Consiglio Nazionale delle Ricerche
Istituto di Scienza e Tecnologie dell'Informazione "A. Faedo"
Artificial Intelligence for Media and Humanities Laboratory

AIMH Lab 2022 Activities for Healthcare

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Outline

Dementia Diagnosis in MRI with Volumetric Transformers

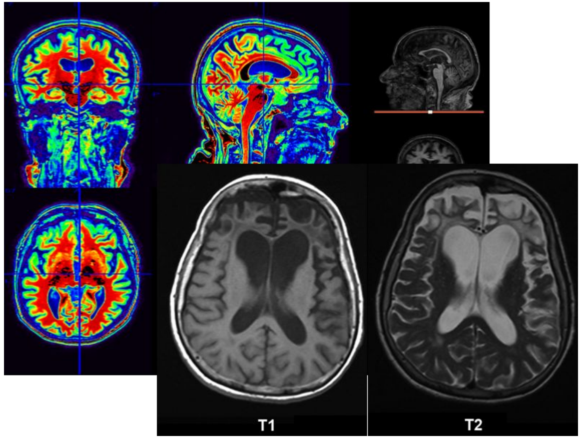
Microscopy Cell Counting under Raters' Uncertainty

Optimized AI for Real-time Pupillometry

Dementia Diagnosis in MRI with Volumetric Transformers

Early Diagnosis from MRI

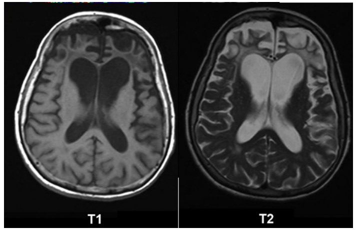
- Study on Behavioral Frontotemporal Dementia (bvFTD) diagnosis from MRI
- Binary classification (bvFTD vs control) from whole-brain MRI
- Volumetric 3D attention models
- Cross-dataset Evaluation



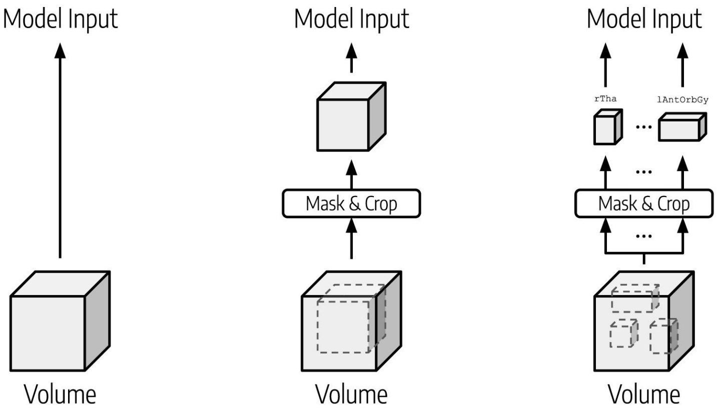
Di Benedetto et al. "Deep networks for behavioral variant frontotemporal dementia identification from multiple acquisition sources." Computers in Biology and Medicine 148 (2022): 105937.

Evaluation of Input Processing

- T1 Weighted
  - modulated (mwp) vs non-modulated (wm)
  - whitened vs non-whitened



- Region Masking / Selection
  - Whole-brain volume as input
  - Frontotemporal Region (FT) as input
  - Several Regions as inputs (ROI)



(a) Whole-brain (b) Frontotemporal mask (c) ROIs

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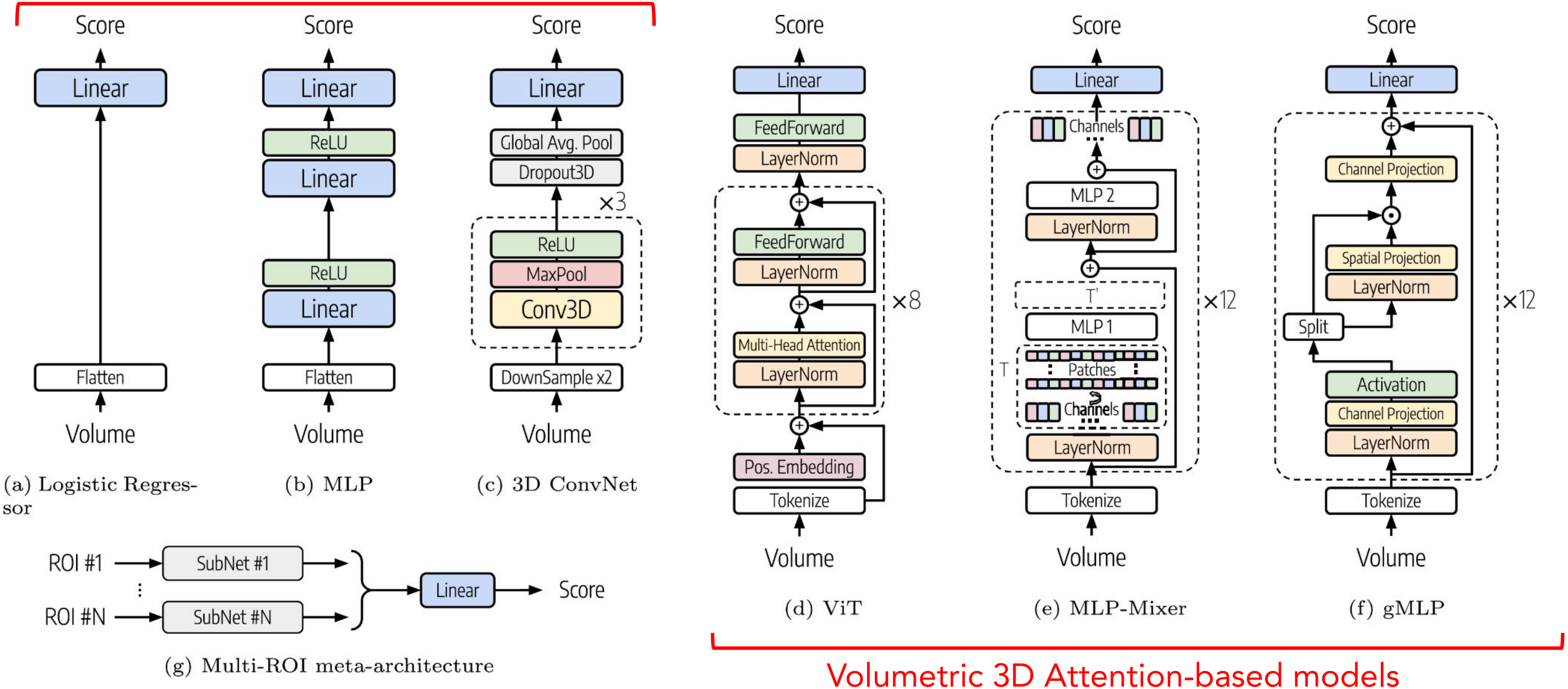
Volumetric Models

Baselines



Volumetric 3D Attention-based models

Di Benedetto et al. "Deep networks for behavioral variant frontotemporal dementia identification from multiple acquisition sources." Computers in Biology and Medicine 148 (2022): 105937.

Cross-dataset Evaluation

- Datasets
  - FTLDNI (110 Control, 50 bvFTD)
  - CMND (24 Control, 30 bvFTD)
- AuROC (train and validation on CMND & blind test on FTLDNI, mean+-std on 5 runs)

AuROC (%, $\text{mean}_{\pm\text{std}}$) on FTLDNI and CMND datasets. None = Whole Volume; FT = Frontotemporal Masking; ROI = Per-ROI Processing

