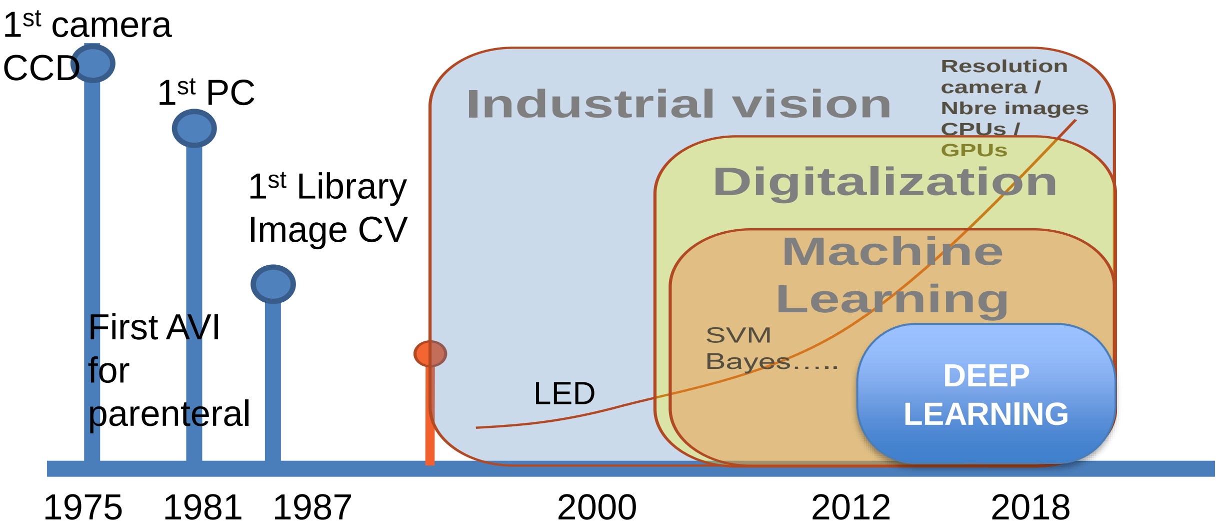
Mastering AVI

Part9: Future trends in AVI

Instructor Lead: Romain Veillon / Fernand Koert / Sébastien Koch

AVI is a fast evolving technology



Key Take Away:

- AVI is a young, maturing technology
- Many changes over the last 30 years, next one is deep learning

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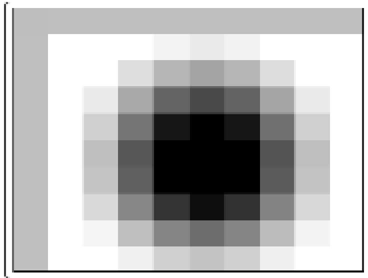
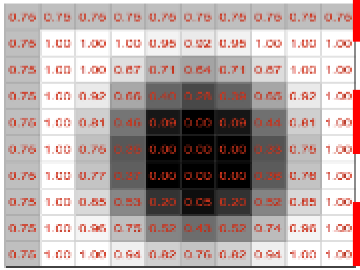
- What is a di





0.75	0.75	0.75	0.75	0.75	0.76	0.75	0.76	0.75	0.76
0.75	1.00	1.00	1.00	0.95	0.92	0.95	1.00	1.00	1.00
0.75	1.00	1.00	0.87	0.71	0.64	0.71	0.87	1.00	1.00
0.75	1.00	0.92	0.66	0.40	0.28	0.38	0.65	0.92	1.00
0.76	1.00	0.81	0.46	0.09	0.00	0.09	0.44	0.81	1.00
0.76	1.00	0.76	0.36	0.00	0.00	0.00	0.33	0.75	1.00
0.75	1.00	0.77	0.37	0.00	0.00	0.00	0.36	0.78	1.00
0.75	1.00	0.85	0.53	0.20	0.05	0.20	0.52	0.85	1.00
0.75	1.00	0.96	0.75	0.52	0.43	0.52	0.74	0.96	1.00
0.75	1.00	1.00	0.94	0.82	0.76	0.82	0.94	1.00	1.00

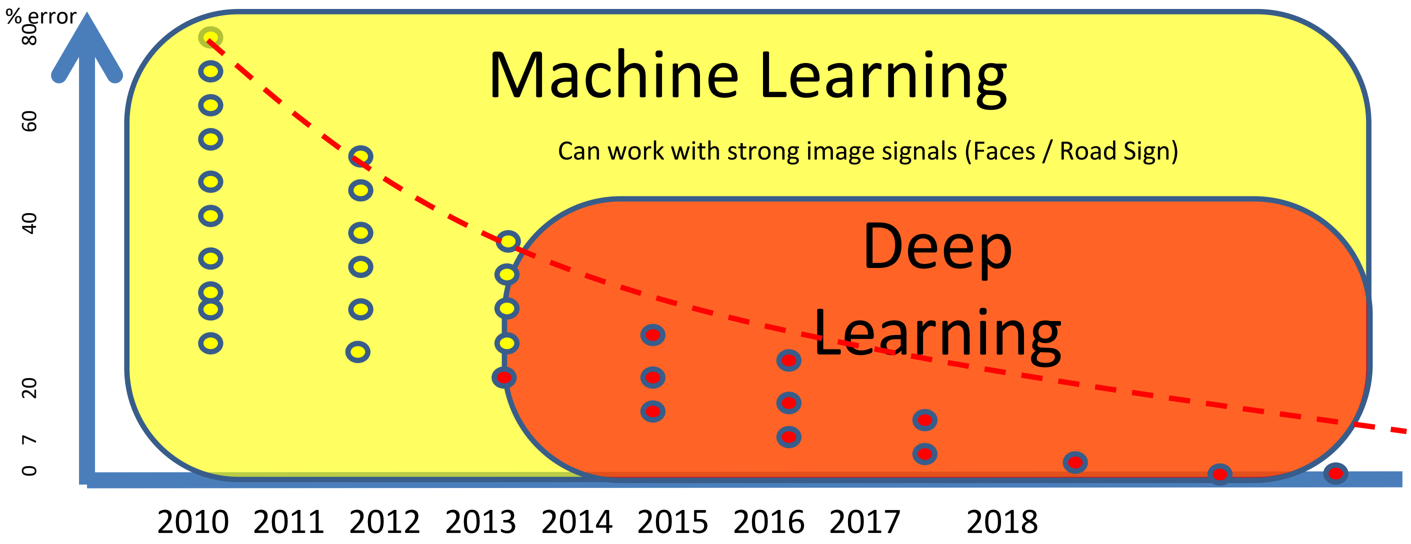
1 particle image **Image with grey levels…** **Digital Image = matrix grid of figures in X and Y**

