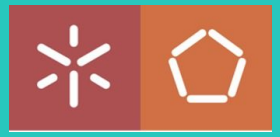
PhageScan

An automated viral particle classifier



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Introduction to Bacteriophages

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Overview

- Viruses that thrive by infecting and replicating within bacterial cells
- Species-specific
- Maintain life cycle by co-evolving with target-species[1]
- Three different life styles:
    - Lysogenic
    - Lytic
    - Chronic
- Valuable biological assets with therapeutical interest[2]

1 Koskella, 2014 (https://doi.org/10.1111/1574-6976.12072)

2 Sulakvelidze, 2001 (https://doi.org/10.1128/aac.45.3.649-659.2001)

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Phage morphology

- Tailed phages are composed by:
  - Icosahedral capsid (genetic material storage)
  - Tail (to attach to and infect host)
- Tailed phages exhibit 3 different morphotypes:
  - Podoviruses: short non-contractile tail
  - Siphovirus: long, flexible, non-contractile tail
  - Myoviruses: long contractile tail with a base plate and spikes

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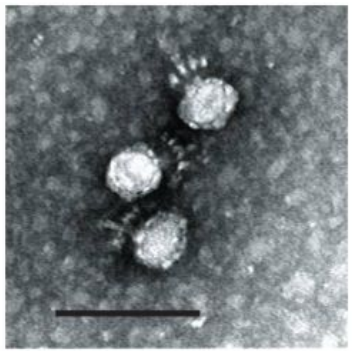
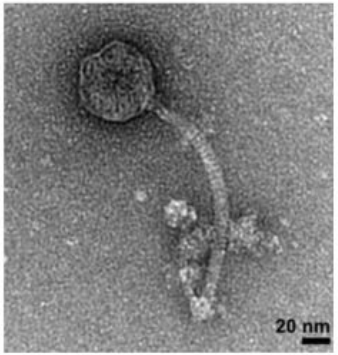
Phage morphology



(a) Podovirus



(b) Siphovirus

(c) Myovirus

Morphotypes of tailed phages [1, 2, 3]

1 Volozhantsev, 2012 - https://doi.org/10.1016/j.ijfoodmicro.2021.109446
2 Demo, 2021 - https://doi.org/10.1371/journal.pone.0248418
3 Mann, 2005 - https://doi.org/10.1371/journal.pbio.0030182

Automated classification of viral particles

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Overview

- Morphology retains visual classification potential!
- Manual identification is laborious and fastidious
- Automated viral classification is growing in popularity
- Several research efforts to develop novel tools

Definition of a "valuable" automated classification tool:

- >75% accuracy[1]

1 Glaeser, 2004 (https://doi.org/10.1016/j.jsb.2003.09.005)

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Application of machine learning techniques

- Gaussian classifiers
- Multi-layer perceptrons
- Naive bayes
- Random forests
- Convolutional Neural Networks

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Goal of this project

Develop a tool to infer virus' taxonomy from TEM micrographs

- Streamline taxonomical classification
- Rough estimation of phage genome size based on TEM micrographs

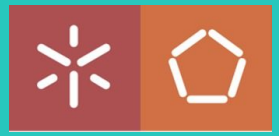
Apply Convolutional Neural Networks (CNNs) to classify morphotypes

- Specifically YOLO (You Only Look Once) algorithms

Why CNNs?

- Versatile models specialized in processing grid-like data (i.e. images)
- Fast, flexible and easy to parametrize
- Strong capability to discern patterns → popular object classifier

Teuwen and Moriakov, 2020 (https://doi.org/10.1016/B978-0-12-816176-0.00025-9)



Introduction to Convolutional Neural Networks

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Introduction to CNNs

Constituted by:

- Input layer (receives raw input data)
- Hidden layers:
  - Convolutional layers (mathematical processing)
  - Pooling layers (downsampling operations)
  - Fully connected layers (vectorial computation)
- Output layer (produces final output)

