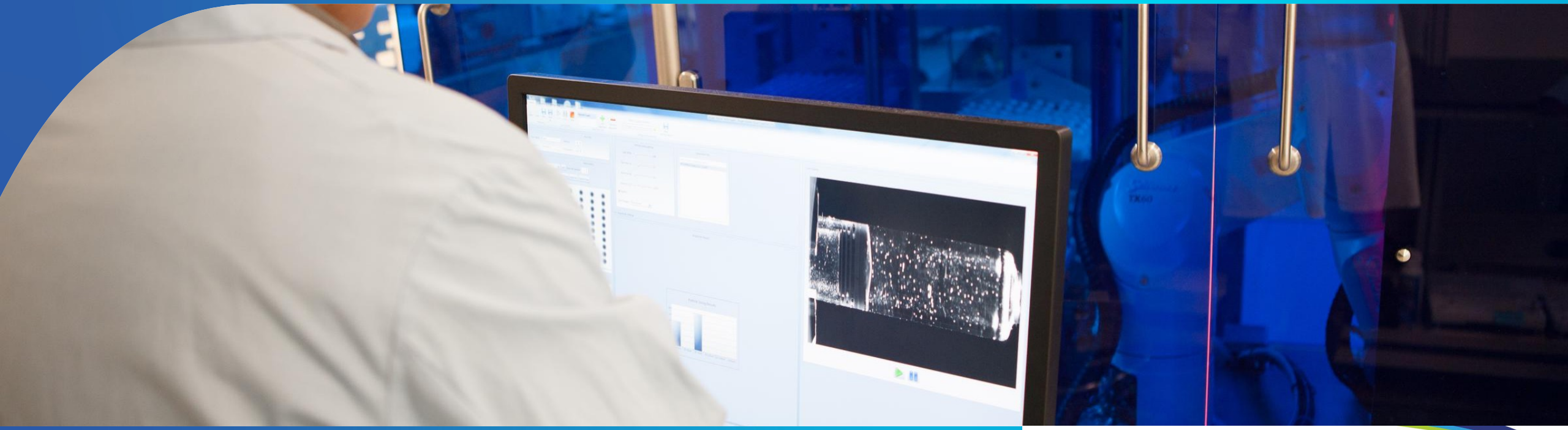


Automated Visual Inspection (AI and Machine Learning)

Jorge Delgado
Process Development Scientific Director

INSPIRING INNOVATION
Transformation & Future
21st REGULATORY CONFERENCE

AMGEN

August 18, 2023

The views expressed herein represent those of the presenter and do not necessarily represent the views or practices of the presenter's employer or any other party


INFORM
PACKAGING DIGEST

HomePharma & MedicalPharmaceutical PackagingAmgen Invests in AI-Assisted Packaging Inspection

Amgen Invests in AI-Assisted Packaging Inspection

Deep learning software overcame an age-old problem of inspection systems: differentiating defects from bubbles in highly viscous solutions in syringes.

In an industry first, the biotech leader has equipped — and validated — an inspection system with artificial intelligence (AI) to boost particle detection 70%, cut false rejects 60%, and differentiate pesky bubbles from unacceptable contaminants in syringes.

Bob Sperber | Feb 24, 2021

1975

First particles AVI machine using Static Division technology

1980 - 2000

Machine Vision advancements allowed the use of vision inspection for multiple purposes

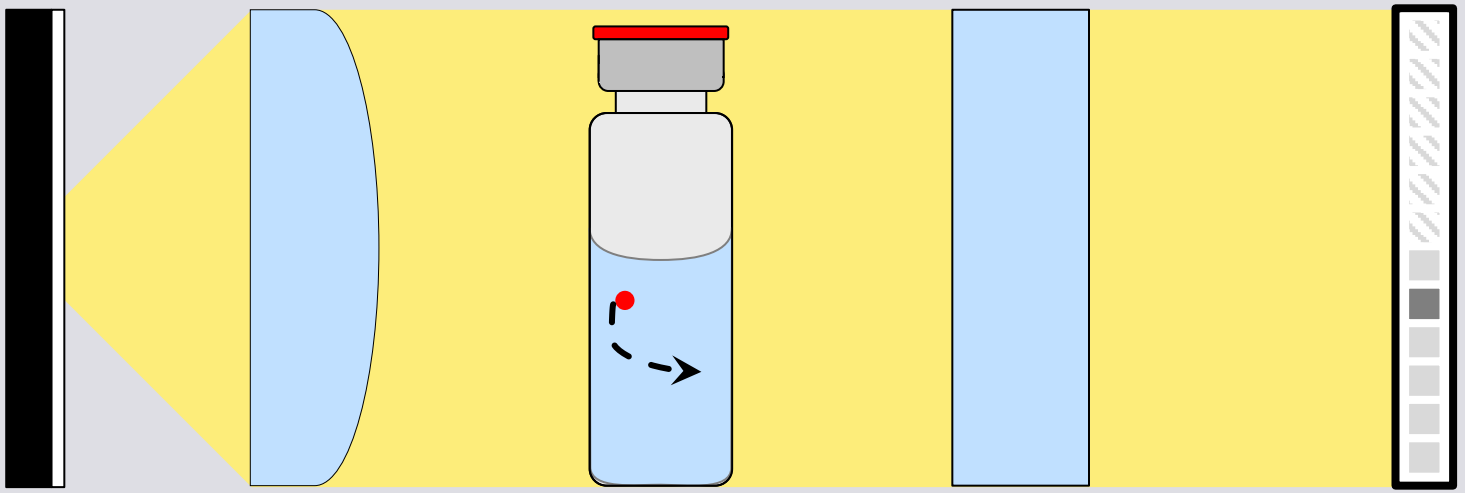
2000 - 2020

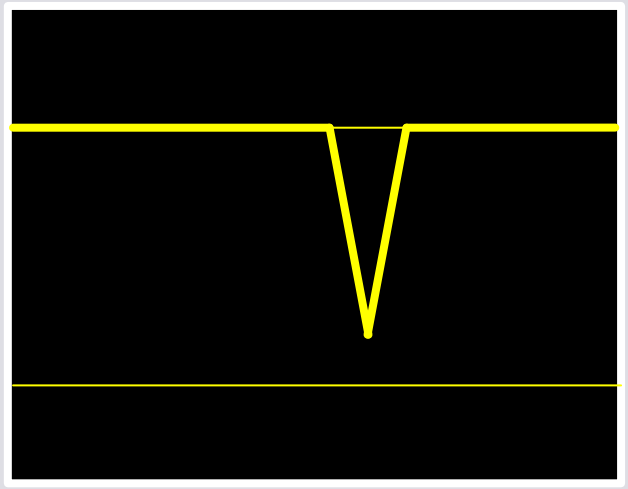
Improvements in Processing Power, Bandwidth and Data Storage allowed the use of Deep Learning in commercial applications

2020

First application of Deep Learning for the Automatic Visual Inspection of Parenteral Drug Products

Static Division Technology





Particles are detected by the variation in voltage created by their shadows against a sensor

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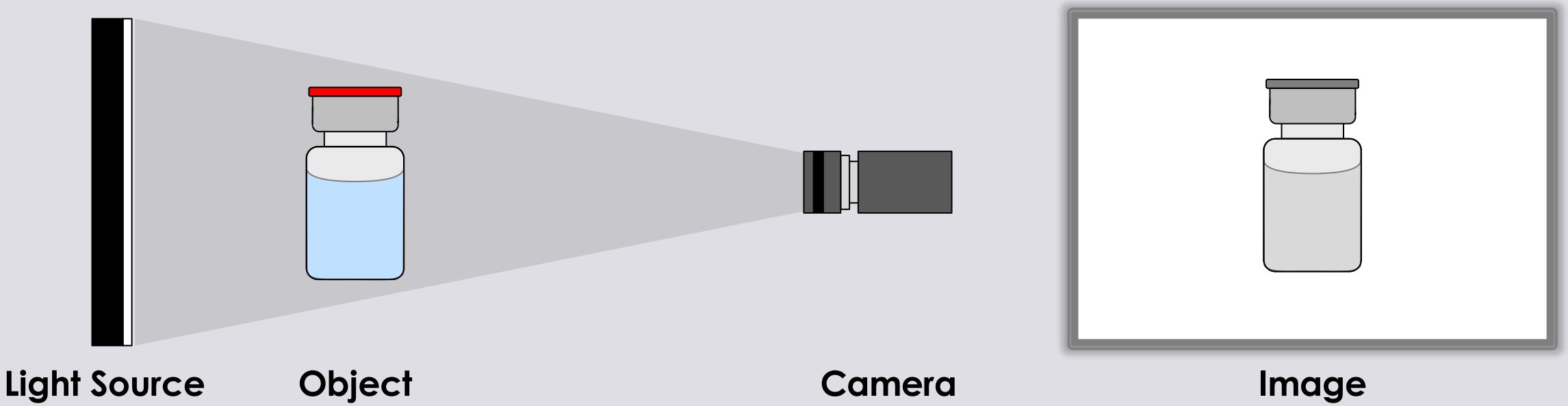
Machine Vision



Machine vision is the integration of hardware and software technologies used to capture, process and analyze images

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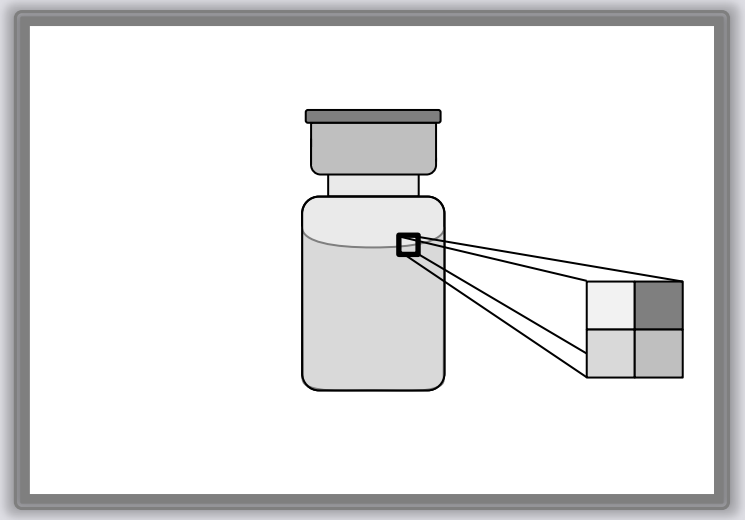
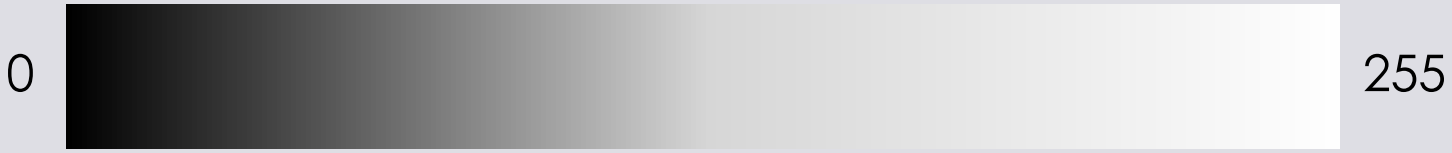
Basic Image Analysis Using Pixels