In computer vision language (python/C++) it is a matrix object:
np.zeros(img.shape, dtype=img.dtype)

Key Take Away:

- **Computer vision see only a matrix**
- **That represent spatial distribution of grey levels**
- **Neural Network will work with image matrix**

Machine Learning versus Deep Learning ?



Key Take Away: **Machine Learning (SVM) never achieved promising results with parenteral**

Problem statement - Challenges

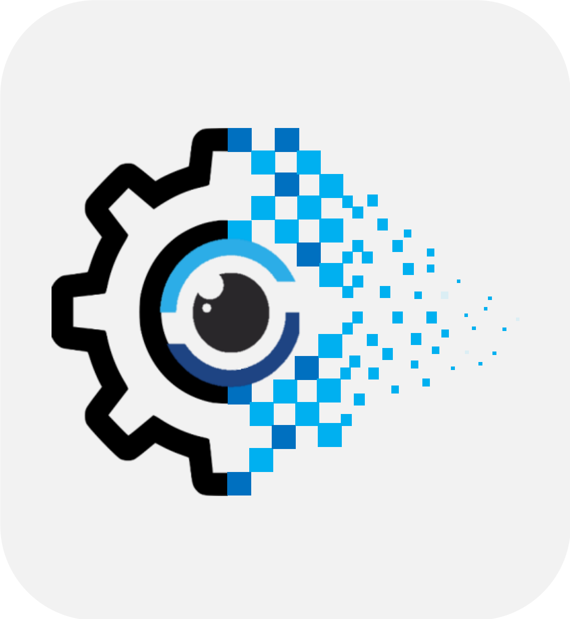
- We believe that Deep Learning will significantly improve Trust and Performance of Automated visual inspection

Suboptimal detection rates for some probabilistic defects

Tedious process around the improvement and test of machine performance

Manual reprocessing of false reject units after automated visual inspection takes a long time

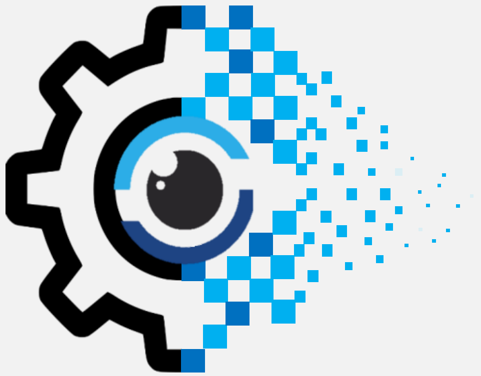
What are Benefits of Deep Learning?