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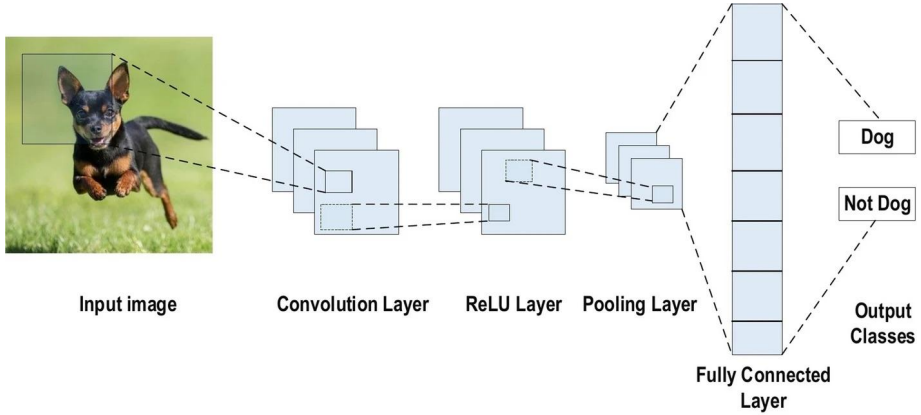
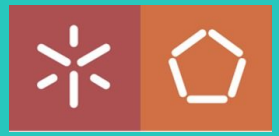
Phage morphology



Schematic representation of a CNN

Source: Alzubaidi et al, 2021 (https://doi.org/10.1186/s40537-021-00444-8)



Methods

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Data collection

- Data collected from PhagesDB and CEB Phage Research Lab
  - 300+ phage TEM micrographs

Noteworthy:

- Vast majority of micrographs are of siphoviruses
- Myoviruses in “relaxed state” and siphoviruses are similar
- Noisy micrographs

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Data preprocessing

- Resizing images to fixed size (640 x 640 px)
- Annotation using bounding boxes and polygons
  - 1 class: “siphovirus”
- Data set augmentation:
  - Random rotations
  - Flips

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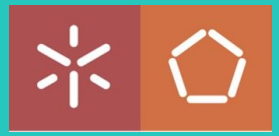
Model training parameters

- Epochs: 10; 25; 50
- Batch size: 16
- Activation function: SiLU (YOLO default)
- Learning rate: 10e-3 (Adam - YOLO default)
- Data set splitting - 80:15:5 (Train:Validate:Test)



Results

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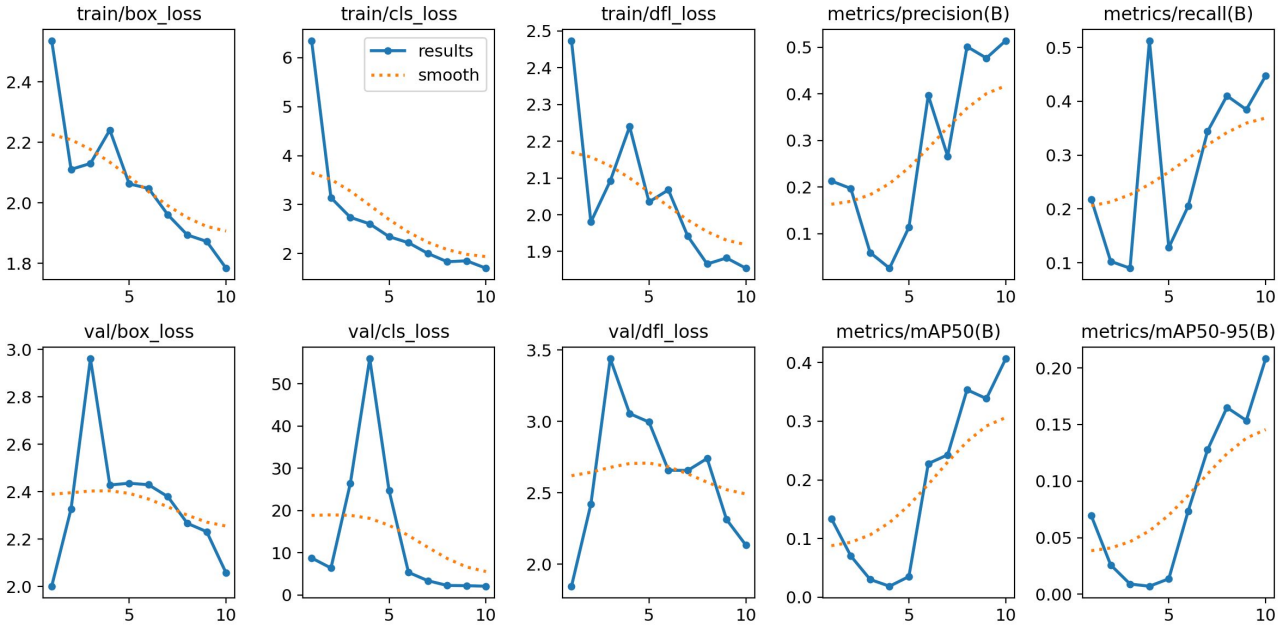
Training results: 10 epochs