242	127
217	191



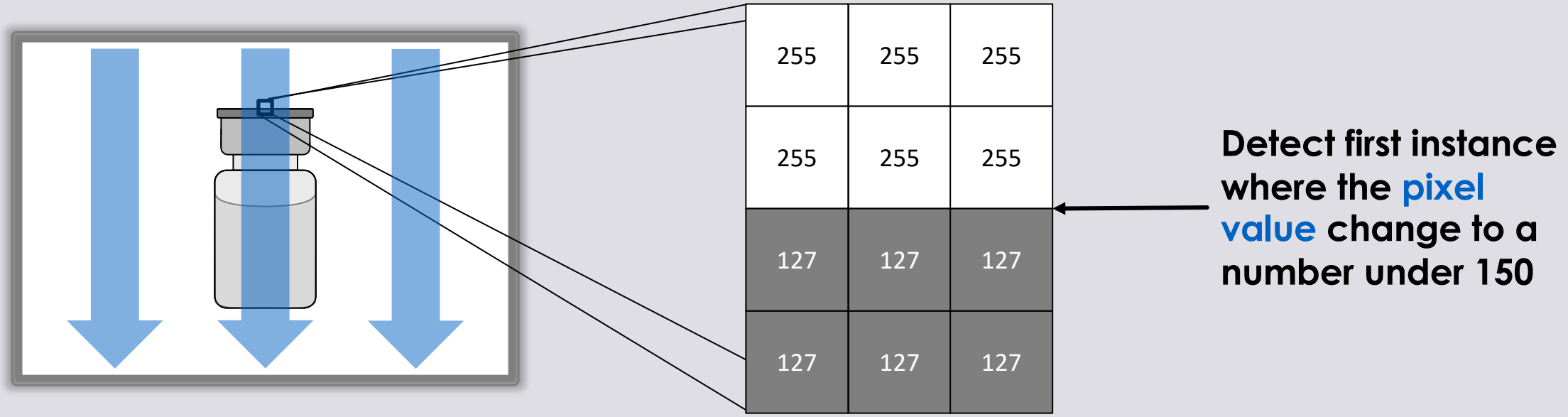
Pixel values in a monochromatic image are from 0 to 255

Image analysis is performed using mathematics based on pixels

The pixel or picture element is the basic unit of programmable color in a computer image

AMGEN

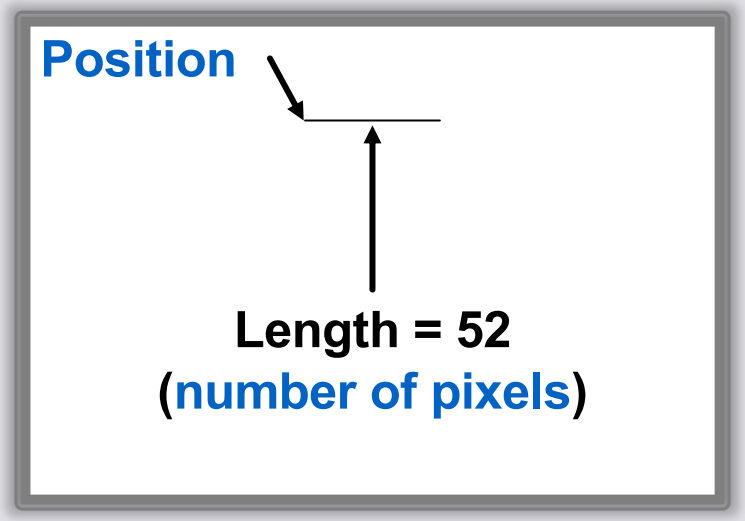
Edges are useful tools to detect objects

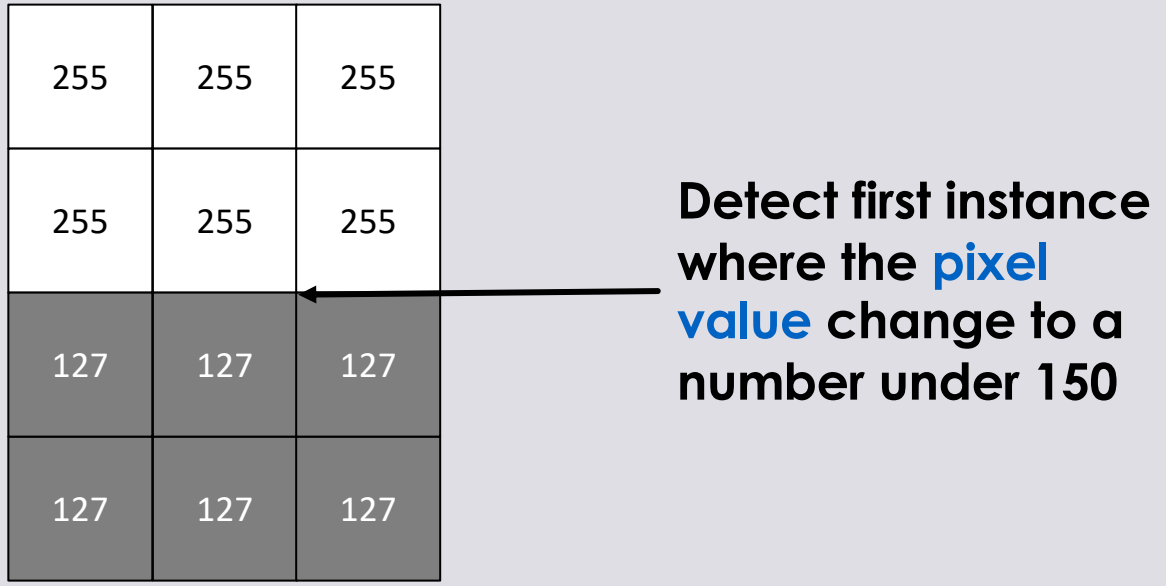


An Edge in an image is a sharp variation of the intensity or brightness of pixels

AMGEN

Edges are useful tools to detect objects





Multiple mathematical computations can be made using the pixel values, number of pixels and position of pixels

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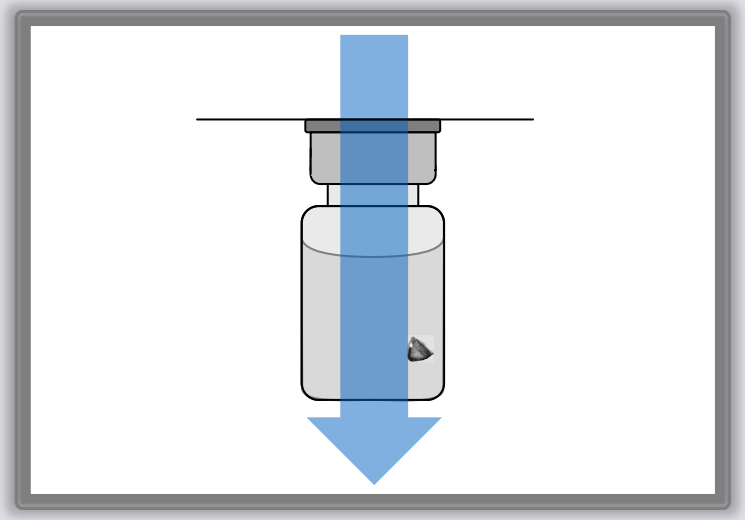
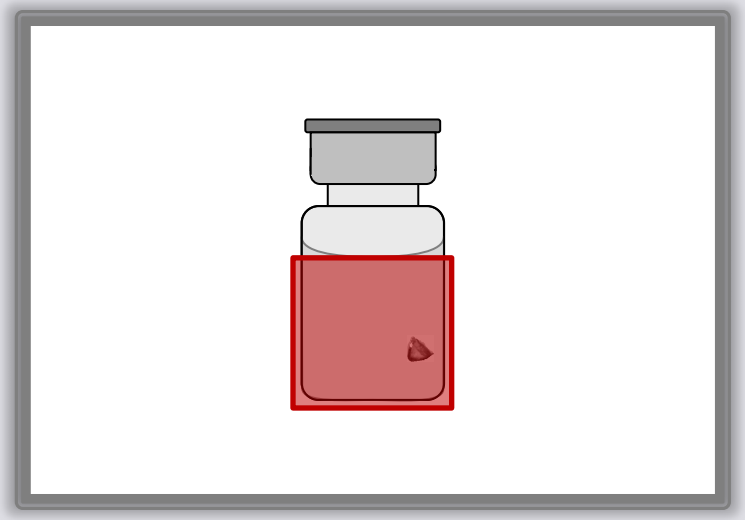
Particle Detection



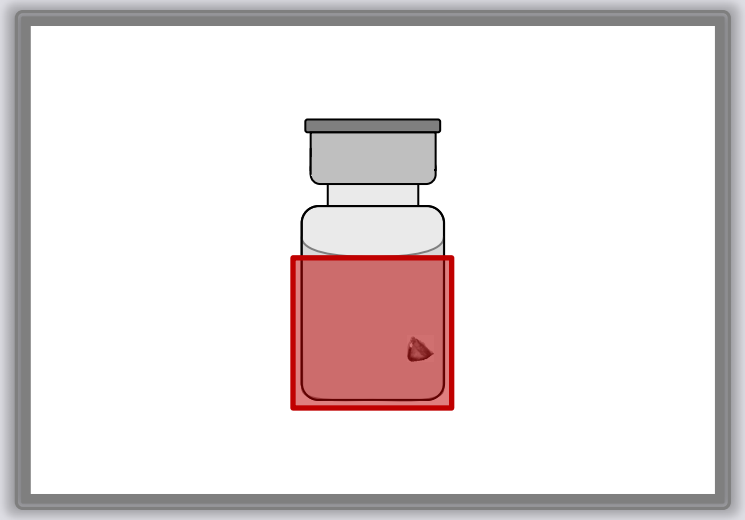
- Identify Object – Edge Tool

Particle Detection

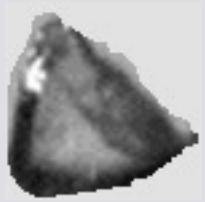


- Identify Object – Edge Tool
- Select Region of Interest (ROI)