Data kind	wm						mwp					
Data crop	None		FT		ROI		None		FT		ROI	
Whitening	✗	✓	✗	✓	✗	✓	✗	✓	✗	✓	✗	✓
	Trained on CMND train split — Tested on whole FTLDNI											
Logistic regressor	$77_{\pm15}$	$64_{\pm13}$	$81_{\pm1}$	$65_{\pm18}$	$85_{\pm3}$	$83_{\pm2}$	$73_{\pm19}$	$78_{\pm9}$	$85_{\pm19}$	$67_{\pm17}$	$28_{\pm9}$	$88_{\pm4}$
MLP	$58_{\pm21}$	$75_{\pm8}$	$47_{\pm9}$	$56_{\pm17}$	$88_{\pm1}$	$84_{\pm2}$	$36_{\pm24}$	$30_{\pm10}$	$23_{\pm5}$	$25_{\pm8}$	$92_{\pm1}$	$91_{\pm5}$
ConvNet 3D	$36_{\pm3}$	$43_{\pm4}$	$45_{\pm8}$	$75_{\pm8}$	$68_{\pm4}$	$67_{\pm2}$	$73_{\pm22}$	$91_{\pm2}$	$48_{\pm36}$	$94_{\pm1}$	$94_{\pm1}$	$90_{\pm4}$
ViT	$41_{\pm10}$	$74_{\pm2}$	$47_{\pm15}$	$78_{\pm1}$	$87_{\pm2}$	$91_{\pm1}$	$59_{\pm30}$	$84_{\pm1}$	$42_{\pm32}$	$91_{\pm0}$	$90_{\pm1}$	$91_{\pm1}$
MLP-Mixer	$69_{\pm5}$	$62_{\pm8}$	$73_{\pm6}$	$70_{\pm7}$	$86_{\pm2}$	$88_{\pm2}$	$80_{\pm2}$	$84_{\pm5}$	$91_{\pm2}$	$88_{\pm3}$	$95_{\pm1}$	$91_{\pm1}$
gMLP	$80_{\pm4}$	$75_{\pm6}$	$79_{\pm5}$	$70_{\pm8}$	$88_{\pm2}$	$90_{\pm2}$	$81_{\pm2}$	$77_{\pm1}$	$85_{\pm1}$	$88_{\pm2}$	$95_{\pm1}$	$91_{\pm1}$

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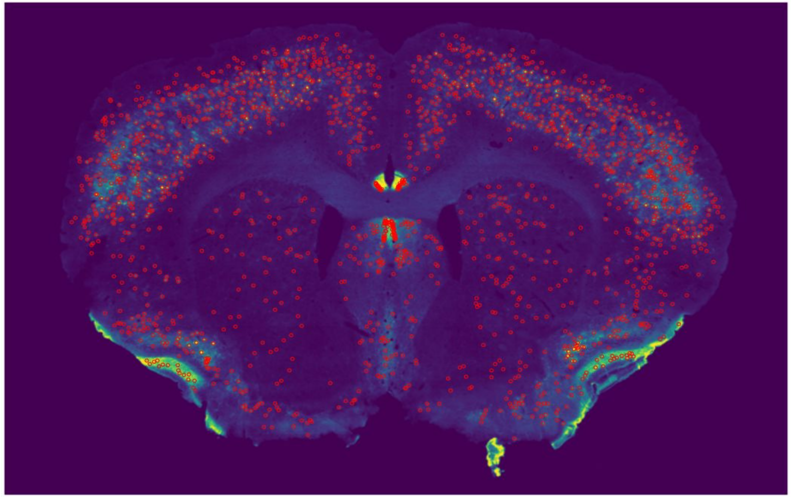
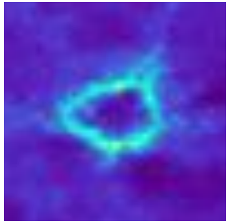
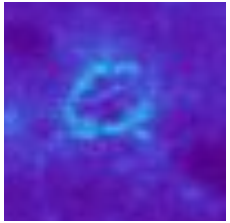
Microscopy Cell Counting under Raters' Uncertainty

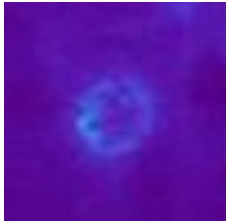
Counting Perineuronal Nets

- Perineuronal Nets (PNNs): structures surrounding neurons that have a role in neuroplasticity
- Goal: estimation of density of PNNs in the brain in “control” and “disease/treatment” conditions
- Slicing, Staining, Microscopy & Count
  - ~60 images with ~120MP
  - 2-3 man-months for counting only
- We would want an AI to do the counting
  - 2-3 months → several minutes
- Let’s pretend to be a neuroscientist

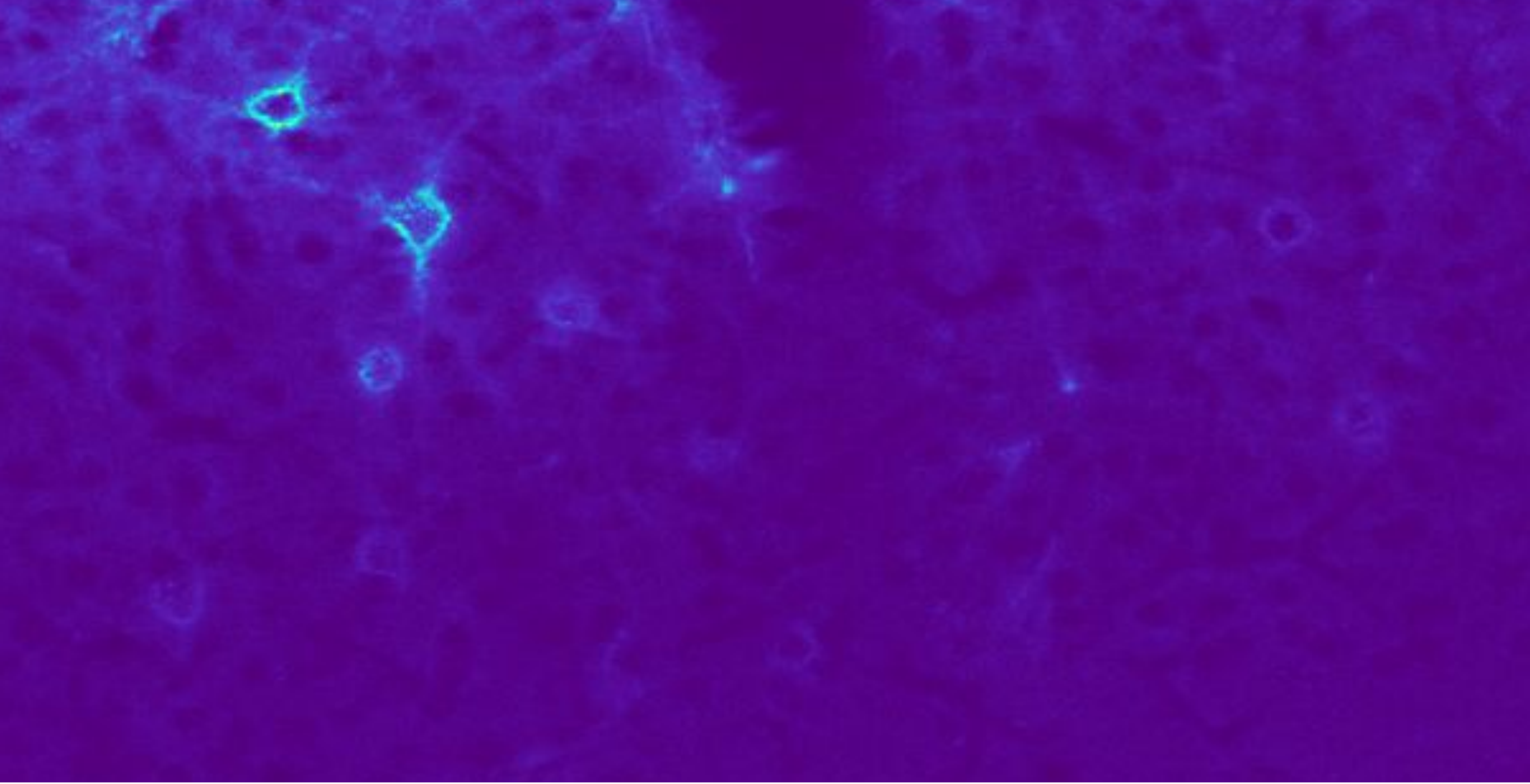








Ciampi, L., Carrara, F., Totaro, V., Mazziotti, R., Lupori, L., Santiago, C., Amato, G., Pizzorusso, T. and Gennaro, C. 2022. Learning to count biological structures with raters’ uncertainty. Medical Image Analysis, p.102500.