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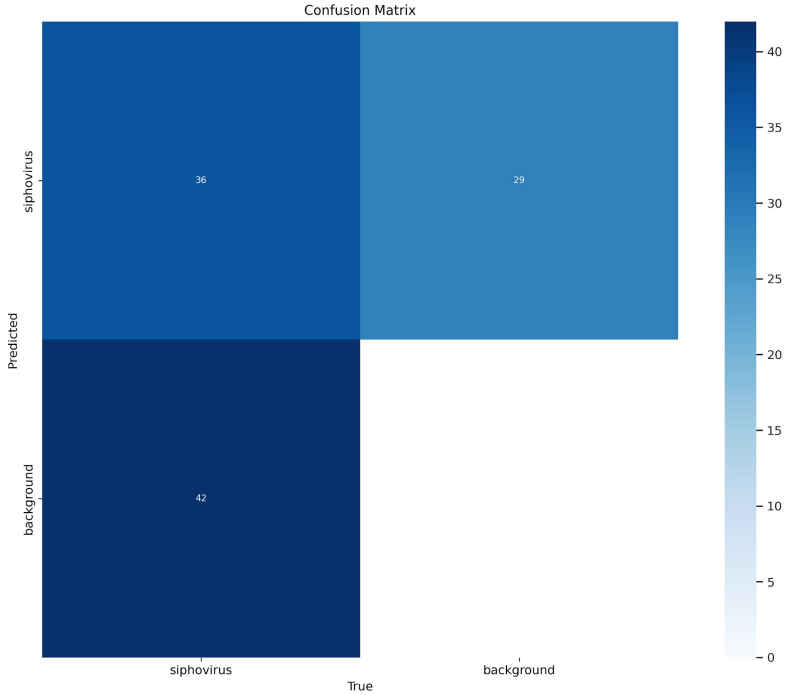
Training results: 10 epochs



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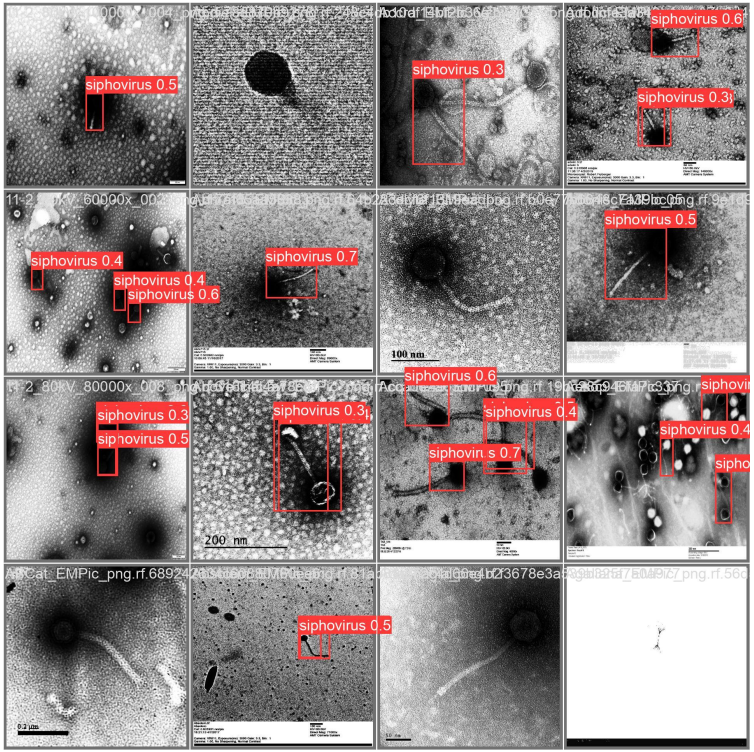
Training results: 10 epochs