Particle Detection



Glass Particle



A blob is a region of an image in which some pixel properties like intensity or color are approximately constant

- Identify Object – Edge Tool
- Select Region of Interest (ROI)
- Process image - Find Blobs

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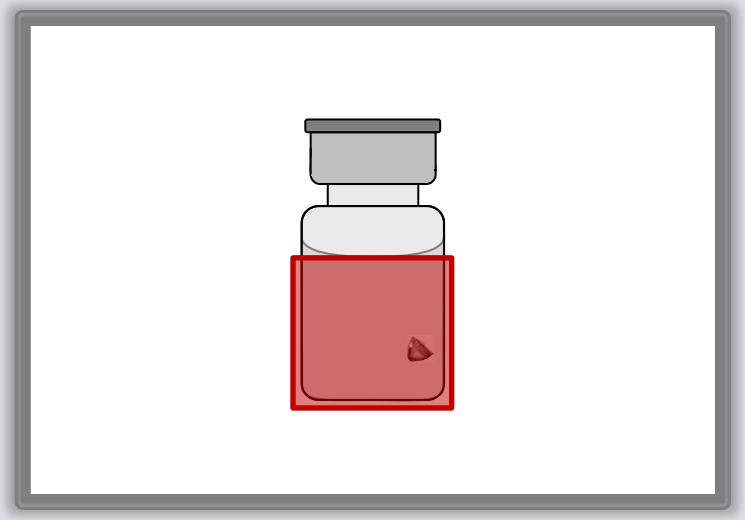
Particle Detection



Glass Particle

A blob is a region of an image in which some pixel properties like intensity or color are approximately constant

- Identify Object – Edge Tool
- Select Region of Interest (ROI)
- Process image - Find Blobs
- Filter image

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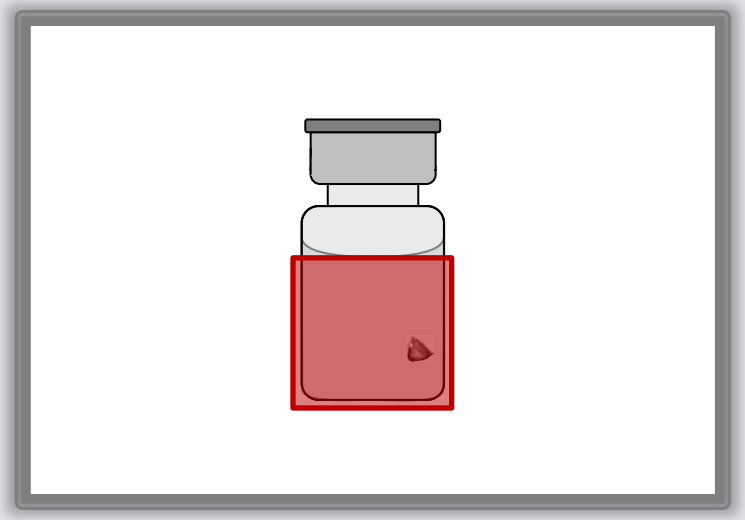
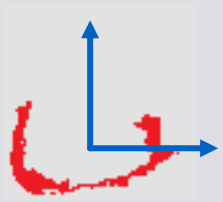
Particle Detection



Glass Particle



- Identify Object – Edge Tool
- Select Region of Interest (ROI)
- Process image - Find Blobs
- Filter image
- Get Center of Mass

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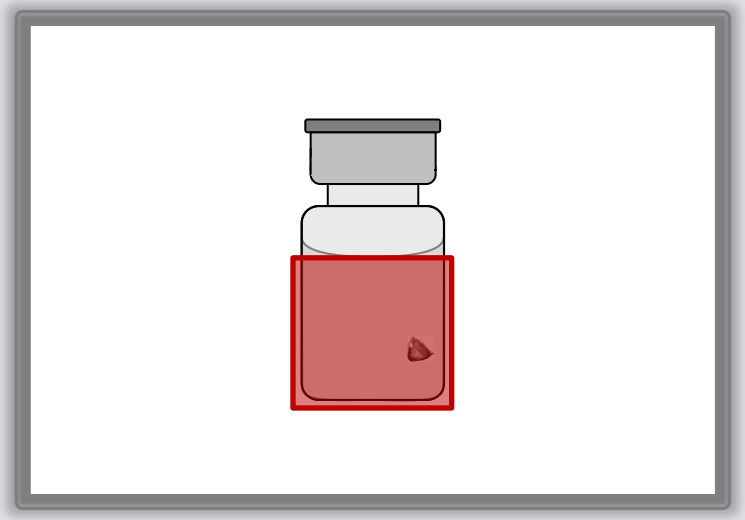
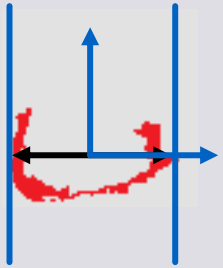
Particle Detection



Glass Particle



Width = 61

- Identify Object – Edge Tool
- Select Region of Interest (ROI)
- Process image - Find Blobs
- Filter image
- Get Center of Mass
- Calculate Width (number of pixels)

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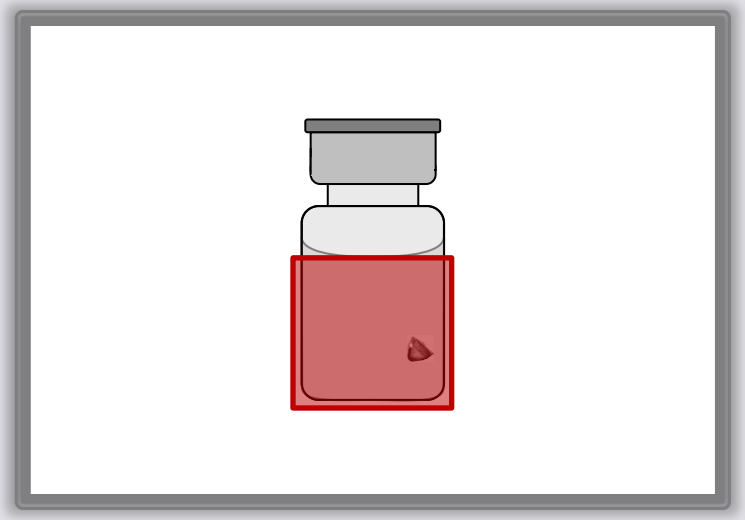
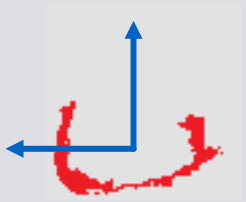
Particle Detection



Glass Particle



Width = 61

- Identify Object – Edge Tool
- Select Region of Interest (ROI)
- Process image - Find Blobs
- Filter image
- Get Center of Mass
- Calculate Width (number of pixels)
- Rotate Center of Mass Angle

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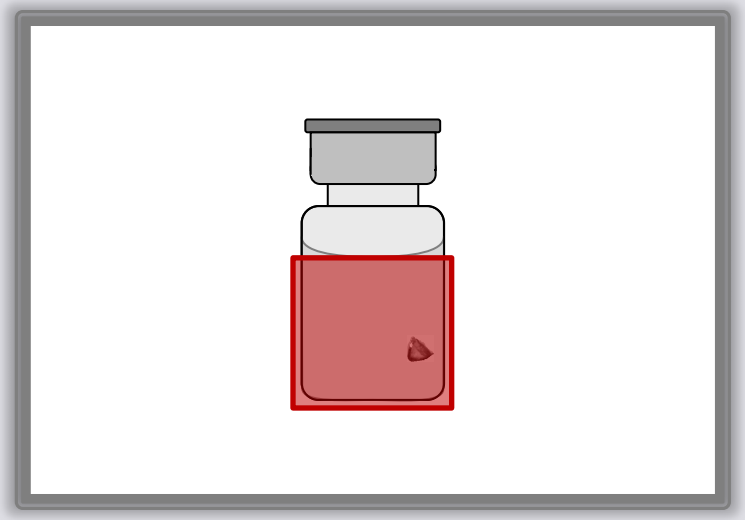
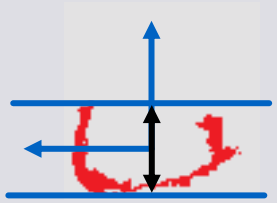
Particle Detection



Glass Particle



Width = 61

Height = 35

- Identify Object – Edge Tool
- Select Region of Interest (ROI)
- Process image - Find Blobs
- Filter image
- Get Center of Mass
- Calculate Width (number of pixels)
- Rotate Center of Mass Angle
- Calculate High (number of pixels)

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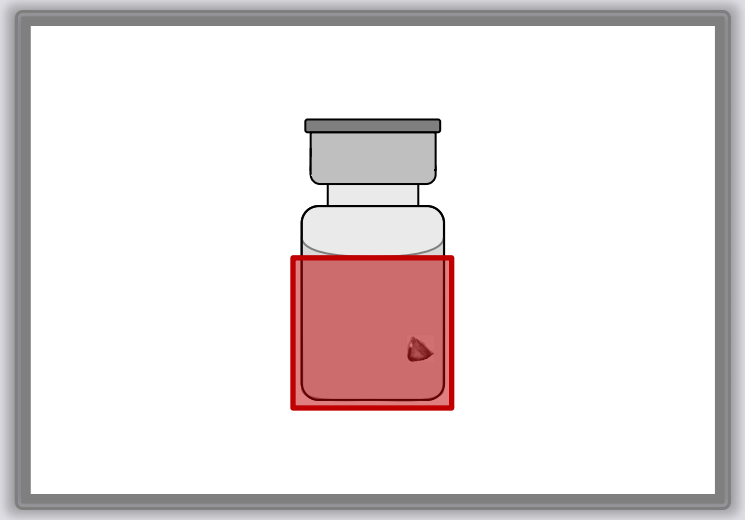
Particle Detection