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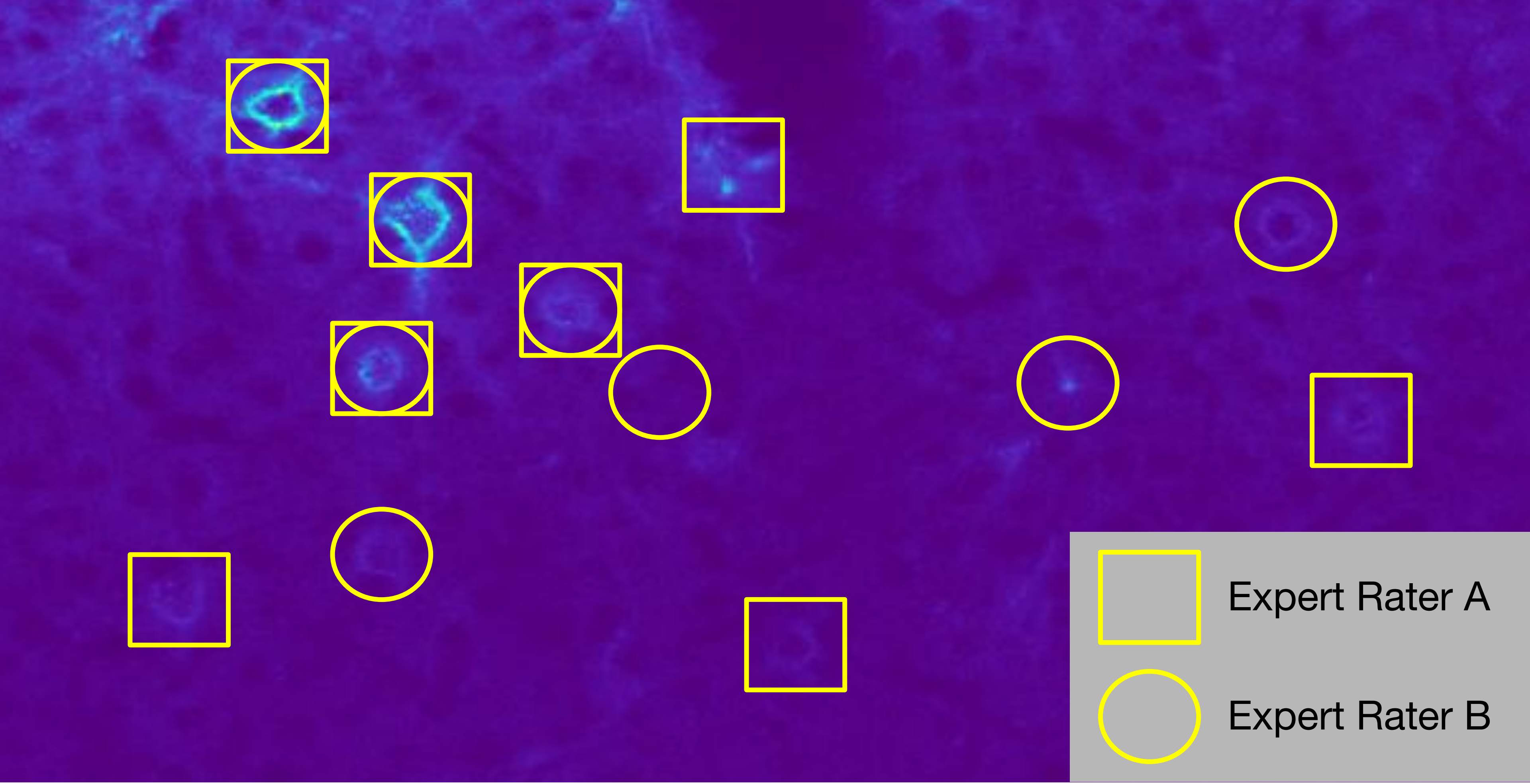

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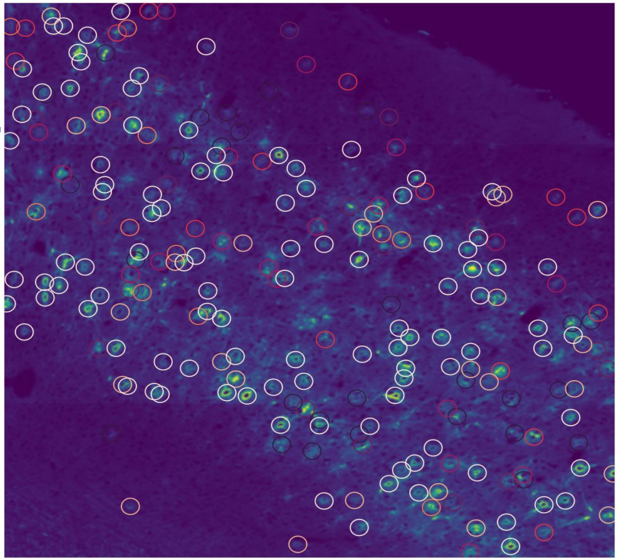
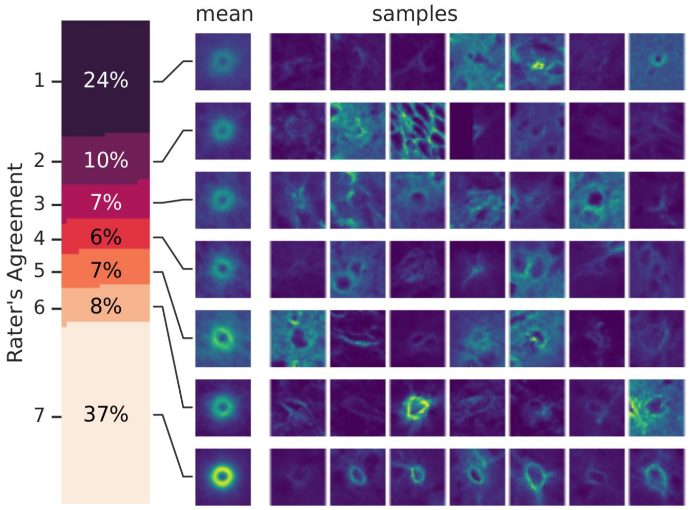
Motivation

- Manually counting non-trivial biological structures may produce weak labels, even with expert raters
  - agreement is ≤ 70% when counting PNNs
- Training AI on weakly labeled datasets may introduce raters' bias into the model
- Naive solution: get more reliable labels by averaging several decisions from multiple raters
  - Expensive
  - You get small datasets (usually not enough for AI)

⇒ use small multi-rater datasets to model uncertainty of patterns

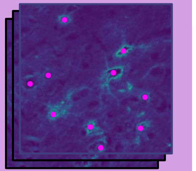
⇒ obtain cell counts at a desired level of certainty



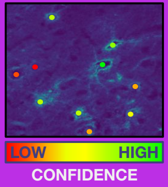


Our Solution: A two-stage Counting Pipeline

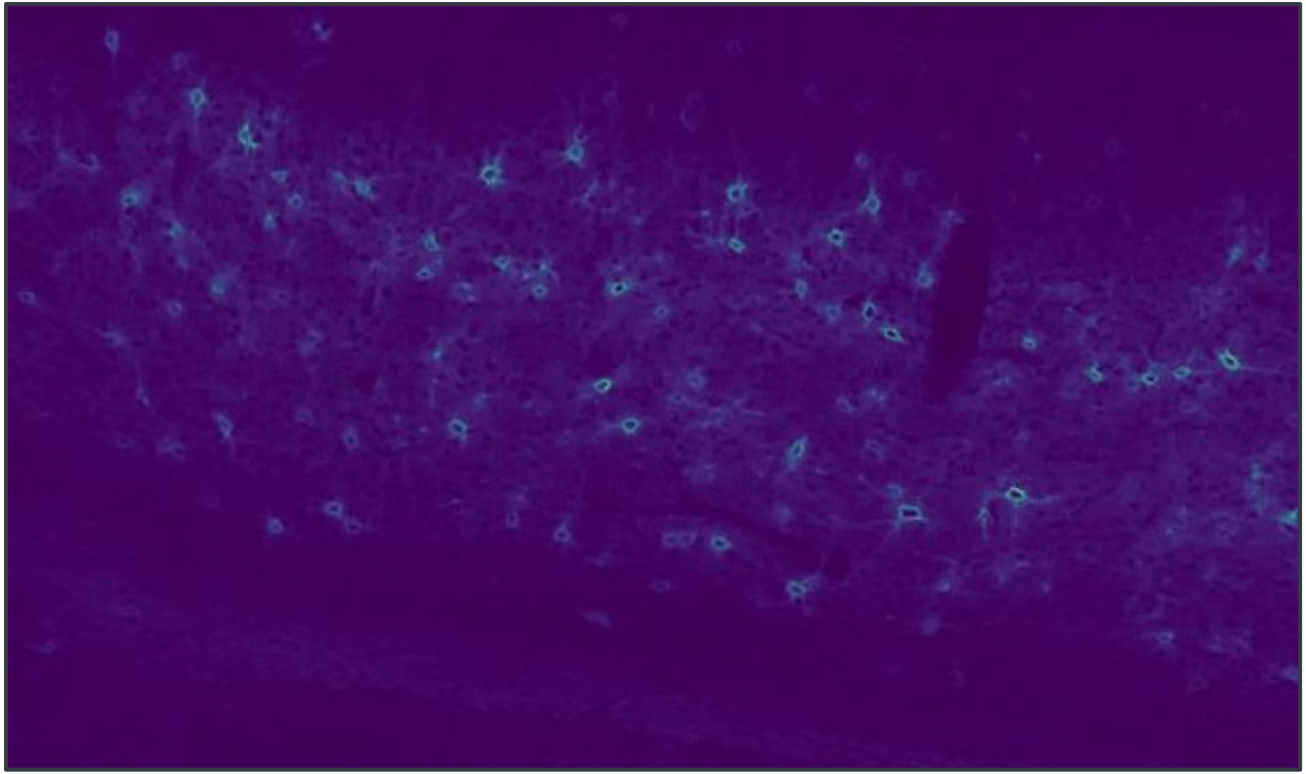
Stage 1:
Localization
(learned from single-rater weakly-labeled samples)