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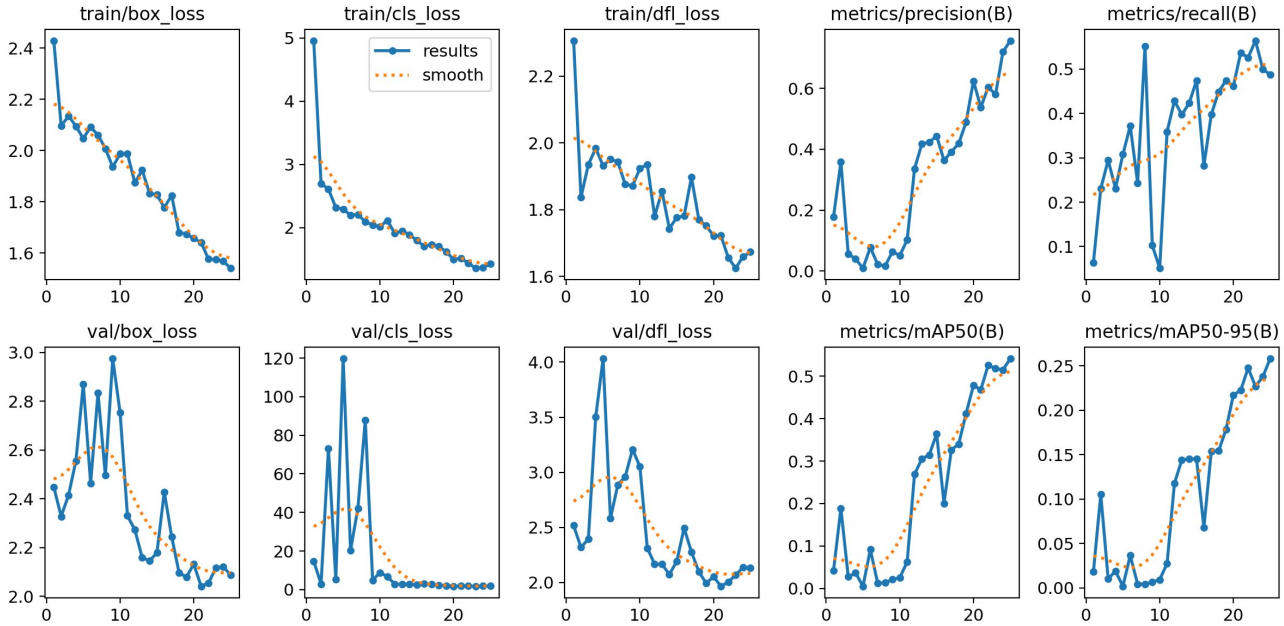
Training results: 25 epochs



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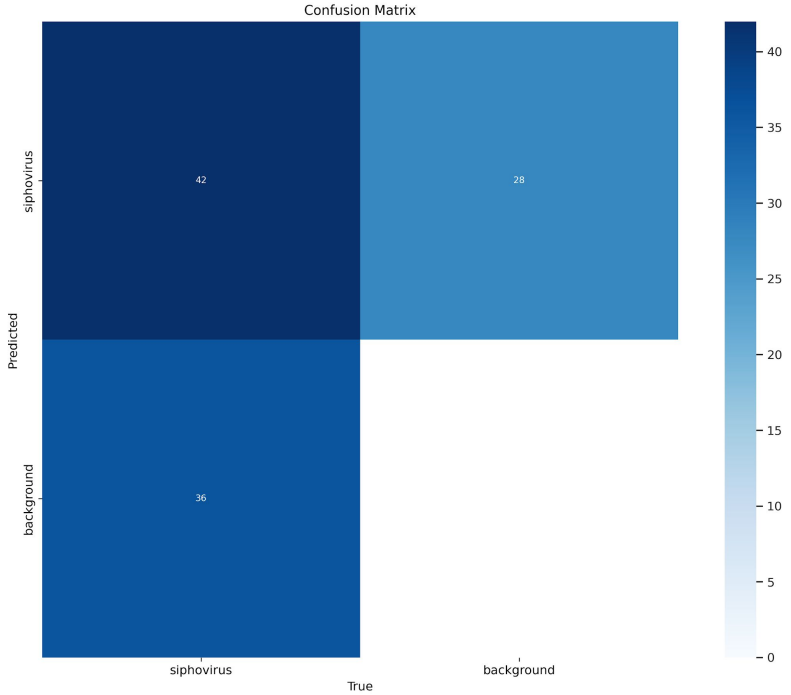
Training results: 25 epochs