Glass Particle

Width = 61

Height = 35

Ratio = Width ÷ Height

Ratio = 1.74

Ratio ≠ 1.00

- Identify Object – Edge Tool
- Select Region of Interest (ROI)
- Process image - Find Blobs
- Filter image
- Get Center of Mass
- Calculate Width (number of pixels)
- Rotate Center of Mass Angle
- Calculate High (number of pixels)
- If ratio ≠ 1, consider it as a particle

AMGEN

Current Automatic Visual Inspection (AVI) Technologies for Particle Detection

- Spin units to promote particles movement and dissipate bubbles
- Tracking system to detect movement, identify particles and differentiate them from bubbles
- Static Division use light transmission method and a diode array to detect light reduction (shadows) caused by moving particles in solution blocking light
- Image subtraction that compares different images of the same static unit and identify changes in the images
- Polarized filters to highlight particle features

Even with multiple techniques, it is still a challenge to effectively detect particles

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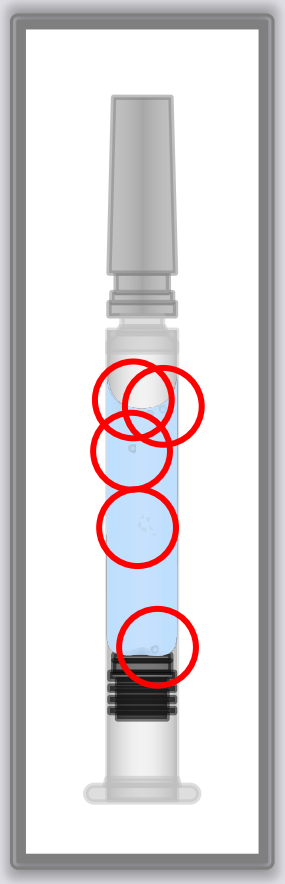
Deep Learning can help overcome some challenges in Automatic Visual Inspection



- Small containers do not promote the movement of particles, i.e., small syringes
- Particles that adhere to the meniscus are difficult to detect
- Bubbles inherent to the formulation of the product that are similar to particles
- Glass particles in solution similar to bubbles
- Heavy particles allocated on top of the plunger
- Protein aggregates inherent to the product are not defects, but are similar to particles
- Viscous or non-clear products

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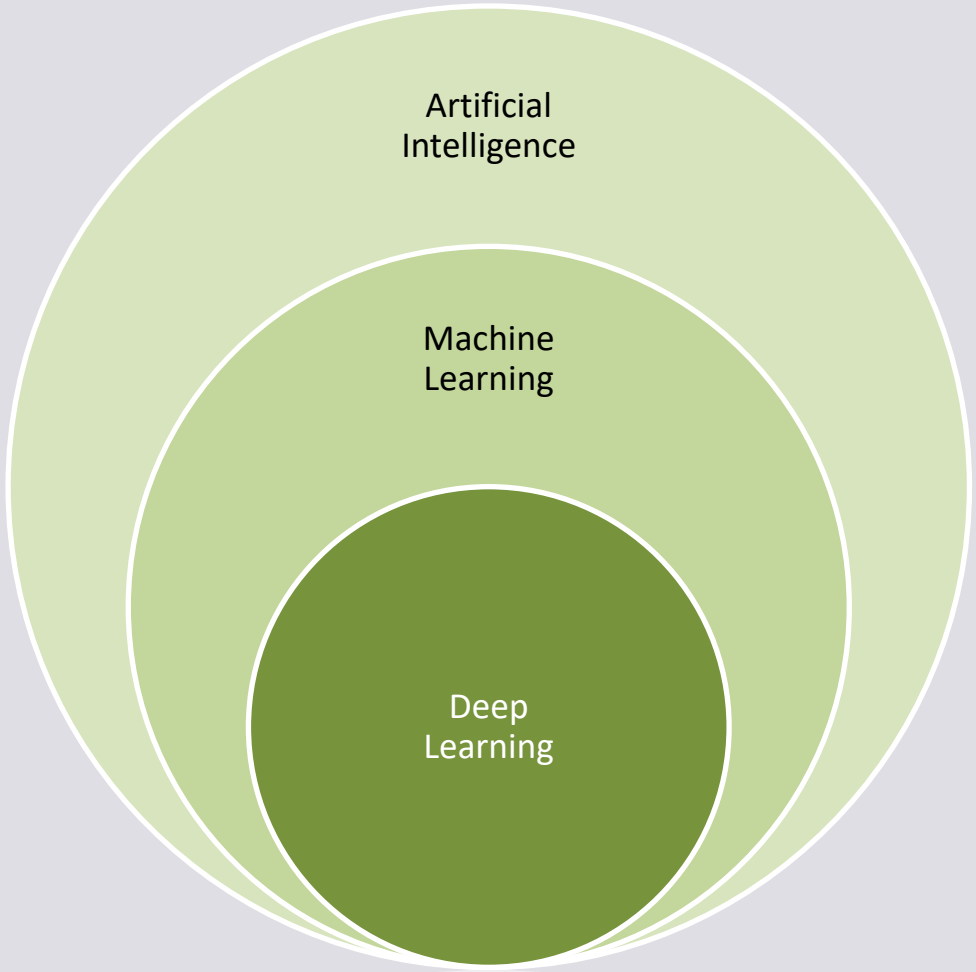
Deep Learning is a Subset of Machine Learning, Which is a Subset of Artificial Intelligence

Artificial Intelligence (AI)
AI involves machines that can perform tasks that are characteristic of human intelligence

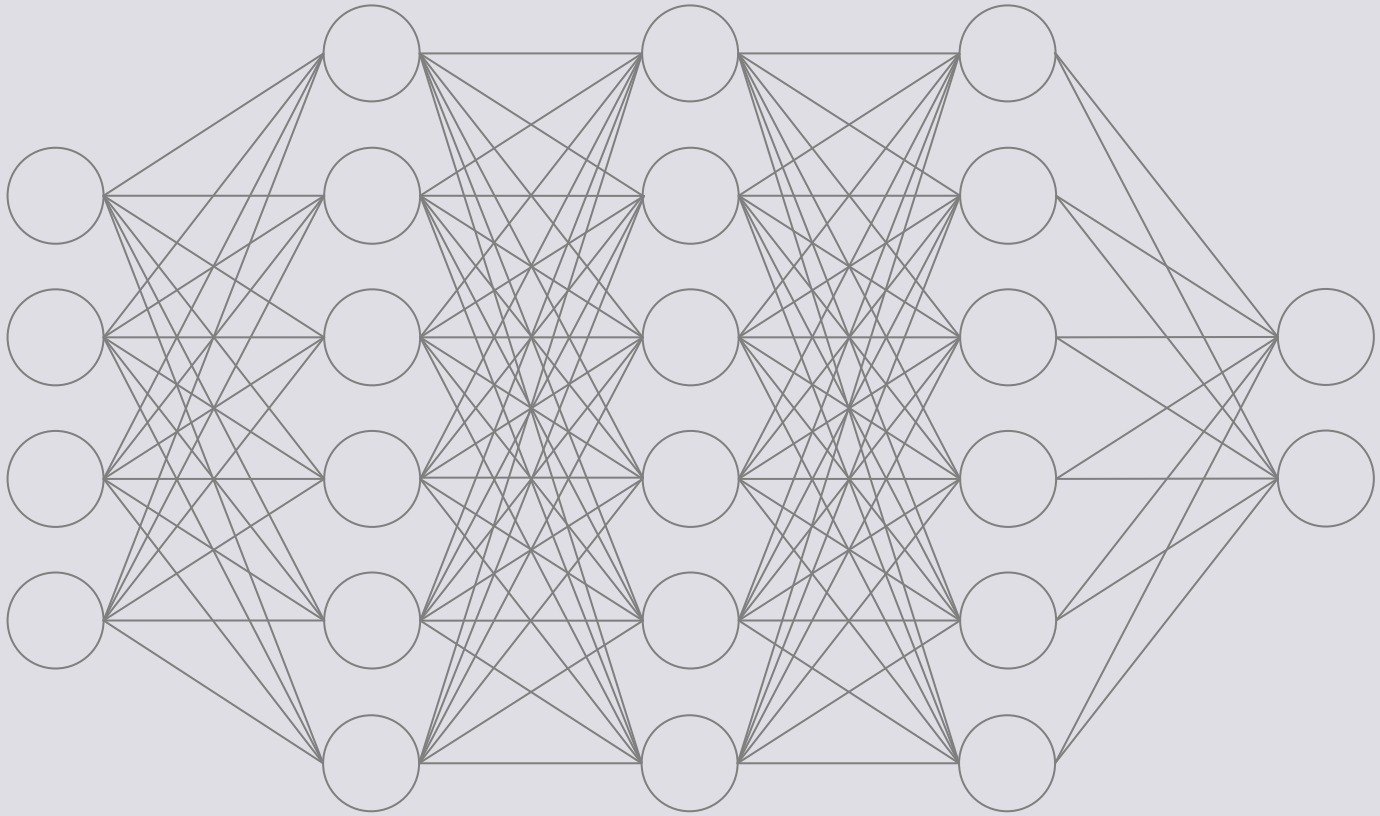
Machine Learning (ML)
A subset of AI which gives the computer the ability to learn without being explicitly programmed

Deep Learning (DL)
A subset of ML inspired by the structure and the function of the brain which use Artificial Neural Networks to find patterns in data and to infer the outcome of something it has never been exposed before