Stage 2:
Scoring
(learned from few multi-rater samples)



Filter & Count



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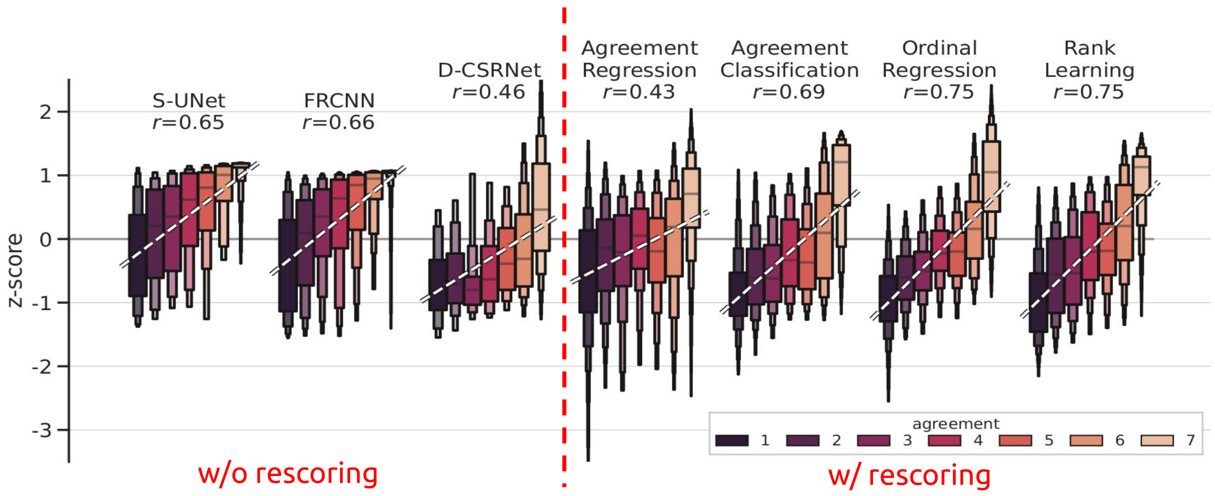
Evaluation

66% → 75%

(Pearson's Correlation between *Predicted Scores* and *Raters' Agreement*)



BASELINE

OURS

Reduction of **Counting Error** across multiple Ground Truth settings

Ground Truth composed by samples found by:

At least one rater	≥ 50% of raters	≥ 70% of raters	All raters
-20%	**-59%**	**-70%**	**-73%**
(19.13 → 14.87)	(14.67 → 6.00)	(15.80 → 4.73)	(13.87 → 3.73)

		Raters' Agreement			
	g_ϕ	Any ($a \geq 1$)	≥ 50% ($a \geq 4$)	≥ 70% ($a \geq 5$)	100% ($a = 7$)
S-UNet	w/o	19.13	14.67	15.80	13.87
	AR	19.73 (+0.60)	11.20 (−3.47)	9.53 (−6.27)	7.27 (−6.60)
	AC	17.53 (−1.60)	**6.00** (−8.67)	**4.73** (−11.07)	**3.73** (−10.13)
	OR	14.87 (−4.27)	7.00 (−7.67)	5.80 (−10.00)	5.13 (−8.73)
	RL	16.13 (−3.00)	6.93 (−7.73)	7.67 (−8.13)	6.07 (−7.80)
FRCNN	w/o	10.07	8.67	8.33	6.13
	AR	13.73 (+3.67)	10.53 (+1.87)	9.40 (+1.07)	8.73 (+2.60)
	AC	11.27 (+1.20)	7.00 (−1.67)	6.33 (−2.00)	5.27 (−0.87)
	OR	10.13 (+0.07)	6.40 (−2.27)	5.93 (−2.40)	4.13 (−2.00)
	RL	**9.67** (−0.40)	6.60 (−2.07)	8.00 (−0.33)	6.00 (−0.13)
D-CSRNet	w/o	89.53	15.67	9.00	8.33
	AR	89.53	18.33 (+2.67)	12.73 (+3.73)	7.40 (−0.93)
	AC	89.53	16.47 (+0.80)	10.13 (+1.13)	5.53 (−2.80)
	OR	89.53	15.67	9.53 (+0.53)	5.53 (−2.80)
	RL	89.53	15.73 (+0.07)	10.33 (+1.33)	5.93 (−2.40)

AR = Agreement Regression. AC = Agreement Classification. OR = Agreement Ordinal Regression. RL = Agreement Rank Learning.

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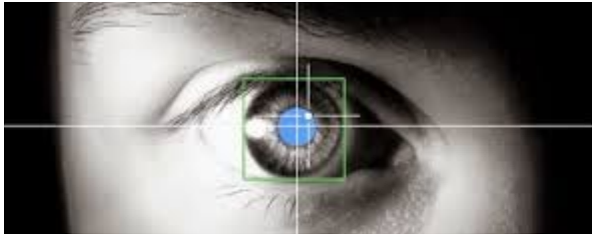
Optimized AI for Real-time Pupillometry

Pupillometry

- Pupillometry: measure pupil fluctuations over time; proxy for cognitive/emotional processing

- Alteration in pupil dynamics can be a translational biomarker for neurodevelopmental disorders (e.g., autism, Rett syndrome).

- Commercial eye/pupil trackers are **expensive** and **technical skills** are needed (fallback: offline recordings and manual segmentation).



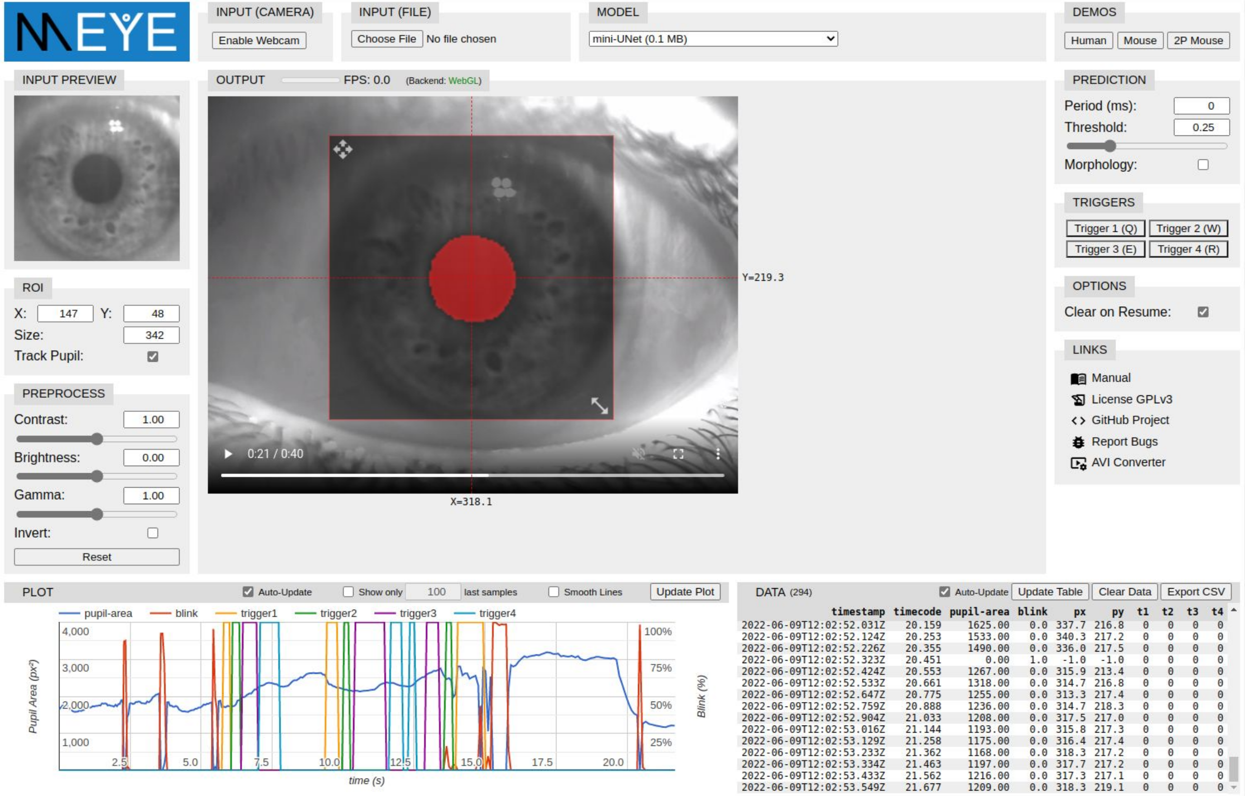
⇒ exploit AI to build a cheap and accessible setup for pupillometry!

