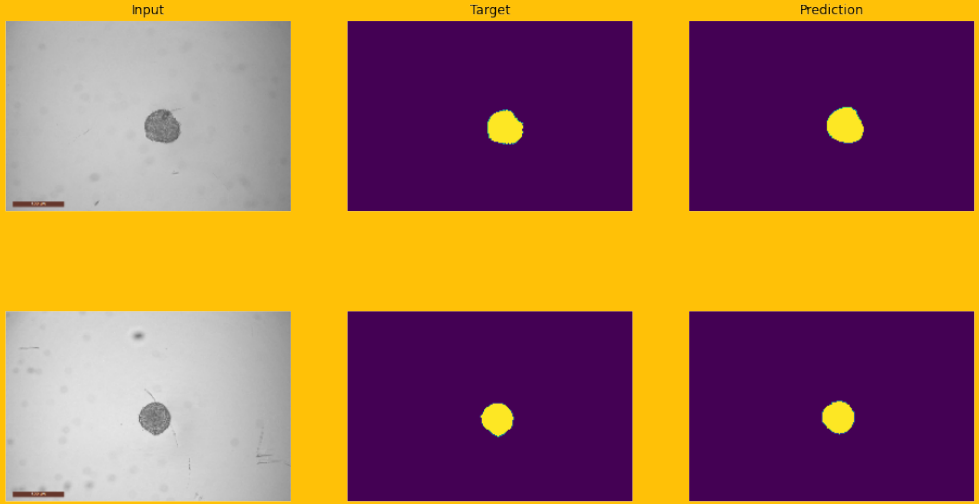
Metric used: Mean Jaccard.

Method	BL5S	BN10S	BN2S	FL5C	FL5S	FN2S
Watershed	0.73	0.64	0.45	0.63	0.44	0.41
U-Net	0.75*	-	-	0.93	-	-

U-Net



U-Net



Schedule

Schedule

Activities	2020	2021	2022	2023
Course work	•	•		
Literature review	•	•	•	•
Dataset implementation		•	•	
Method execution		•	•	•
Results publication			•	•
Method iteration			•	•
Thesis writing	•	•	•	•

Final Considerations

Final Considerations

Found Challenges

- Handcrafted features lack versatility.
- Well annotated spheroids masks.

Our Contribution

- New unique spheroid dataset.
- Self-supervised segmentation for spheroids.

Thank You

Doubts and Suggestions

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