Artificial Neural Network

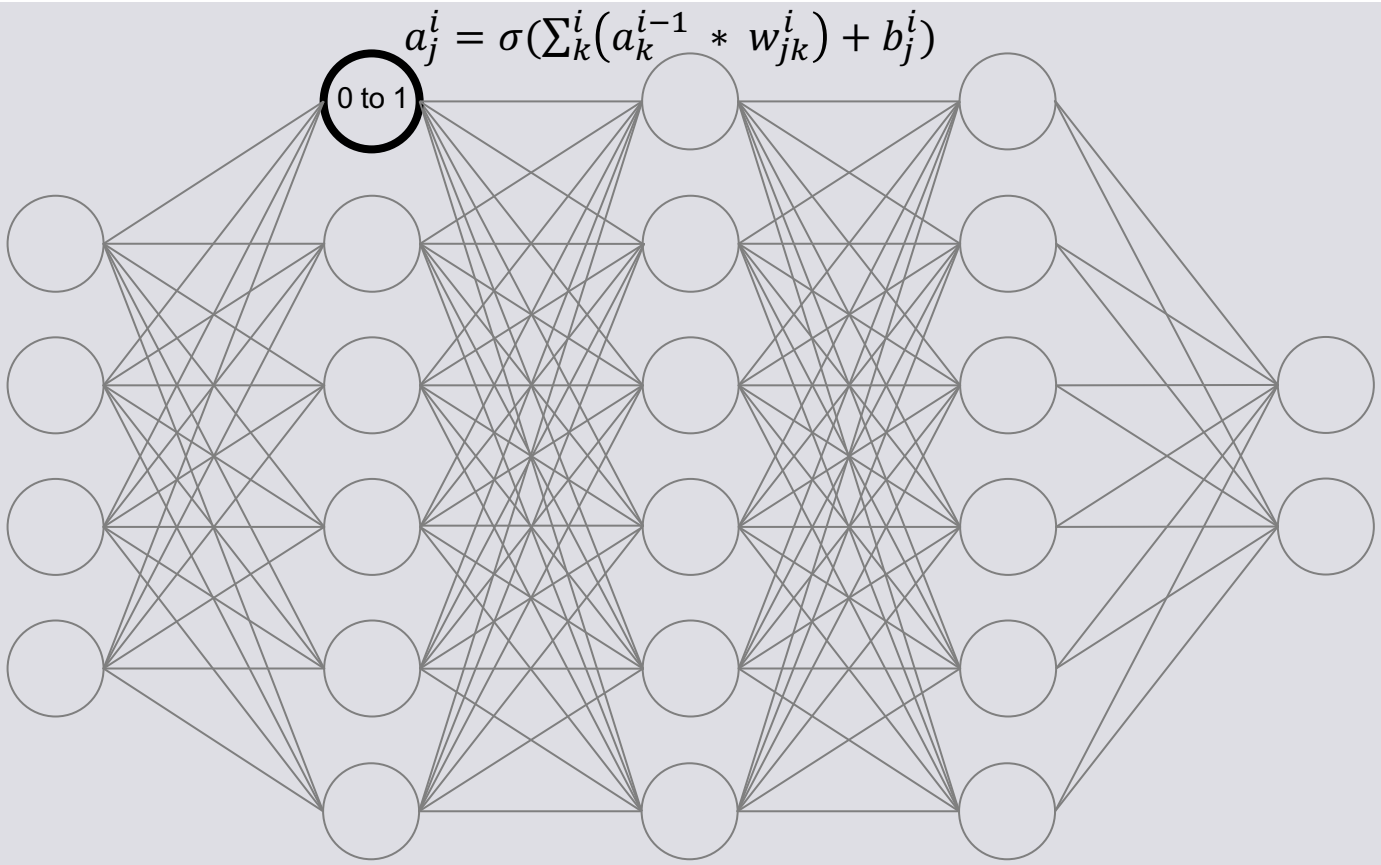
Computing system based on interconnected neurons or nodes (circles) arranged in layers



Artificial Neural Network

Computing system based on interconnected neurons or nodes (circles) arranged in layers

Each neuron is a mathematical equation that use previous neurons and weight values as input



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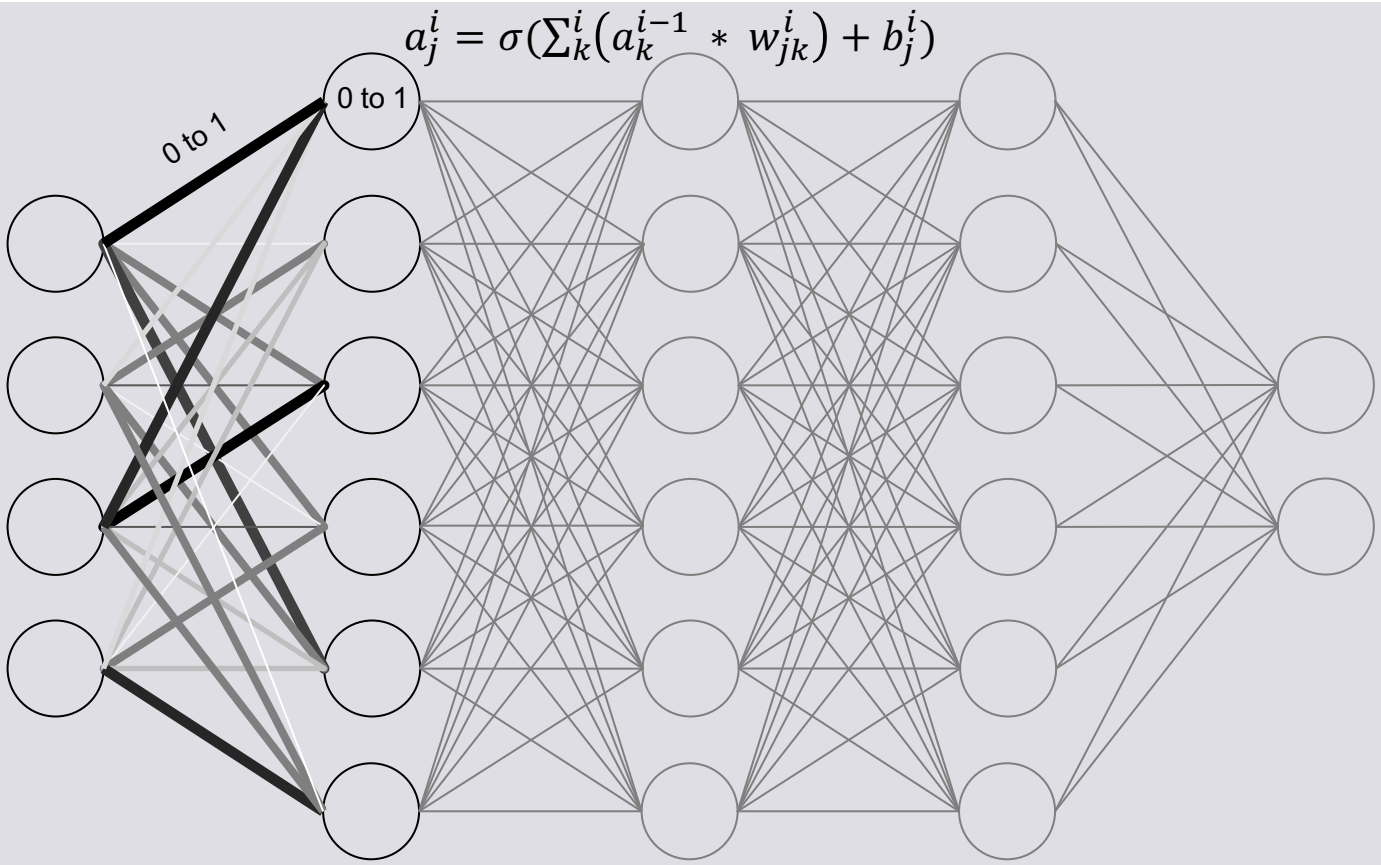
Artificial Neural Network

Computing system based on interconnected neurons or nodes (circles) arranged in layers

Each neuron is a mathematical equation that use previous neurons and weight values as input

Each connection or line is a weight value indicating how important is the relation between neurons