Mazziotti, R., Carrara, F., Viglione, A., Lupori, L., Verde, L.L., Benedetto, A., Ricci, G., Sagona, G., Amato, G. and Pizzorusso, T. 2021. MEYE: Web App for Translational and Real-Time Pupillometry. Eneuro, 8(5).

MEYE

A real-time, open source, easy-to-use, portable tool for pupillometry in online video streams and offline recordings.

Optimized pupil segmentation model (0.1MB) provides fast segmentation of pupils in different scenarios (human & mice, IR and 2P lightning).



Runs in your browser! At Home!

https://www.pupillometry.it/

Also in Python/MATLAB environments:

https://github.com/fabiocarrara/meye

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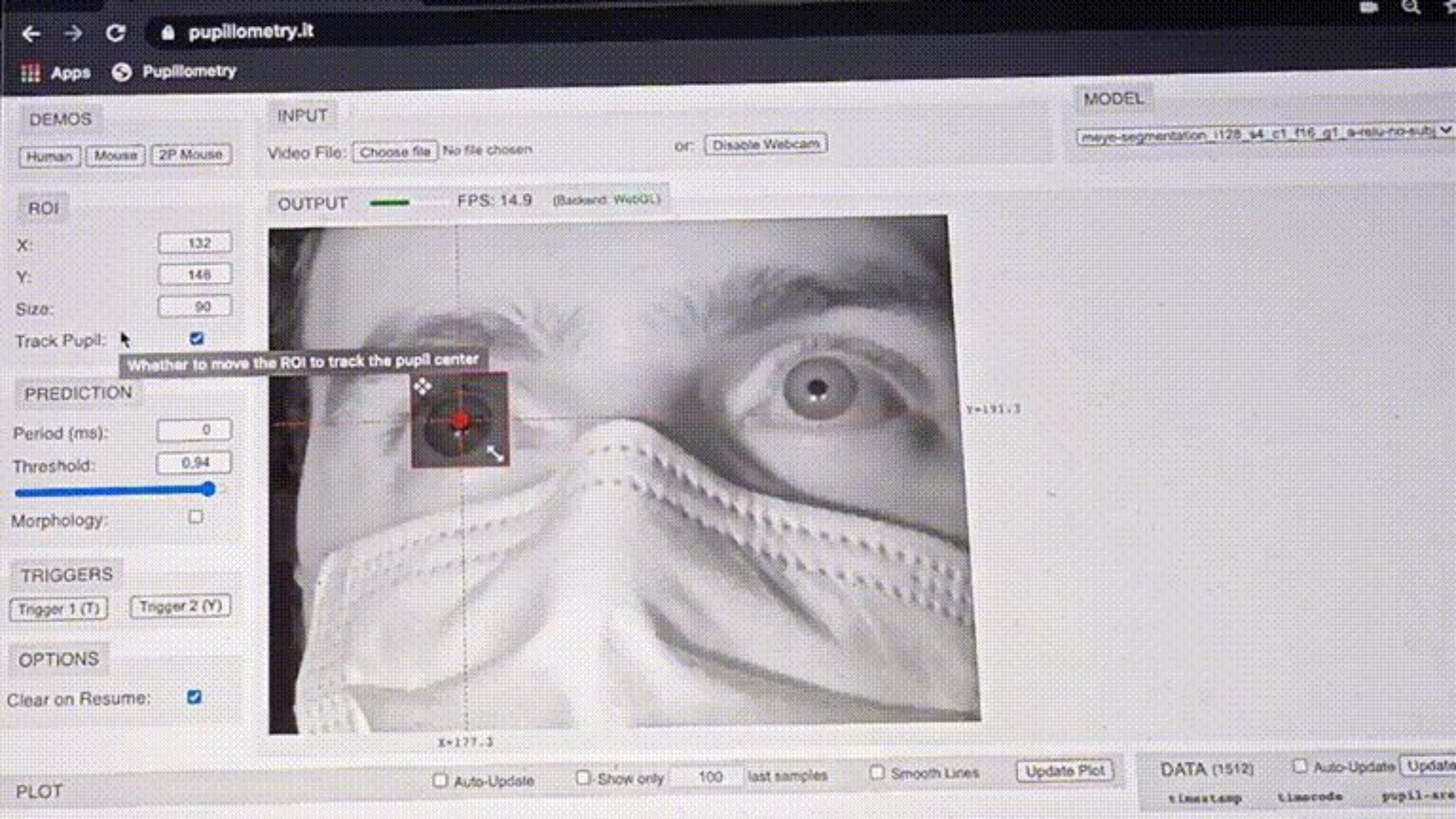
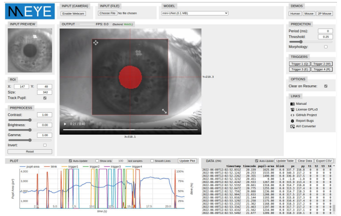


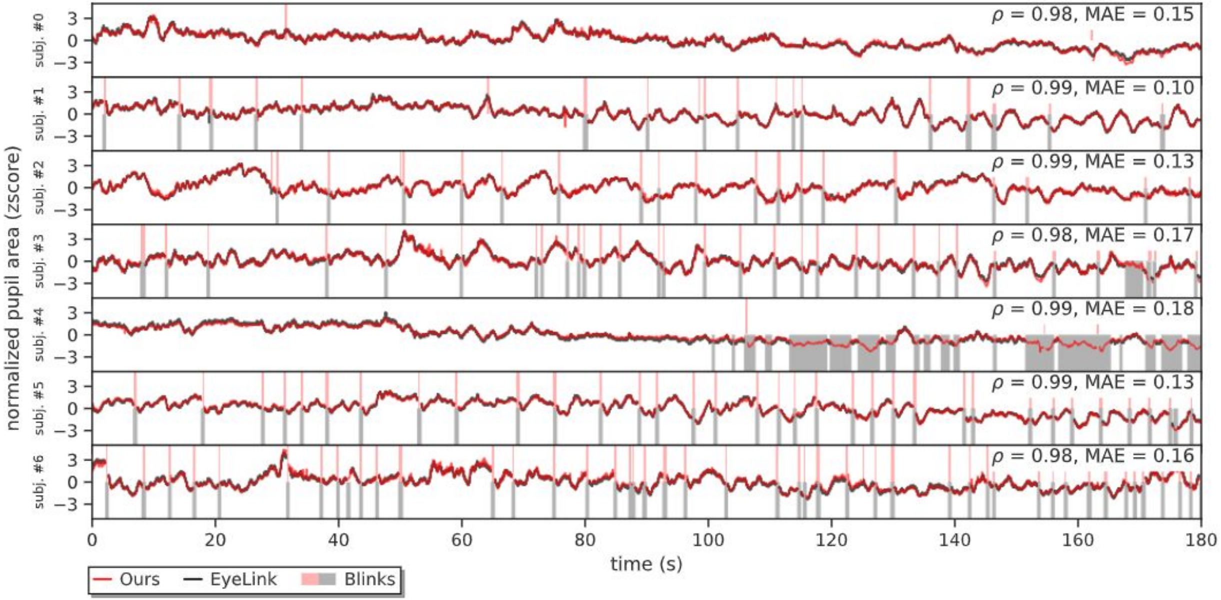
pupillometry.it
Apps
Pupillometry
DEMOS
Human
Mouse
2P Mouse
INPUT
Video File:
Choose file
No file chosen
or:
Disable Webcam
MODEL
ROI
X:
132
Y:
148
Size:
90
Track Pupil:
Whether to move the ROI to track the pupil center
OUTPUT
FPS: 14.9
(Backend: WebGL)
PREDICTION
Period (ms):
0
Threshold:
0.94
Morphology:
TRIGGERS
Trigger 1 (T)
Trigger 2 (Y)
OPTIONS
Clear on Resume:
PLOT
Auto-Update
Show only
100
last samples
Smooth Lines
Update Plot
DATA (1512)
Auto-Update
timestamp
timecode