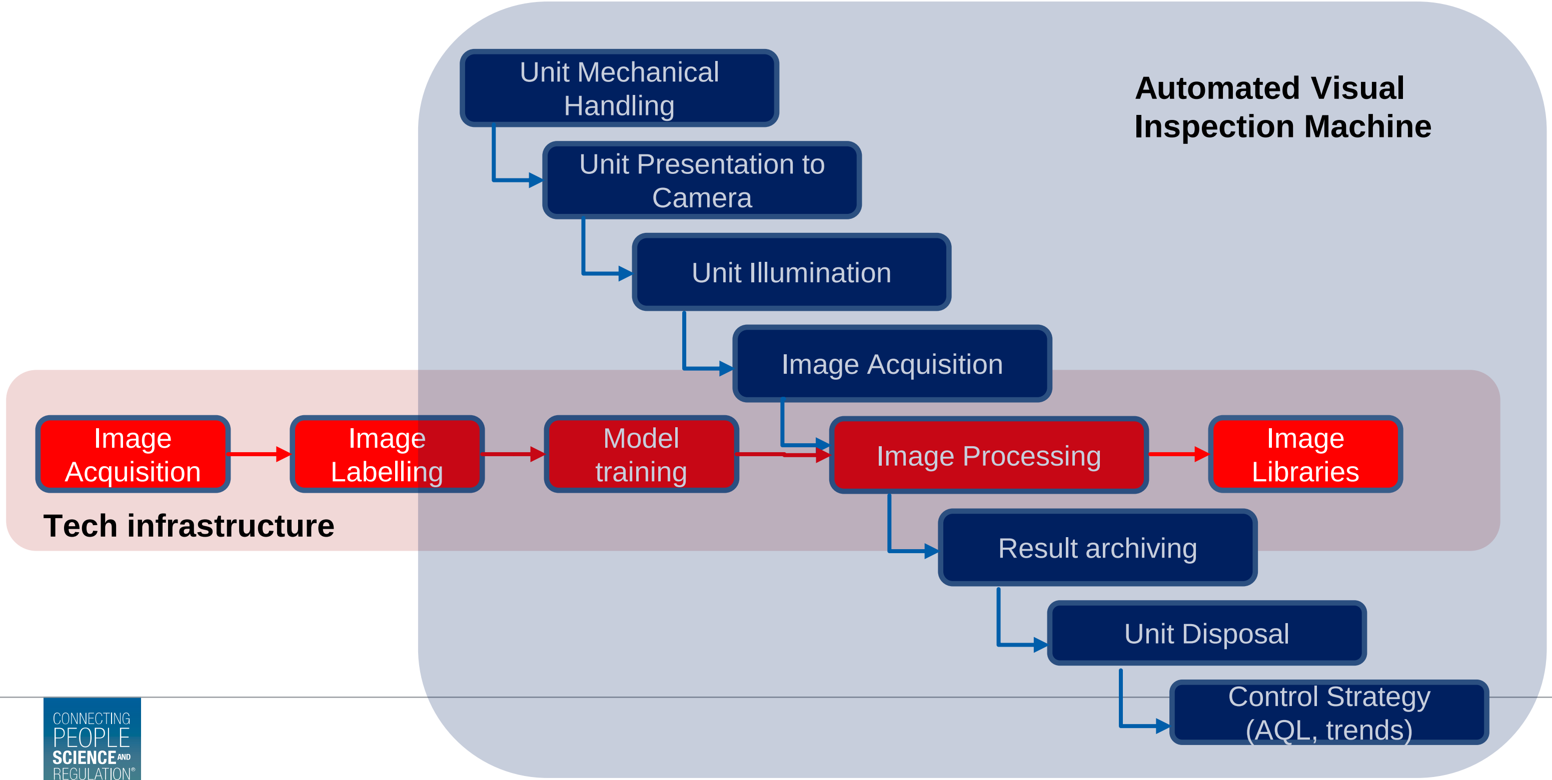
- Deep Learning can significantly improve defect detection on AVI, specifically for defects that are probabilistic
- Deep Learning can be more specific to defect detection and can minimize false rejects
- Deep Learning can allow more generalization of setup across manufacturing network, this brings simplification and harmonization of practices.

Regulatory Landscape for A.I.

- **UNESCO, 2022, Recommendation on the ethics of artificial intelligence, United Nations Educational, Scientific and Cultural Organization (UNESCO)**
- **FDA FRAME initiative too - https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/cders-framework-regulatory-advanced-manufacturing-evaluation-frame-initiative**
- **USP<1790>, May 2022, Visual Inspection of Parenteral**
- **FDA, CDER, Draft May 2023 - Artificial Intelligence in Drug Manufacturing**
- **EMA, Draft July 2023 – Reflection paper on use of Artificial Intelligence**