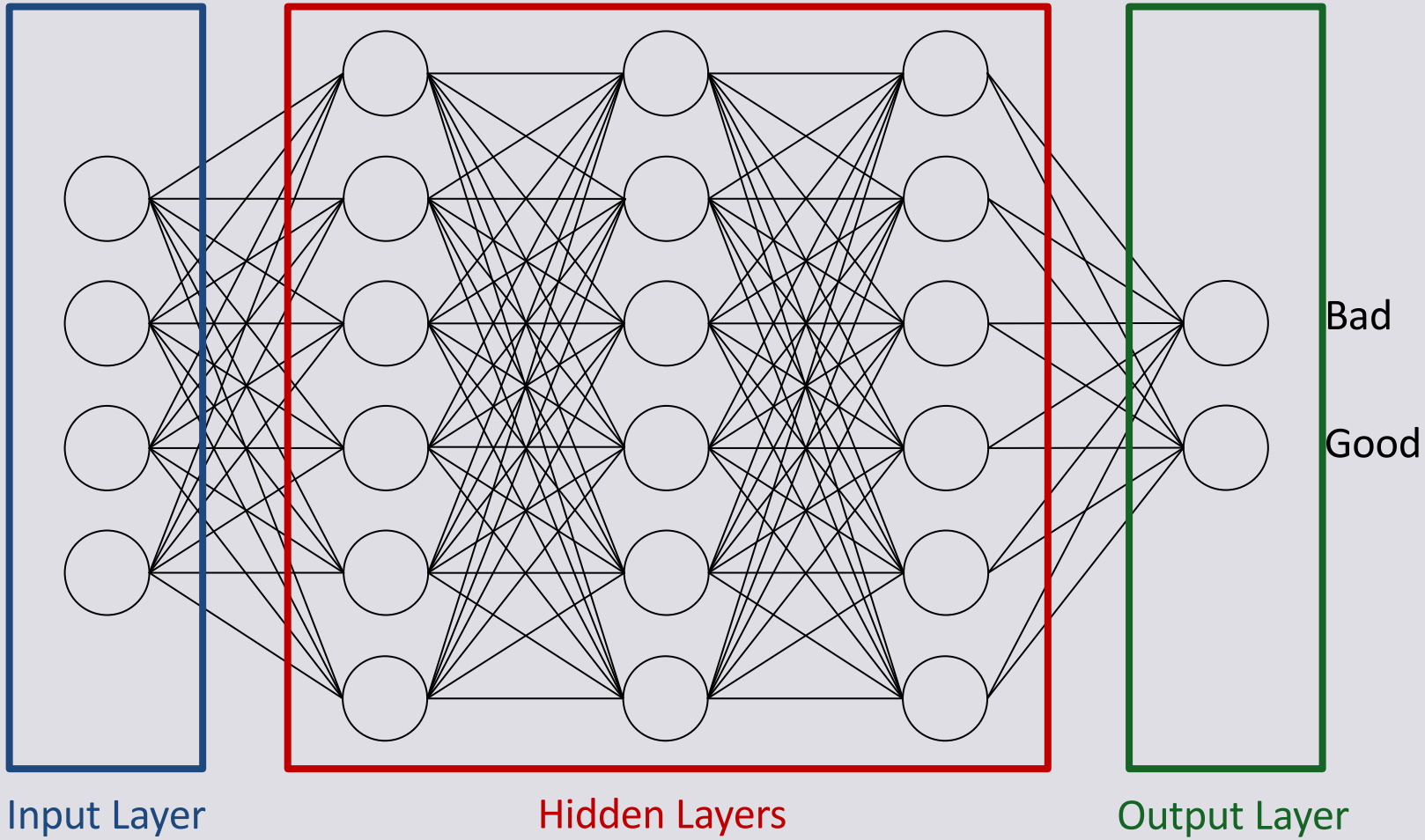


Artificial Neural Network Structure

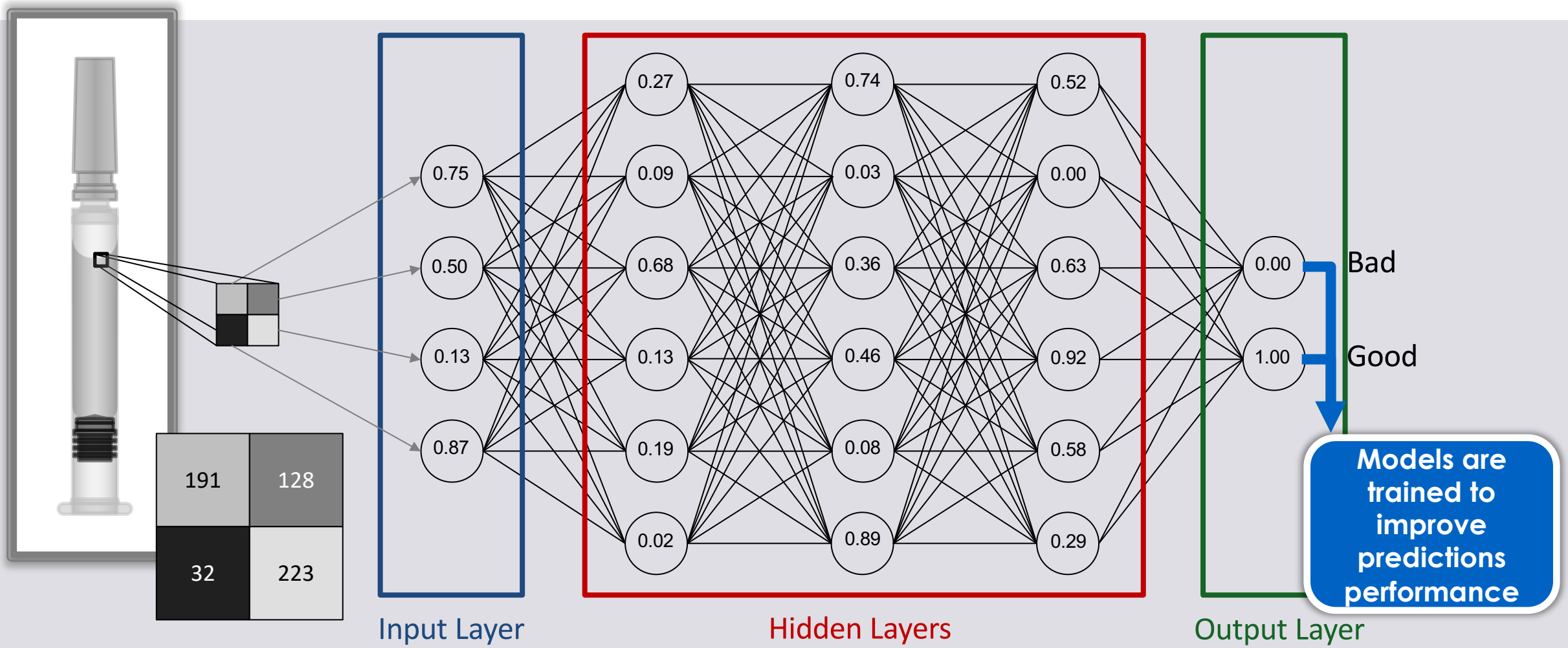
Input Layer – Input from the physical world

Hidden Layers – used for processing the inputs through activation functions

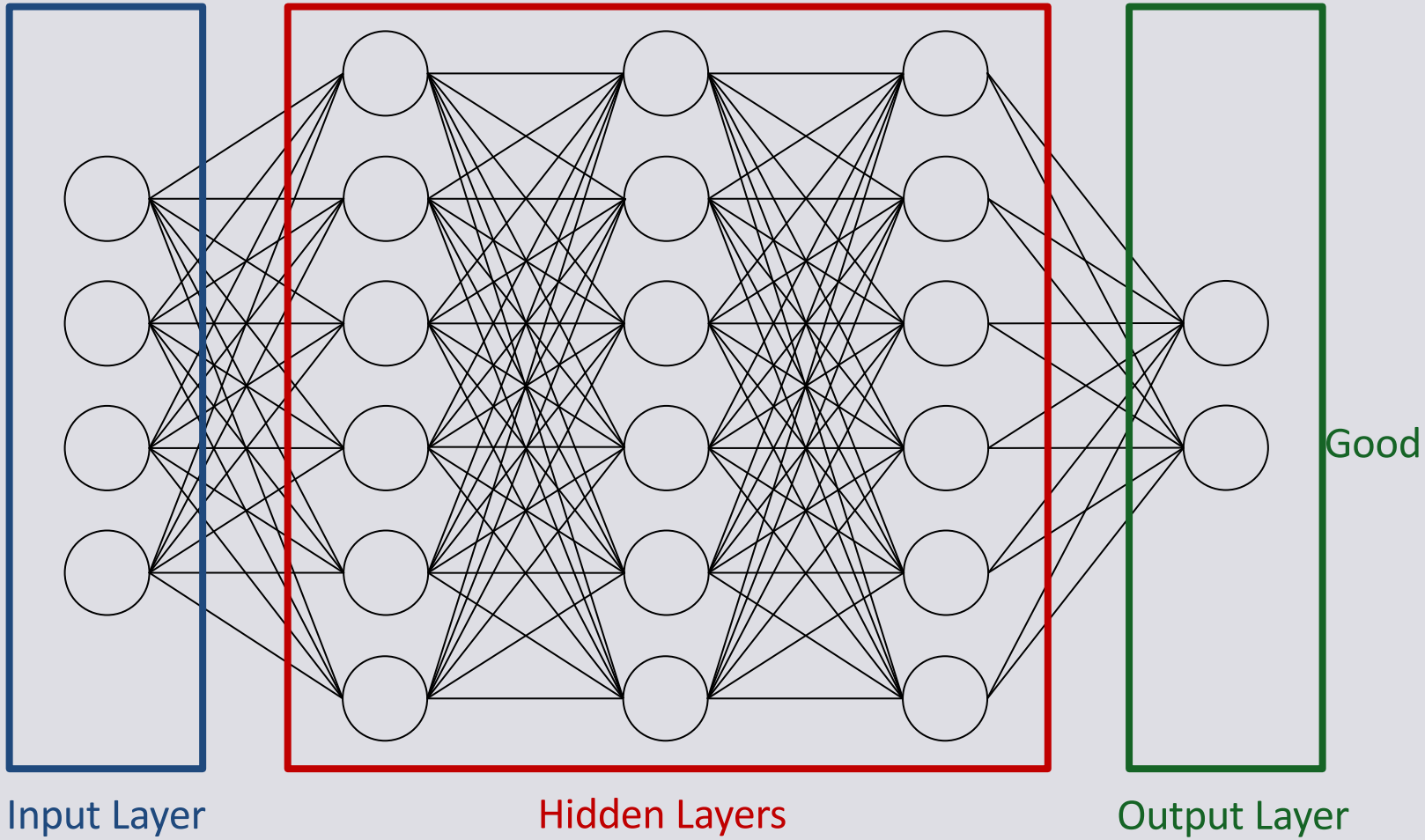
Output Layer – Contains the result of the inference made by the model