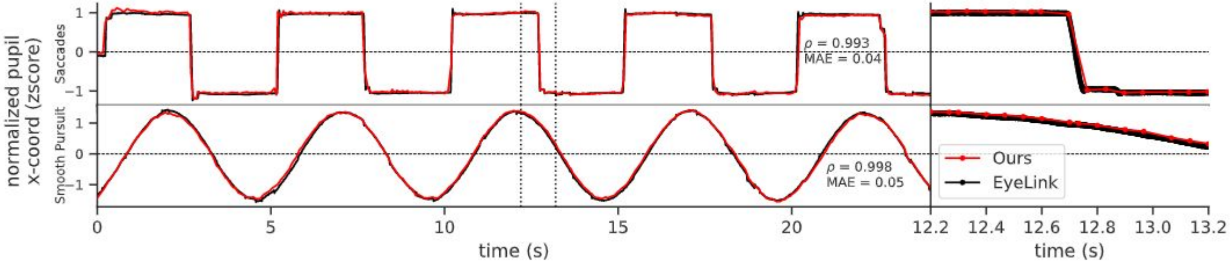
Comparison with EyeLink® 1000



MEye (Free) & USB IR Camera + Varifocal Lens (~50€)

EyeLink 1000 System (many €€€)





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Thanks for your attention!

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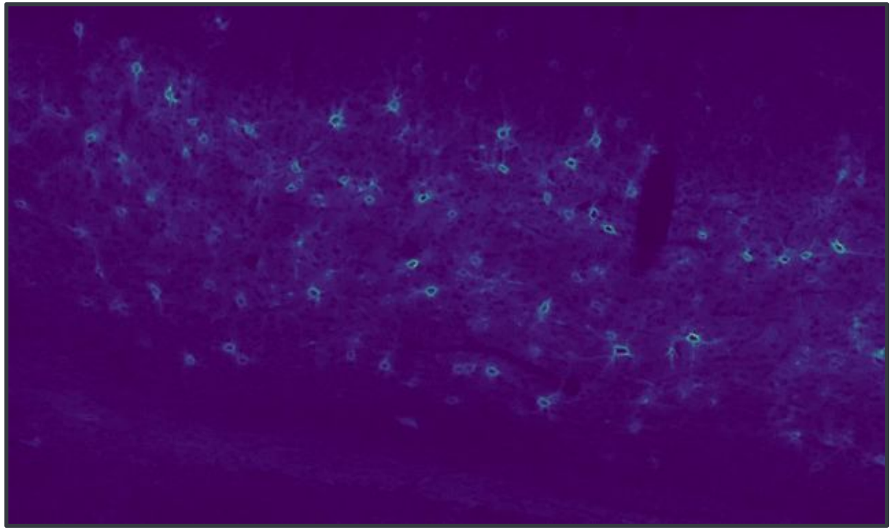
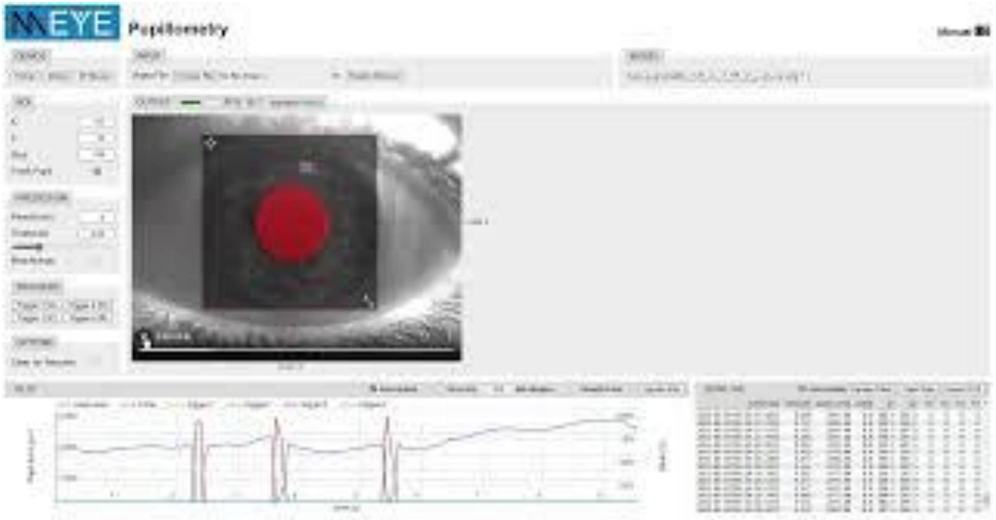
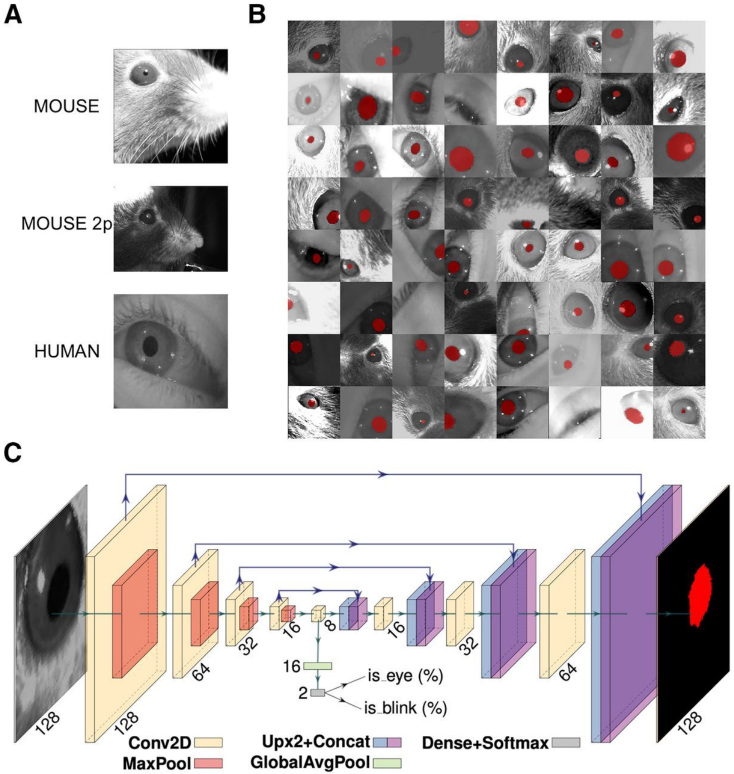




Extra Slides

Architectural Optimization for Fast Pupillometry



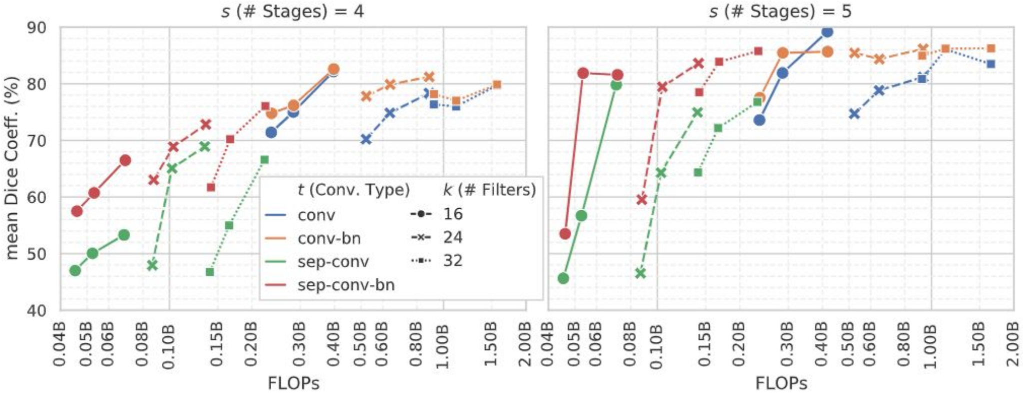


Fig. 2. Effectiveness (y-axis, mean Dice Coefficient, %) vs. Efficiency (x-axis, FLOPs in billions) trade-off of the explored architectures for image segmentation when varying the number of encoder/decoder stages s, the convolutional block type t, the number of convolutional kernels in the first stage k, and the network growing factor γ. Each line represents a class of architectures with a fixed t, a fixed k, and an increasing γ varied in $\{1, 1.2, 1.5\}$.