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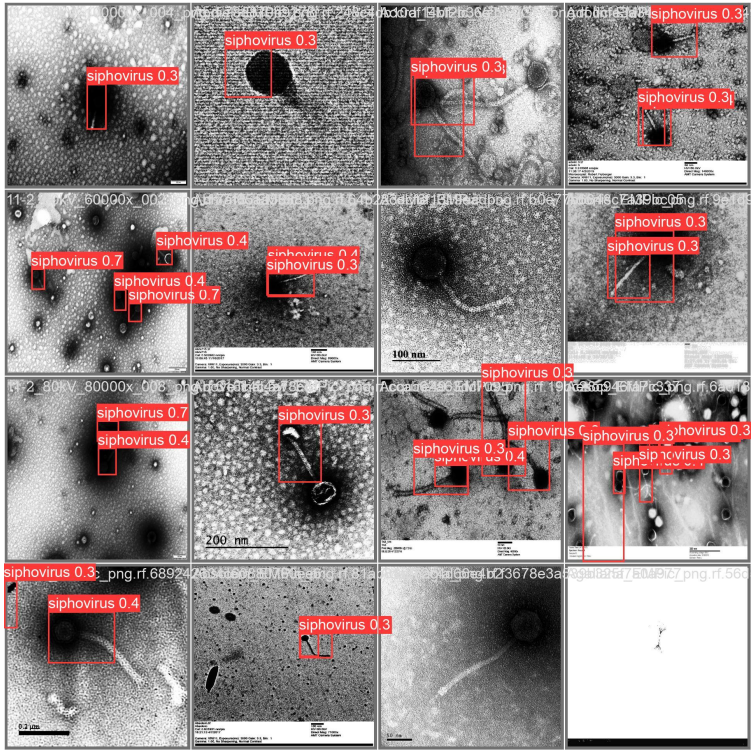
Training results: 25 epochs



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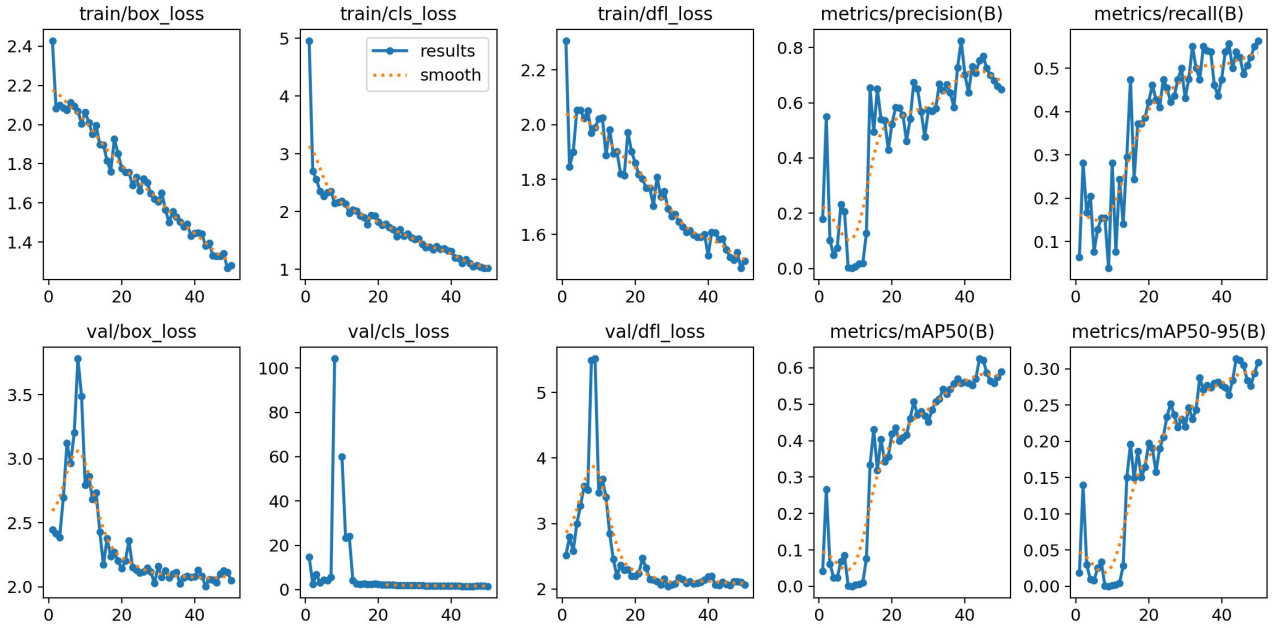
Training results: 50 epochs