Scope of Change with Deep Learning = image processing



Convolutional Neural Network for image Classification

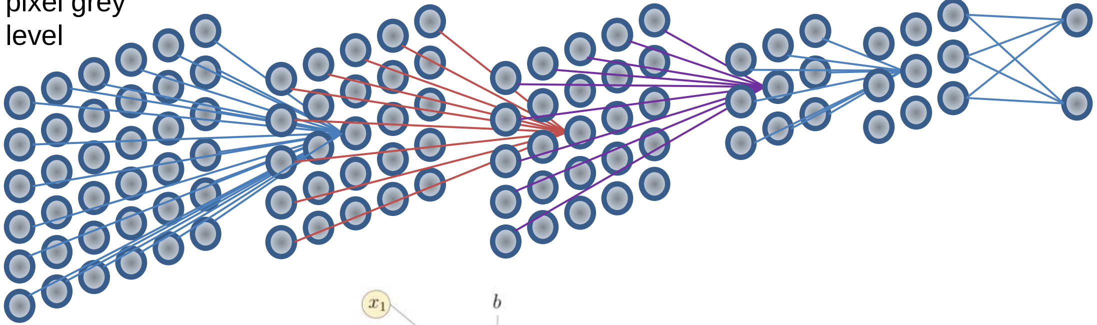
Conform images

Crack images

First layer to input each pixel grey level

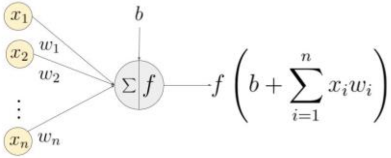
Early layers to detect big features

Last layers for final defect classification



Conform class

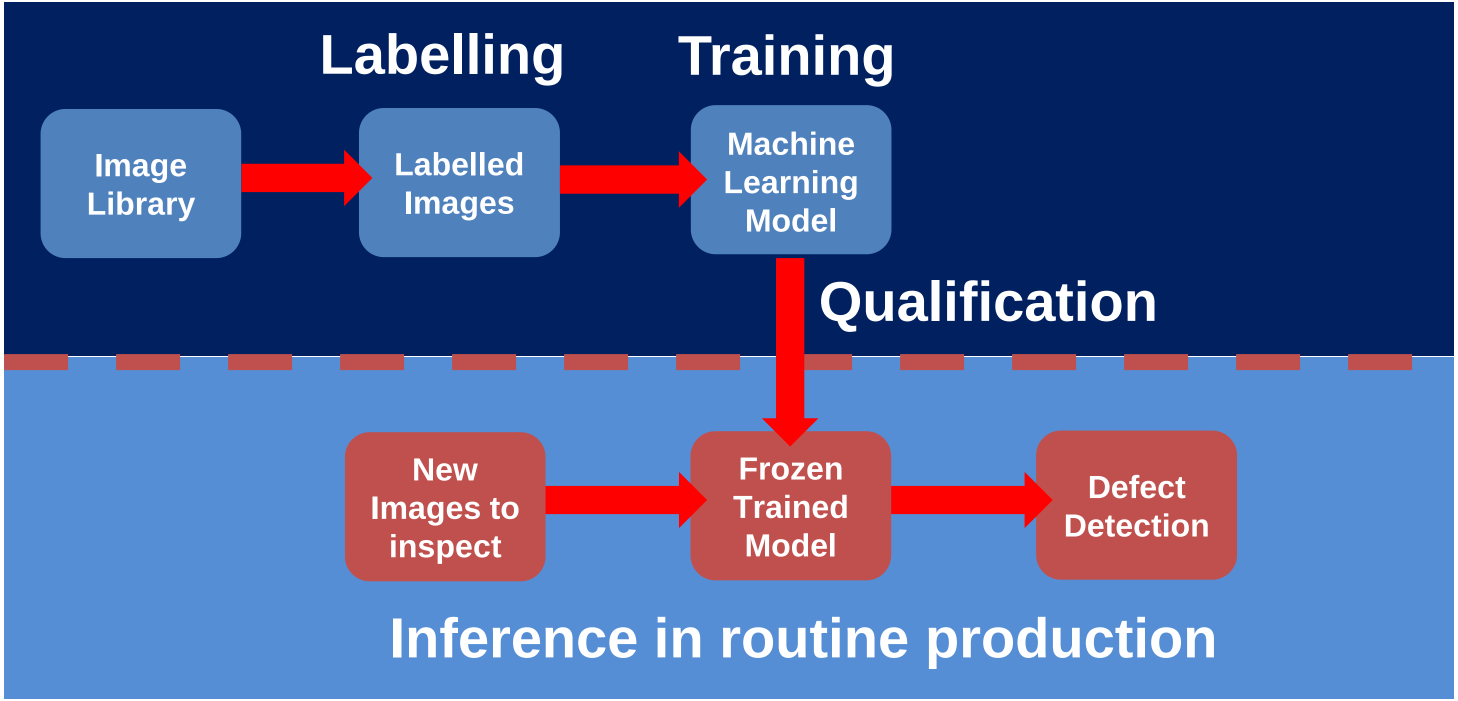
Crack class



Each neuron is a weighted sum of others with bias

Many Layers designed to optimize image classification, containing from 3 to 50 million parameters to adjust

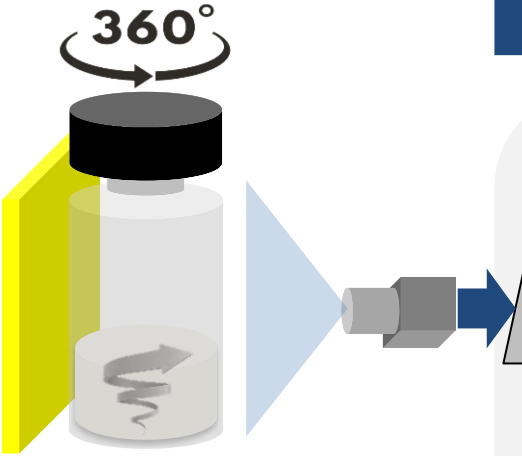
Deep Learning is Supervised Learning with Human in the Loop



AI Model after training and qualification is versioned and locked without any further improvement during routine production.

If improvement is required the model goes back to development and requalification.

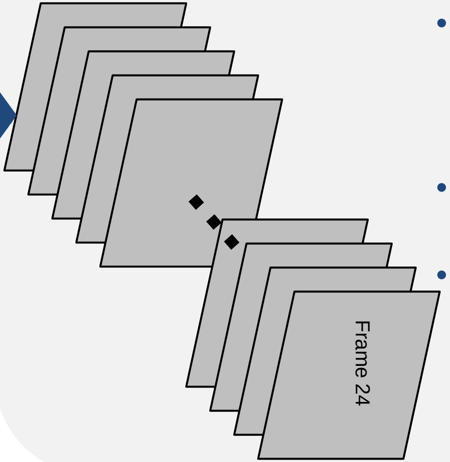
System Risk Assessment – Deep understanding of process flow is required



AVI machine takes i.e. 24 frames during vial rotation

Vision setup for image acquisition, pre-processing, DL model, Post processing

For each of 24 Frames:



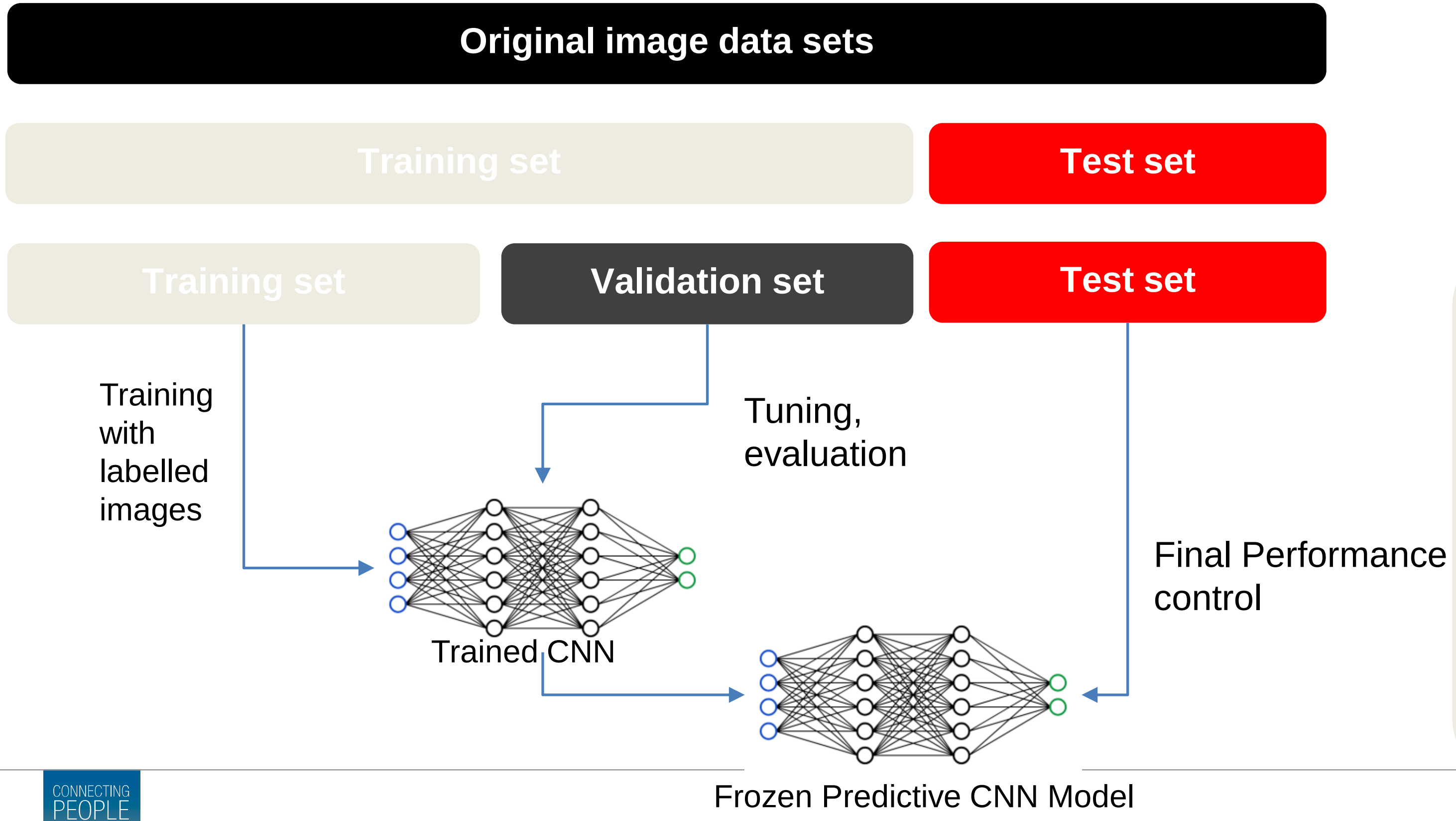
- Pre-processing many intermediate images (centering – AOI – filtering – data reduction) = traditional computer vision
- Processing by Deep Learning model to classify defects
- **Archive classification results in a register for each frame number**

For All Frames = post processing rules: Trajectory analysis / recurrence voting / consecutive frames results

Pass / Fail in shift register

Automated Visual Inspection Deep Learning Case Study

image sets with principle of independence – no leakage



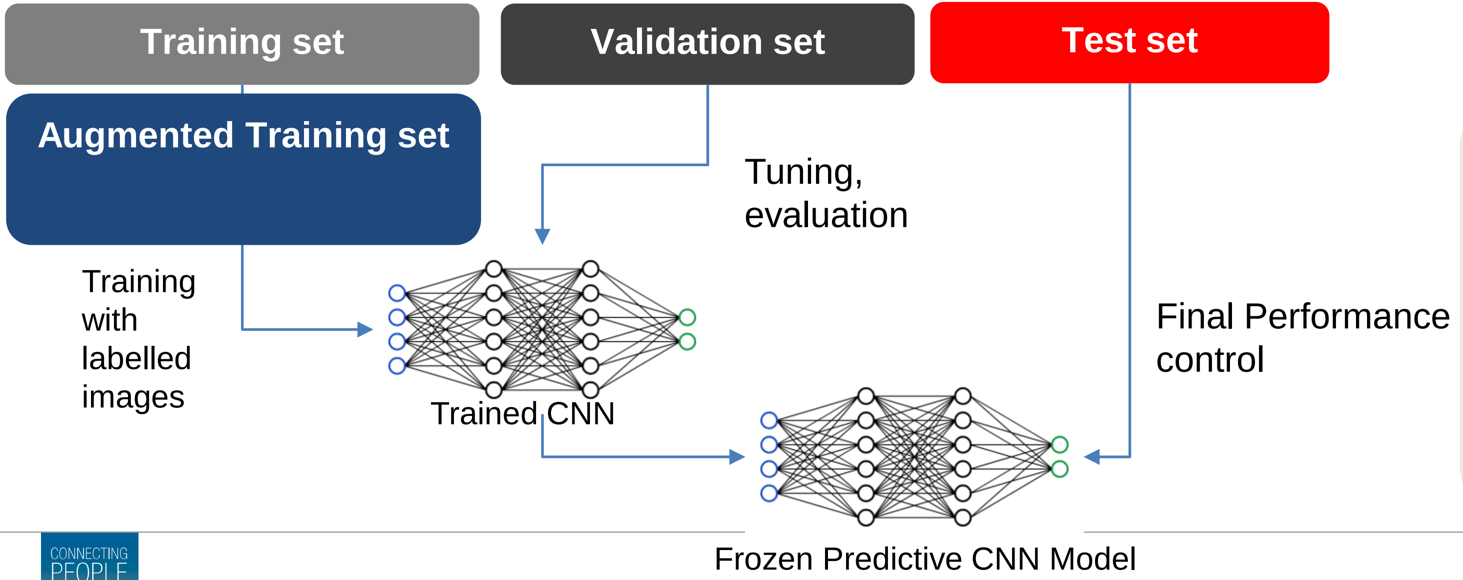
Data science Terminology:

Validation set is not used in the GMP sense, it may be confusing as it comes from data science cross validation concept to ascertain errors during training

How to use fully independent test sets in AVI ? Why Data Augmentation ?

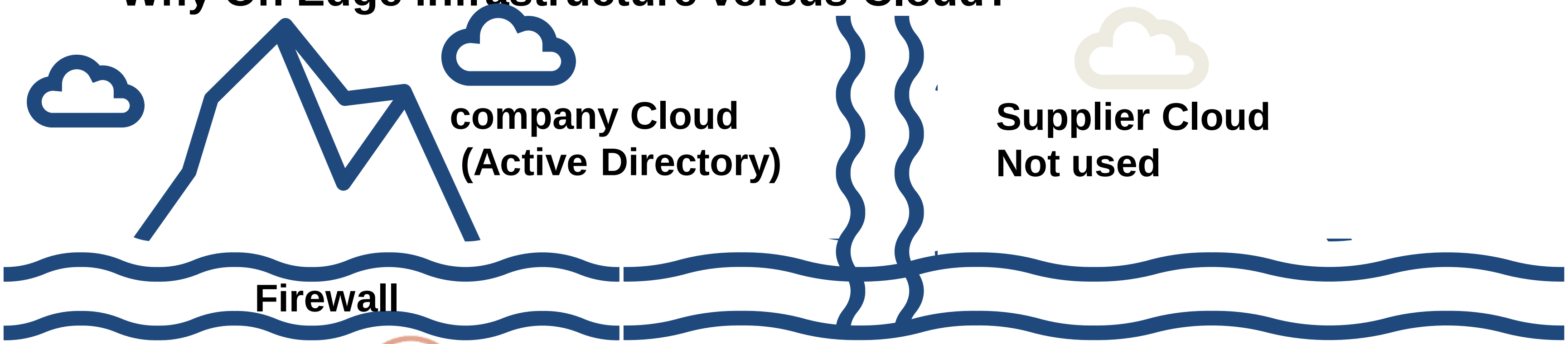
1 physical defect set for training and validation during training: true defect zone + wide polymorphism

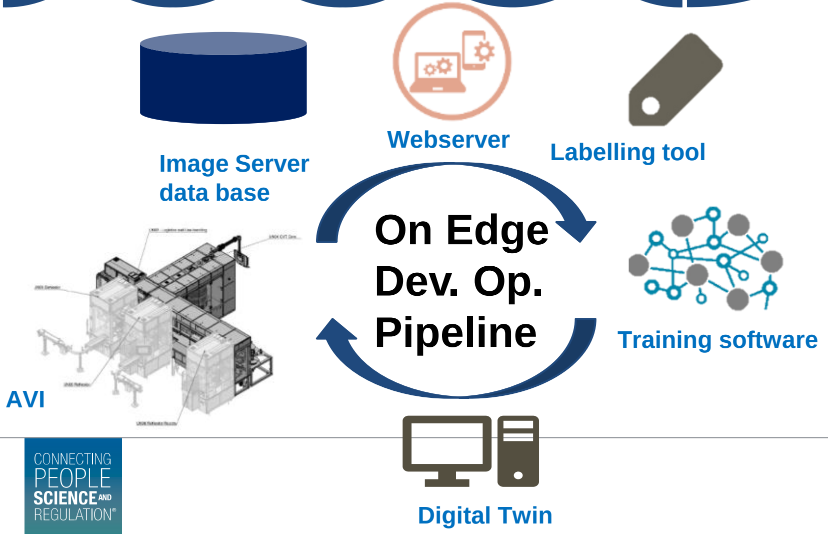
1 new physical defect set for testing performance: true defect zone + wide polymorphism



Risk:
Using same physical test kit and split it may present similar images in training and test set and may bias evaluation of the model

Why On Edge infrastructure versus Cloud?