Artificial Neural Network Prediction

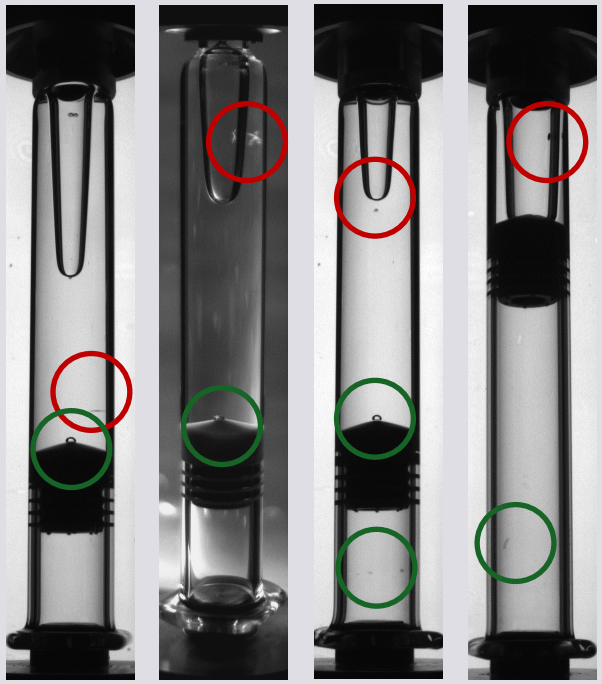


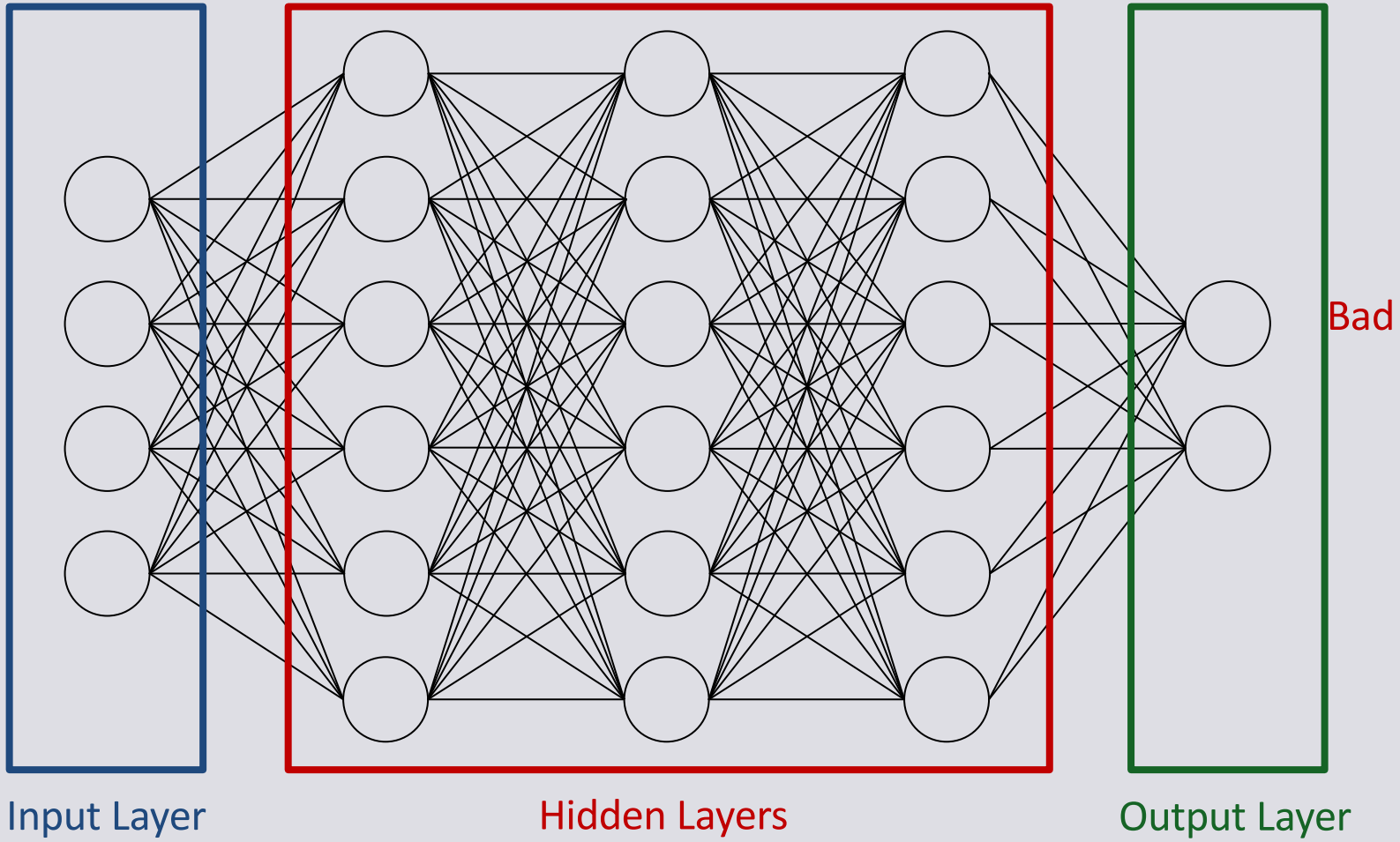
Artificial Neural Network - Training - Good



*Test units made in the laboratory to simulate defects

Artificial Neural Network - Training - Bad





*Test units made in the laboratory to simulate defects

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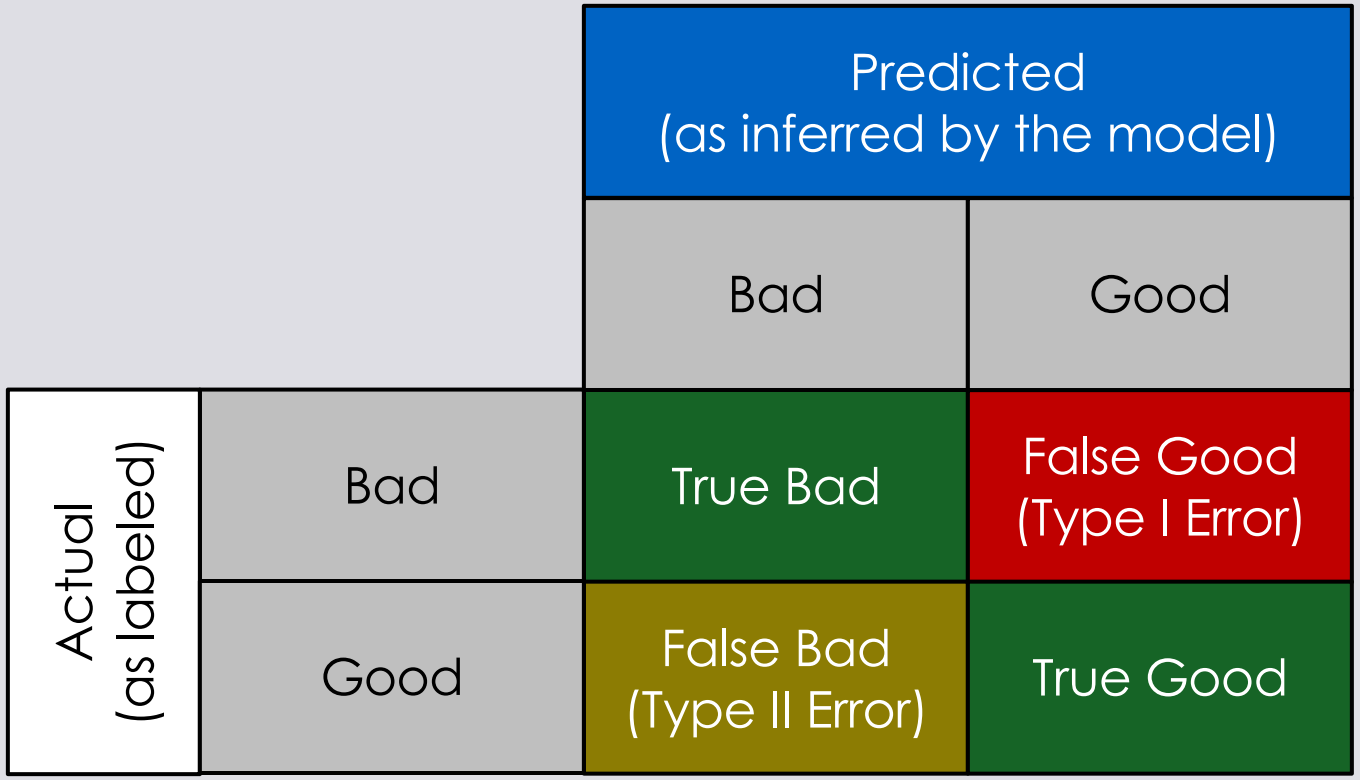
Model Testing – Confusion Matrix

A confusion matrix is a tool used to measure the performance of a Deep Learning model by summarizing the number of correct and incorrect predictions made



Detection Rate = Predicted Bad ÷ Actual Bad
False Fails = Predicted Bad ÷ Actual Good

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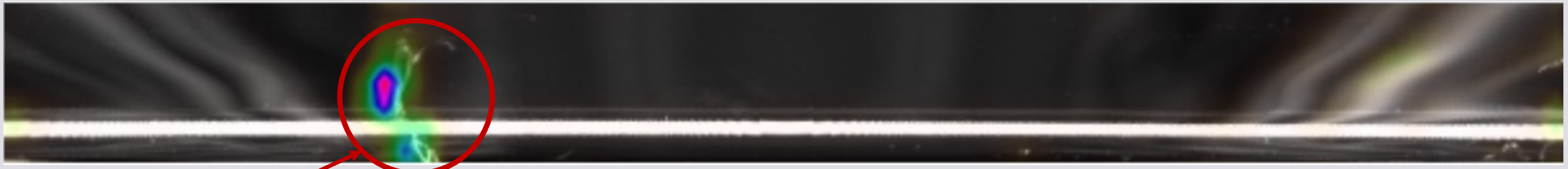
Deep Learning Heat Map



Original Image

Heatmap

Heat maps are used to highlight the areas in the image which influenced the neural network in the inference made

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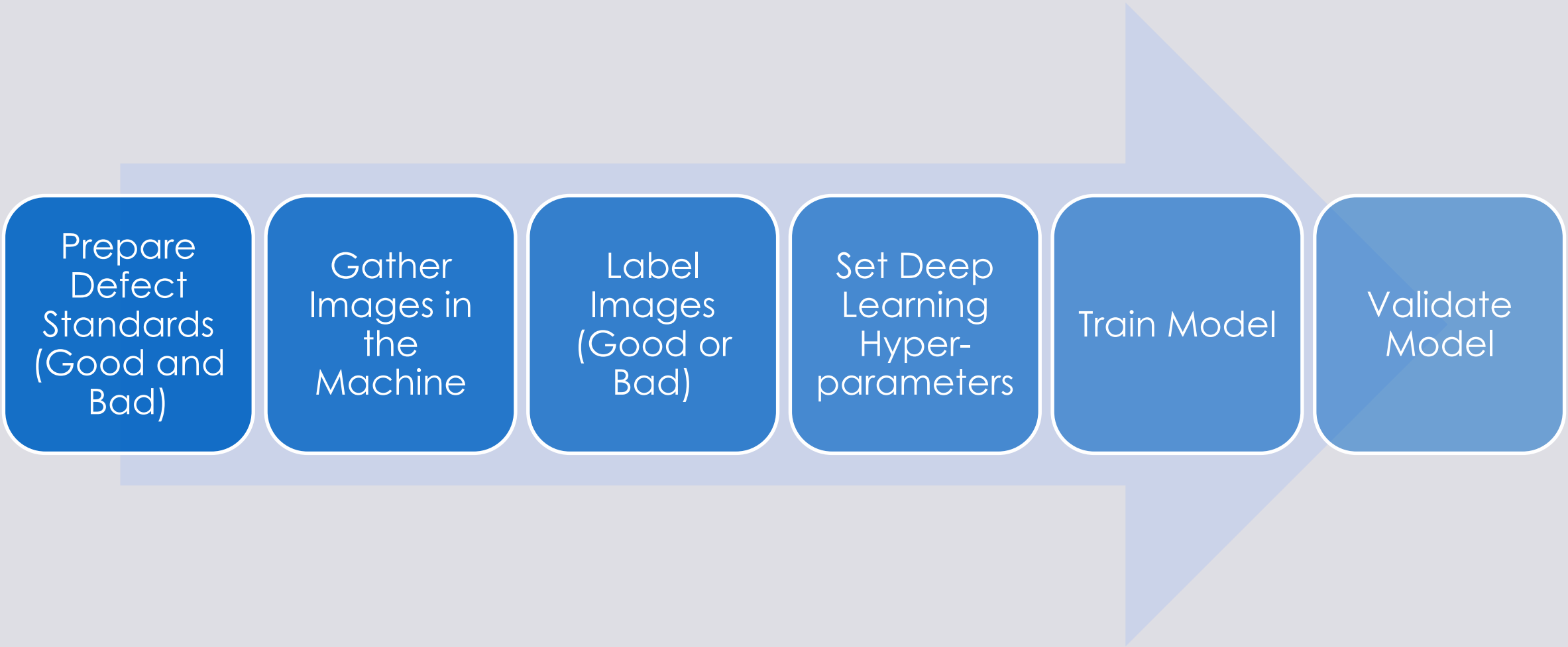
Deep Learning Model Generation