Model	Pretrain	mean Dice	FPS (Web†)	FPS (Keras‡)	FLOPs	# Params.
DeepLabv3+/ResNet-50	ImageNet	80.1%	<1	28.7	14.1B	26.8M
DeepLabv3+/Lite-MobileNet-V3-Small	ImageNet	69.0%	18.8	34.8	0.3B	1.1M
Ours ($s = 4$, $t =$ conv, $k = 16$, $\gamma = 1.5$, $a =$ false)	none	84.0%	23.2	45.2	0.2B	0.03M

† Dell Laptop - *CPU*: Intel® Core™ i7-9750H 2.60GHz, *GPU*: Intel® UHD Graphics 630, *TensorFlow.js Backend*: WebGL, *Browser*: MS Edge 90.0.818.56.
‡ Ubuntu 20.04 - *CPU*: Intel® Core™ i9-9900K 3.60GHz, *GPU*: GeForce RTX 2080 Ti, Python 3.6.9 + TensorFlow 2.4.1.

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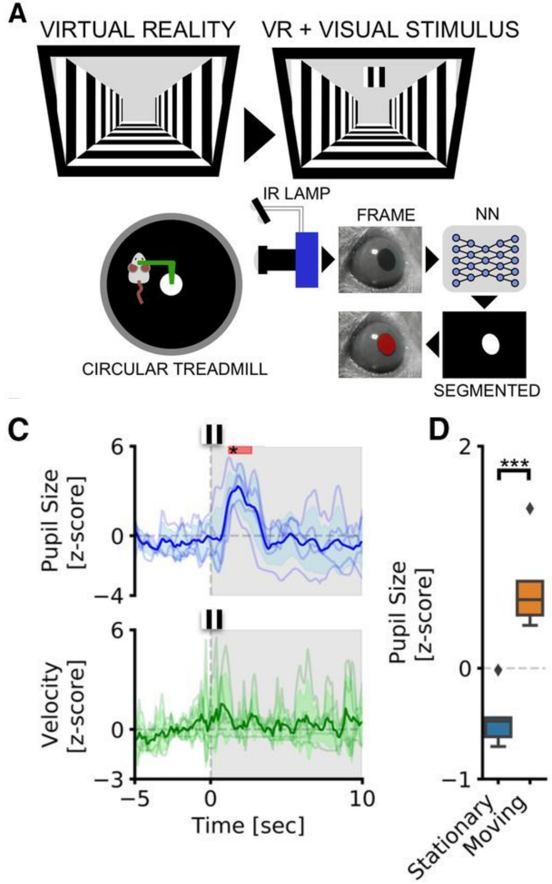
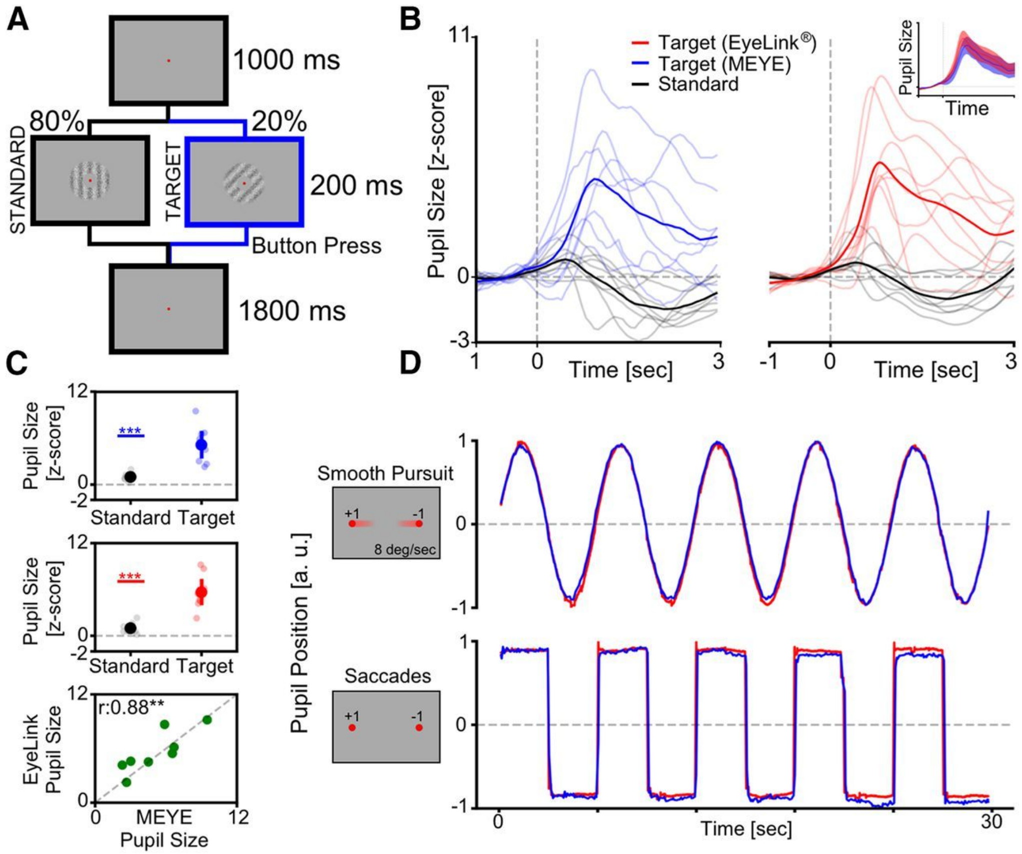
Evaluation on Mice and Humans





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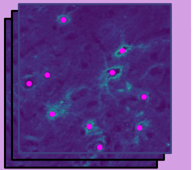
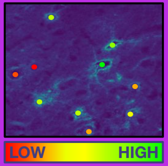
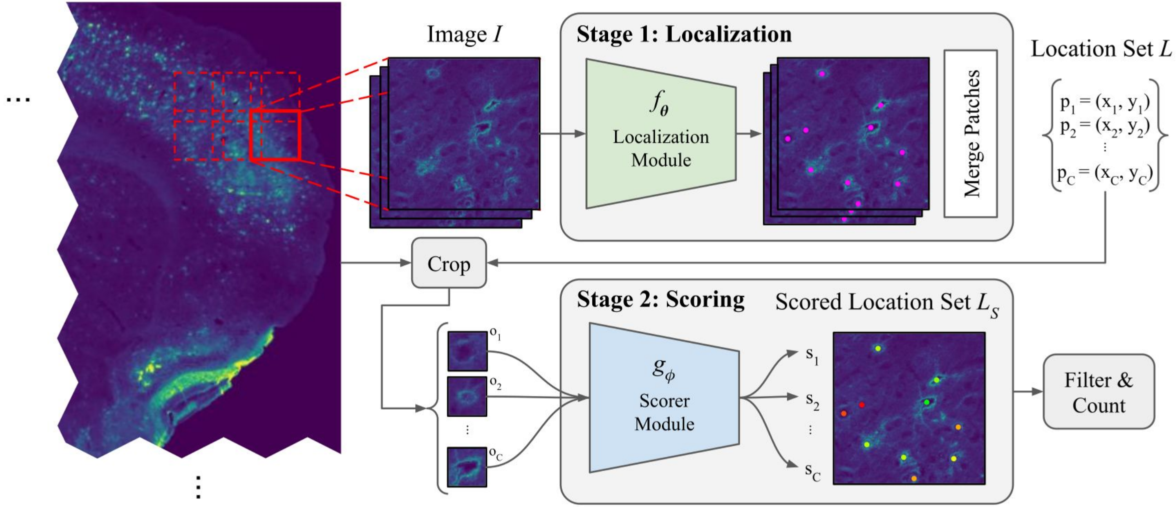
Stage 1:
Localization
(learned from single-rater weakly-labeled samples)



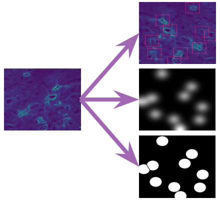
Stage 2:
Scoring
(learned from few multi-rater samples)