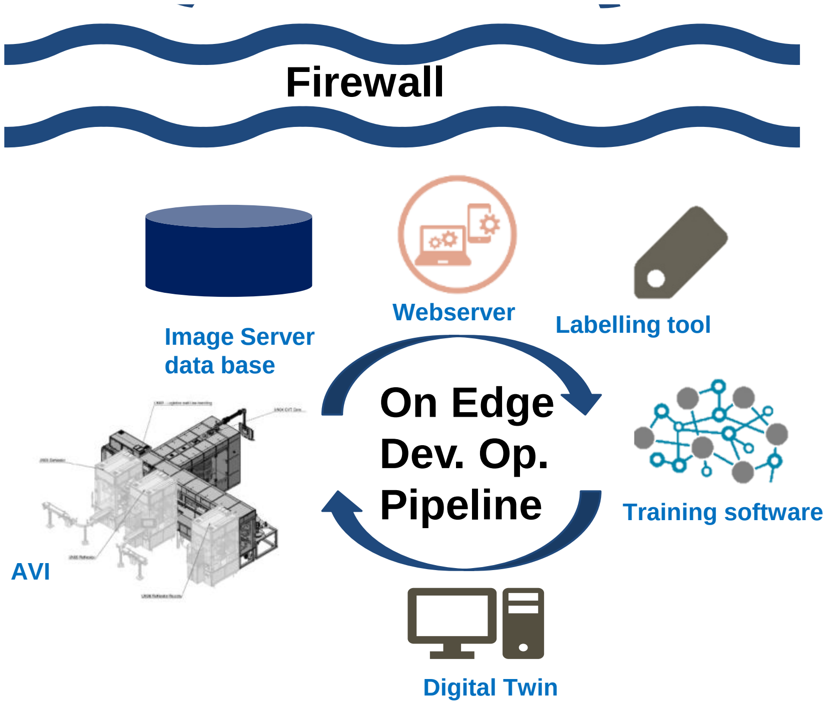
+ On Edge = faster flow of massive image storage to stay behind firewalls cybersecurity rules

+ On edge = we buy softwares from supplier to avoid servicing on cloud (no 3rd party mngt)

+ On edge = we can use GMP infrastructure for data integrity and access control

- On Edge infrastructure is more validation effort and cost

On Edge infrastructure – how to validate this ?



- URS for image dBase structure and metadata
- URS for image storage and retention app
- URS for image labelling / training and digital twin app
- Network landscape definition
- System Risk assessment
- Lab tests on dev servers
- Validation servers deployment
- Production servers deployment
- OQ - PQ

Validation Strategy for Deep Learning Models in AVI

Desktop Qualification of Models

- Desktop OQ evaluation of DL model on edge digital twin
- Strong metrics documentation in OQ

On-line performance evaluation

- Digital Image testing OQ to test AVI hardware
- Real defect kit testing PQ to compare to MVI baseline
- Production Lots first control strategy (AQL/trends)

Life cycle Continuous improvement

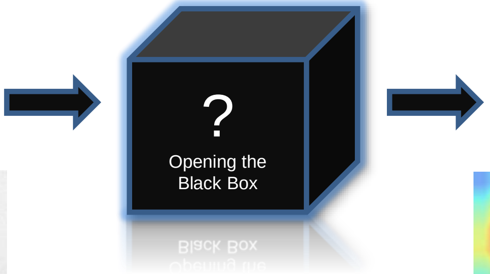
- Data gathering for improvement
- Continuous improvement with change control and new validation of performance

Why visualization of defect activation is key?

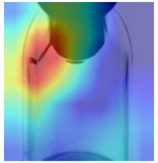
Model

Input

Crack on shoulder



Output



Crack on shoulder is activated by the model (red)

- Heatmap is a powerful tool to bring explainability to the model behavior

- This can show if the model is activating detection in the corresponding defect region

How to evaluate the performance of a Deep Learning Model ?

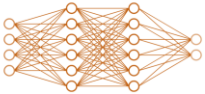
Proposal for Model Desktop Operational Qualification

Input

- List image used in training / val. / test sets, balance sets
- Describe model type / structure / Layer modifs
- Describe the Deep Learning type (classif. / segm…)
- Describe training type (scratch / transfer)
- Describe AI platform (tensorflow/keras/torch)
- Describe optimization function used
- Describe training parameters (rate, batch size)
- Describe hardware used for training
- Describe labelling software used
- Describe who has done the labelling
- Describe data augmentation or use of GAN and control of lightning
- Describe input image pre-processing size and interpolation used

Process

DL Model training



Output

- Document Learning curve with Loss / errors
- Document KPIs (Acc. Precision Recall)
- Document the number of epoch to best fit
- Document the heatmap visualization on test set images
- For multiclass models document by class
- Document confusion matrix on test set images
- Document the name + version of the new trained network
- Document image sequence performance test set
- Evaluate performance with image from a new test kit never used (totally independent test sets)
- Evaluate False rejects on larger sample sets never shown to the model

The Model Domain of application must be controlled

AI models can be developped, trained and validated for a specific use case and defect class.

If same model is used in another domain of application, the performance must be verified.

Model Domain of application

Product / presentation

Training set

Validation set

Test set

Defect Classes

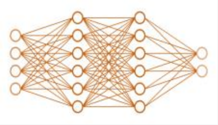
Same Model with different Domain of application