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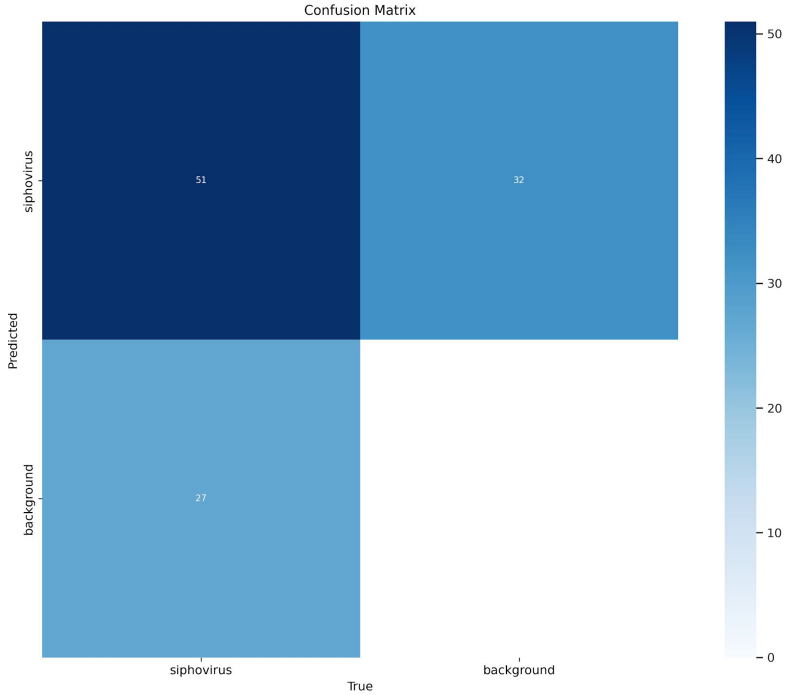
Training results: 50 epochs



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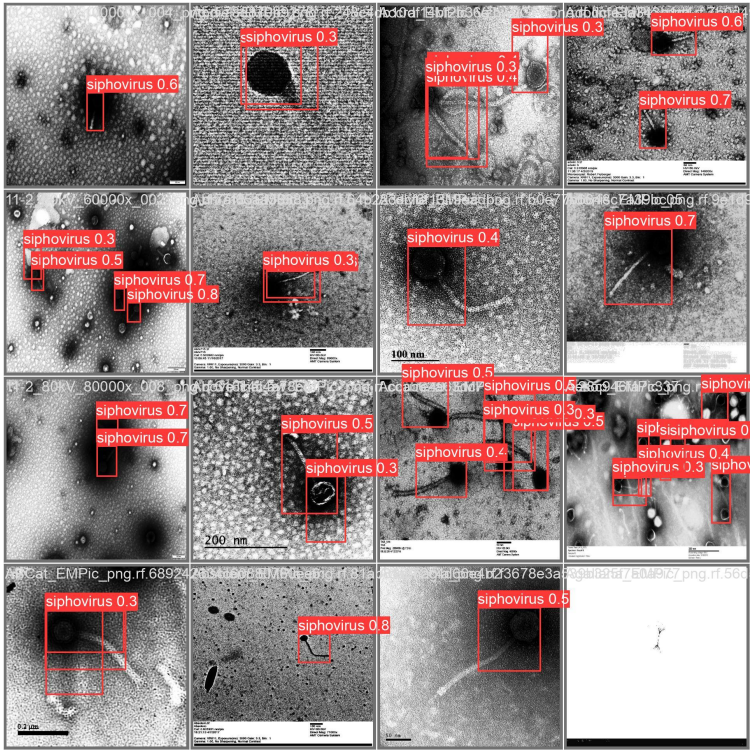
Training results: 50 epochs