Filter & Count



- **Three localization strategies f_θ:**

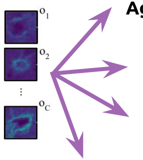


Detection (*FRCNN*)

Density Estimation (*D-CSRNet*)

Segmentation (*S-Unet*)

- **Four scoring strategies g_θ:**



Agreement Regression (AR)

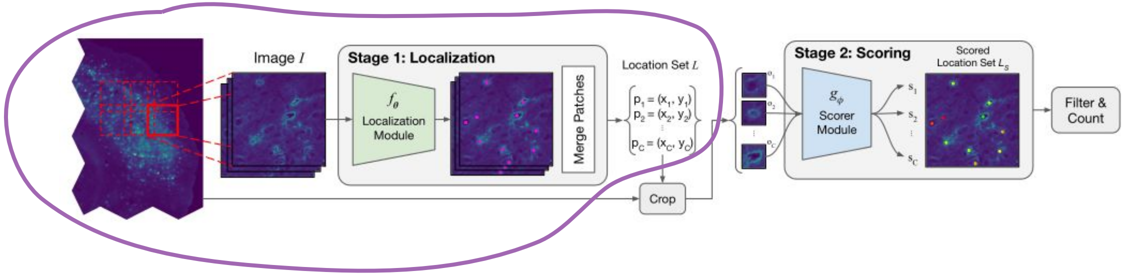
Agreement Classification (AC)

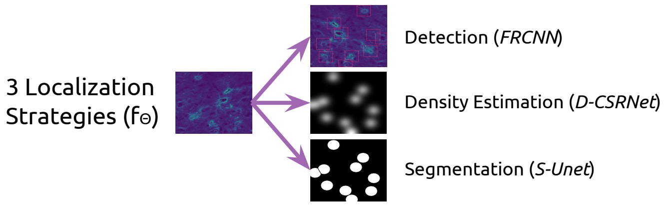
Agreement Ordinal Regression (OR)

Agreement Rank Learning (LR)

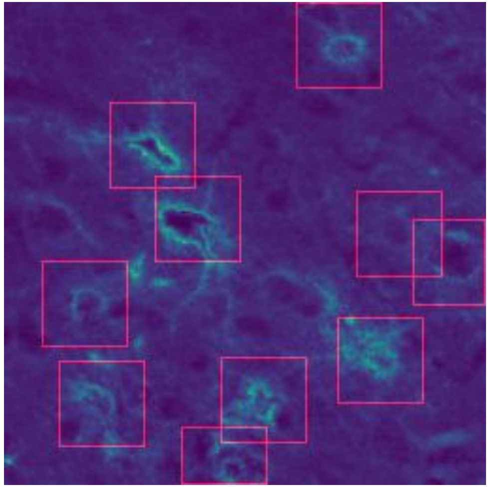
Ciampi, L., Carrara, F., Totaro, V., Mazziotti, R., Lupori, L., Santiago, C., Amato, G., Pizzorusso, T. and Gennaro, C. 2022. Learning to count biological structures with raters' uncertainty. Medical Image Analysis, p.102500.

Stage 1: Localization

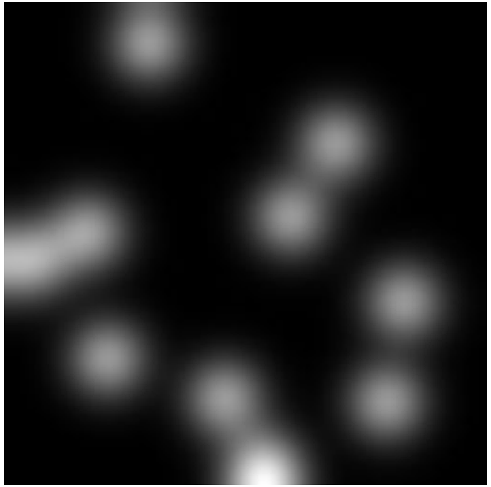




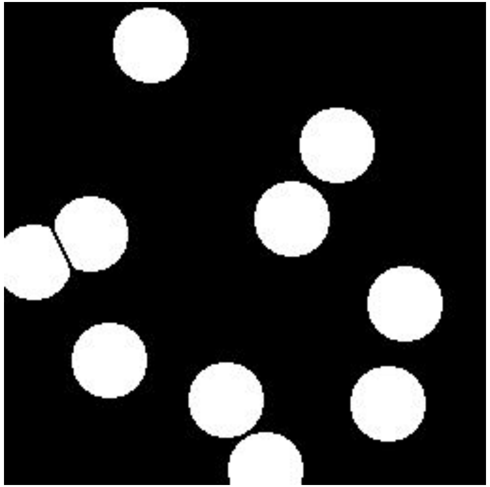
1. ***Detection (FRCNN)***



2. ***Density Estimation (D-CSRNet)***

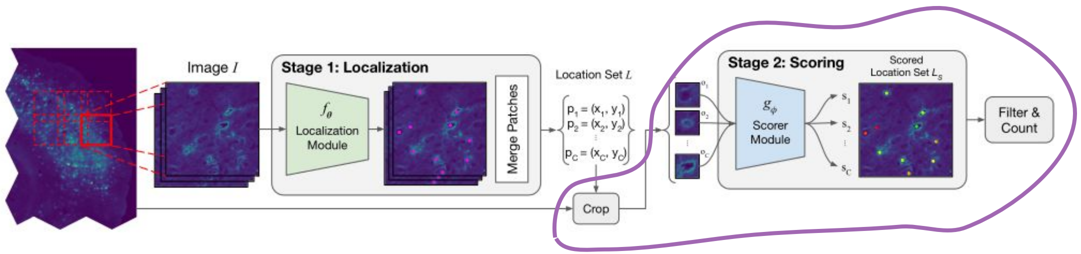


3. ***Segmentation (S-Unet)***

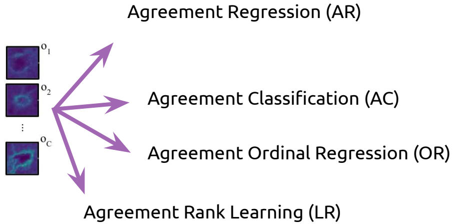


Ciampi, L., Carrara, F., Totaro, V., Mazziotti, R., Lupori, L., Santiago, C., Amato, G., Pizzorusso, T. and Gennaro, C. 2022. Learning to count biological structures with raters' uncertainty. Medical Image Analysis, p.102500.

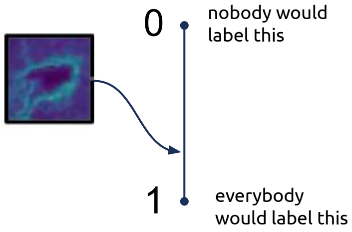
Stage 2: Scoring



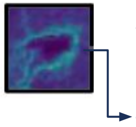
4 Scoring Strategies (g_Θ)



1. ***Agreement Regression (AR)***



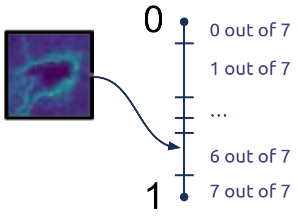
2. ***Agreement Classification (AC)***



CLASSES:

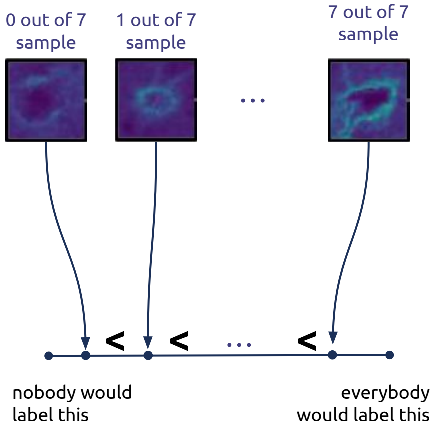
- 0 out of 7 would label this
- 1 out of 7 would label this
- ...
- 6 out of 7 would label this
- 7 out of 7 would label this

3. ***Agreement Ordinal Regression (OR)***



Model learns thresholds during training

4. ***Agreement Rank Learning (LR)***



Model is penalized during training if scores are not sorted properly.

Ciampi, L., Carrara, F., Totaro, V., Mazziotti, R., Lupori, L., Santiago, C., Amato, G., Pizzorusso, T. and Gennaro, C. 2022. Learning to count biological structures with raters' uncertainty. Medical Image Analysis, p.102500.