Product / presentation

Training set

Validation set

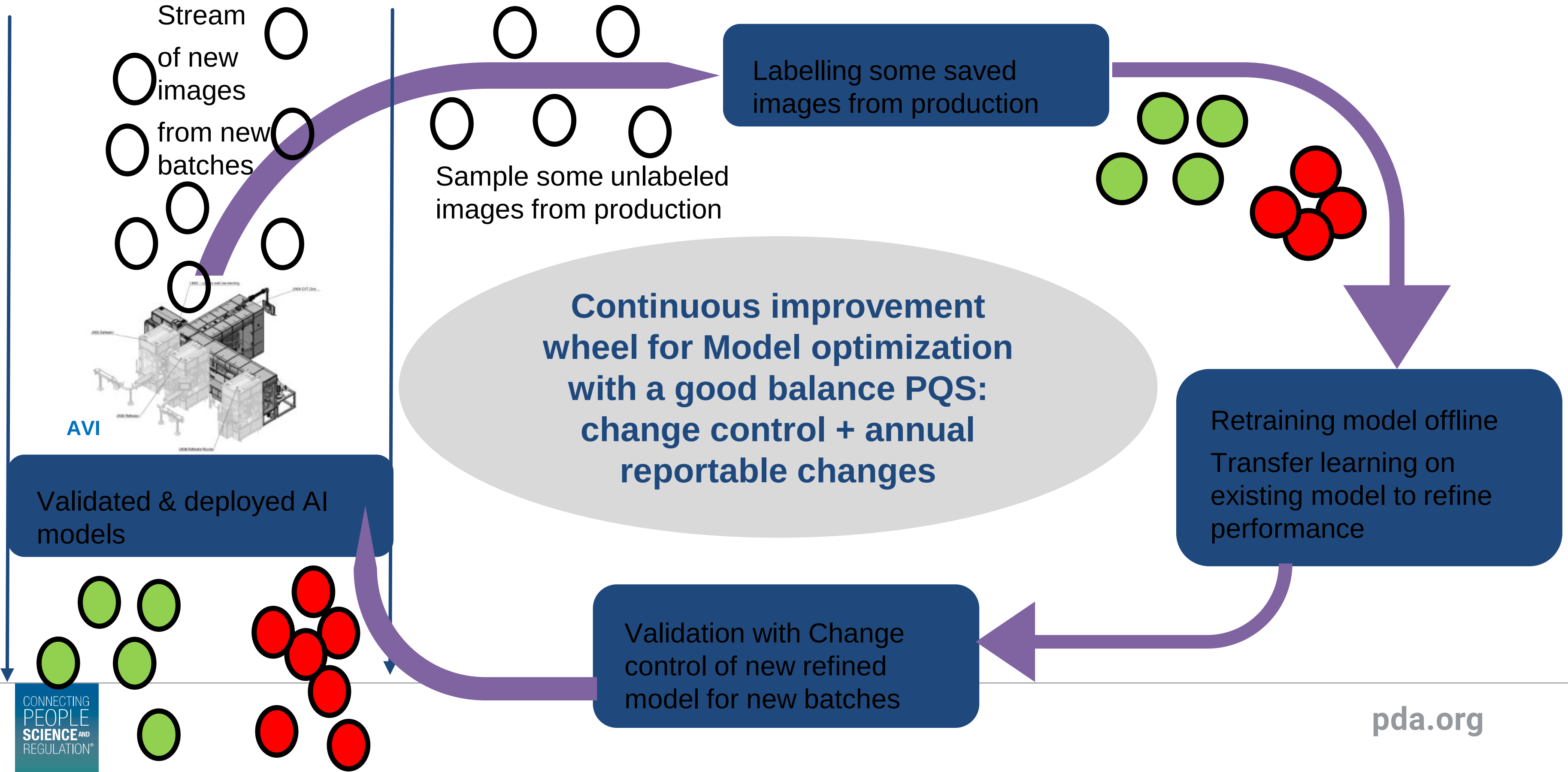
Test set



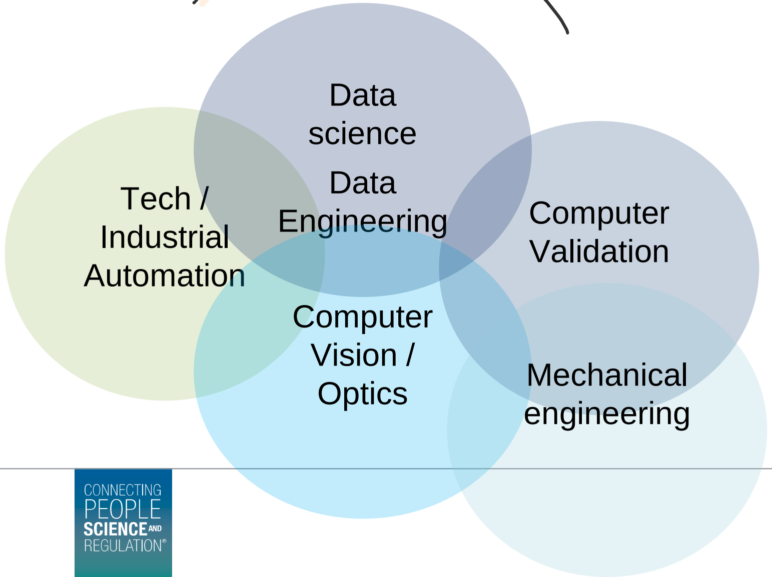
Defect Classes

Life Cycle of Deep Learning Model

Active Learning Loop to speed up continuous improvement with real defects



Competencies to develop in Visual Inspection teams



- **Labelling role**

Create the Job description
Develop tools & training
Upskill some technicians
in a central function team

- **Data engineer visual inspection role**

Create the Job description
Develop tools & training
+ external certification
Upskill / hire some engineers
in production site / visual inspection team

Conclusion

Deep Learning will improve significantly Performance, Generalization and Trust of Visual Inspection process.

- **Deep Learning will require new competencies to hire & train like labelling and data engineering.**
- **The effort for backend infrastructure should not be underestimated in context of GMP, cybersecurity and data integrity rules.**
- **Regulatory risk versus traditional methods, need for ability to carry out change management in PQS.**
- **Validation should be based on robust URS, QRM, deep process knowledge and transparency to bring explainability of A.I.**

Contact: romain.veillon@gsk.com