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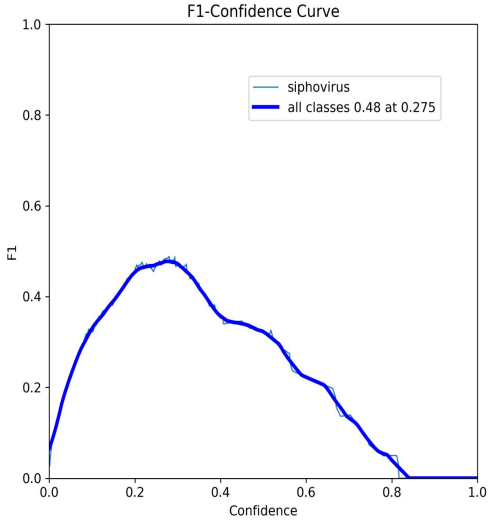
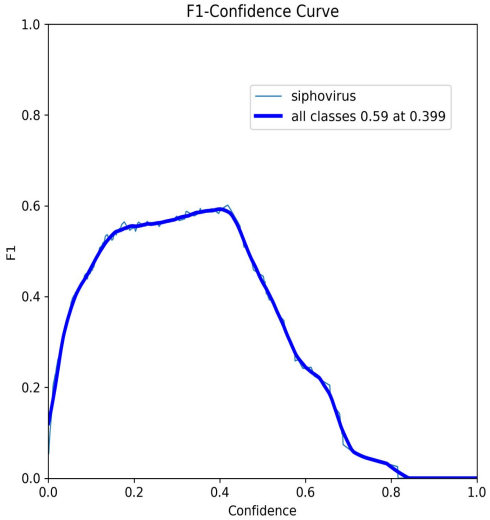
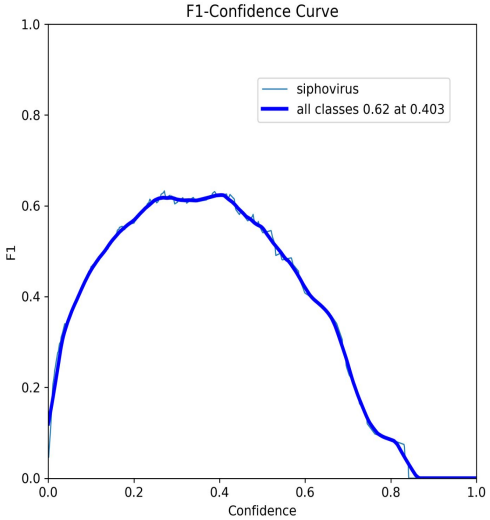
Comparison



10 Epochs



25 Epochs



50 Epochs

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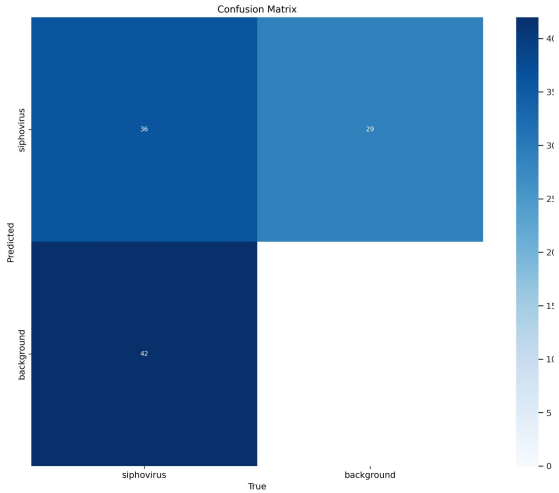

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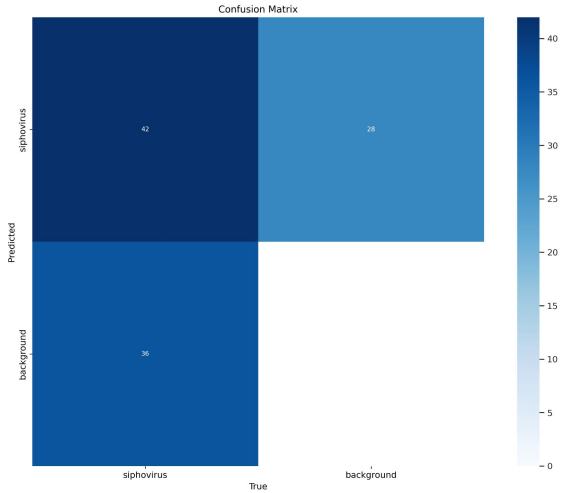

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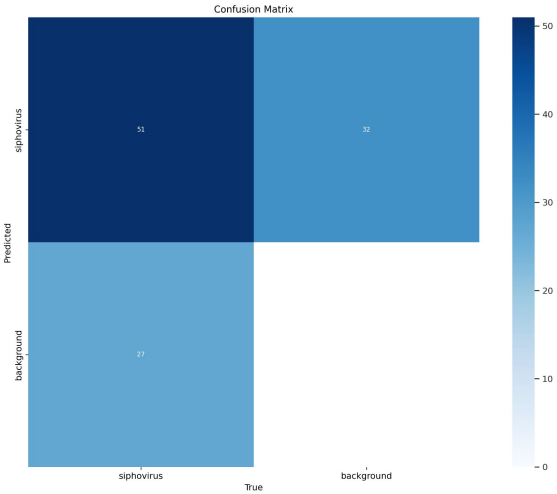

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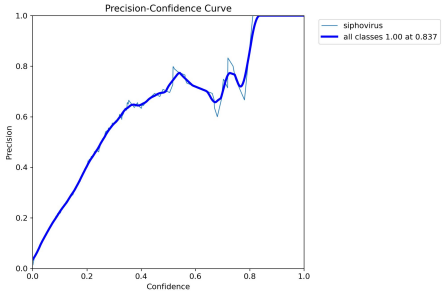

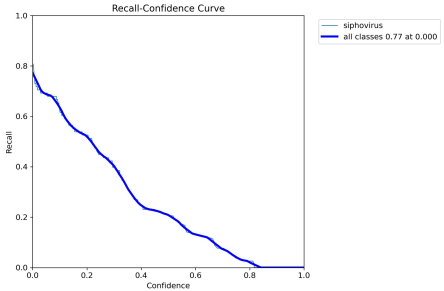

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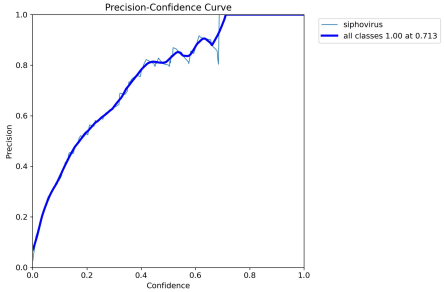

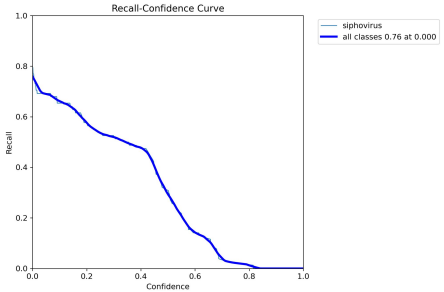

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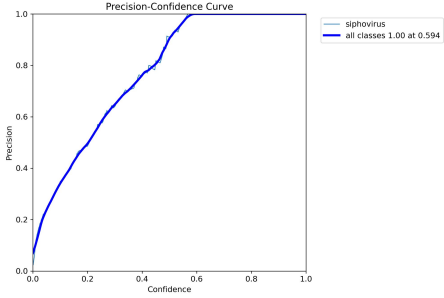

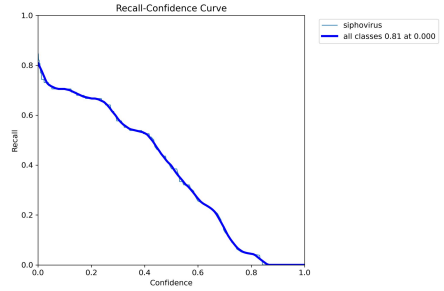

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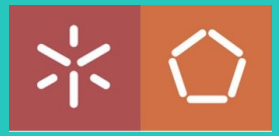

Conclusions

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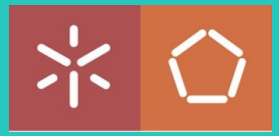
Conclusions

- Reasonable F1 score for 0.6 confidence threshold;
- Model improves through epochs, being the optimized around 40 epochs;
- Overfitting is visible (a problem when using single classes), especially for high confidence thresholds;



Future work

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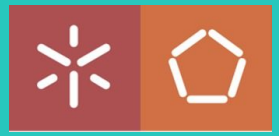
Future work

- Train the model with more classes;
- Increase data variety and quality to improve results;
- Add automated measurement features (exploratory):
  - implement OCR for scale reading;
  - edge detection to isolate capsid;
  - estimate measurements;



Thank you!