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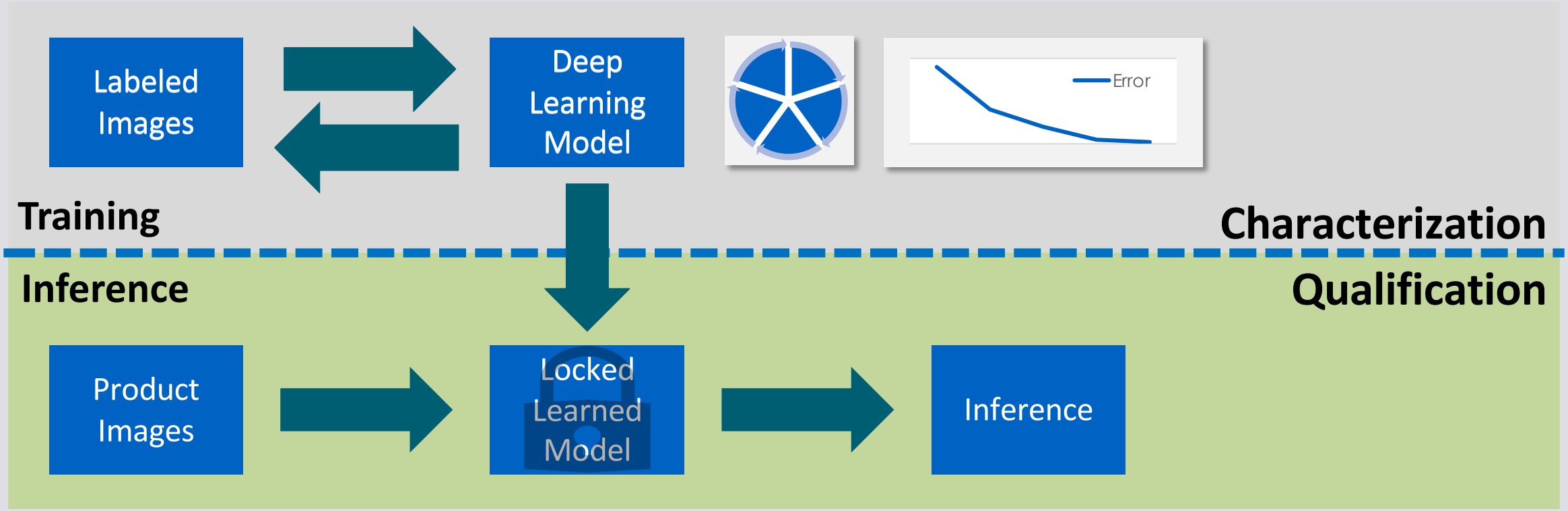
Deep Learning Characterization and Qualification



Once a model is locked, there are no changes in the Neural Network
If 1 image is evaluated 1 million times, 1 million times we will obtain the same result

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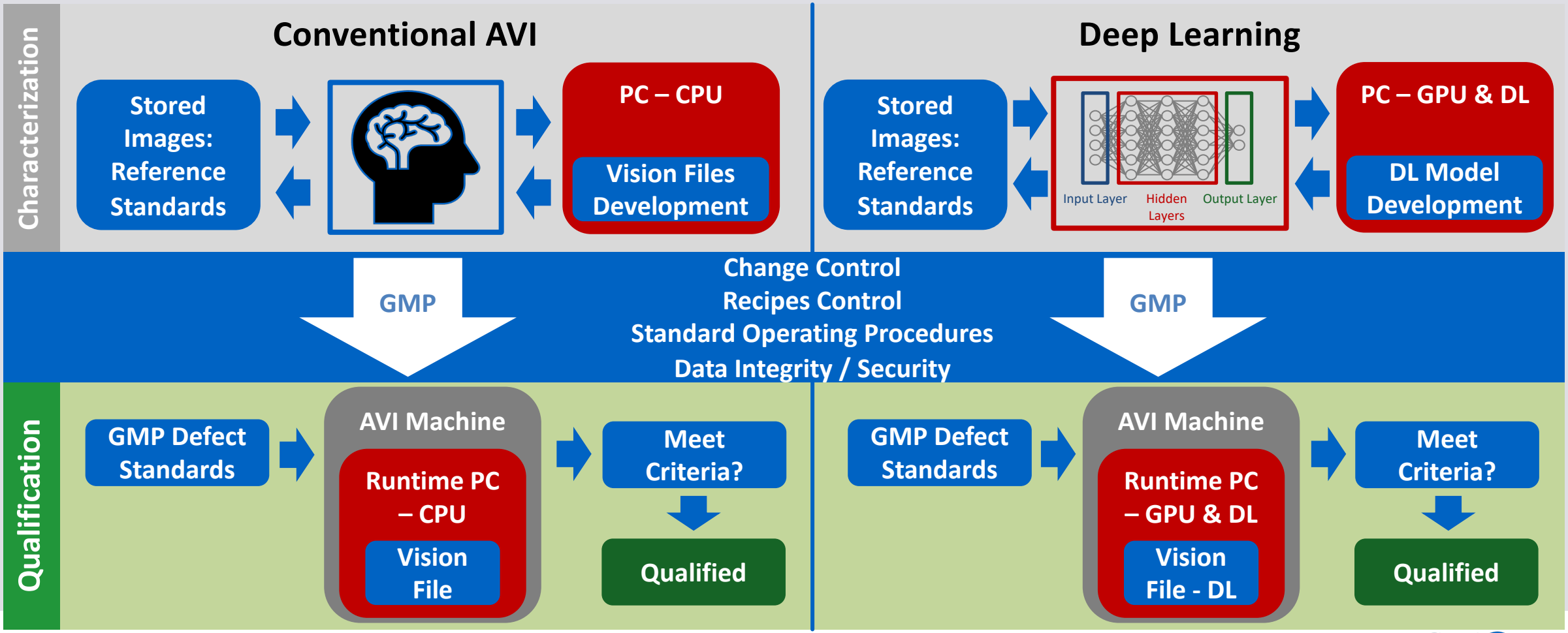
AVI Qualification Approach



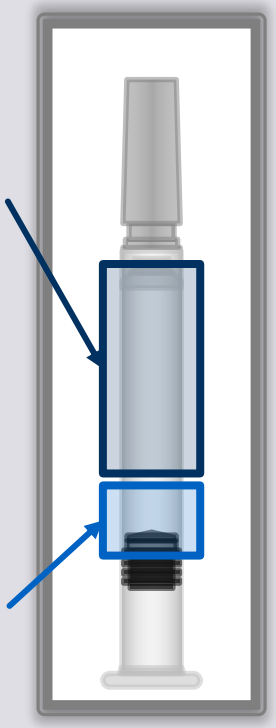
Drug Product Manufacturer | AVI Original Equipment Manufacturer | Machine Vision

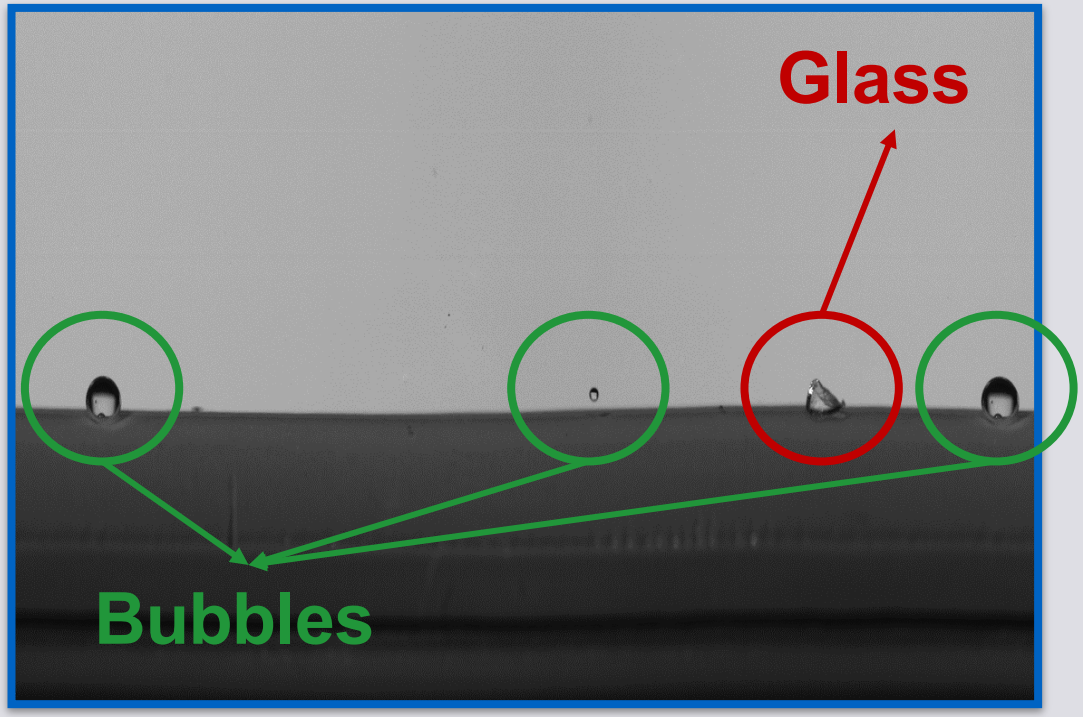
AMGEN

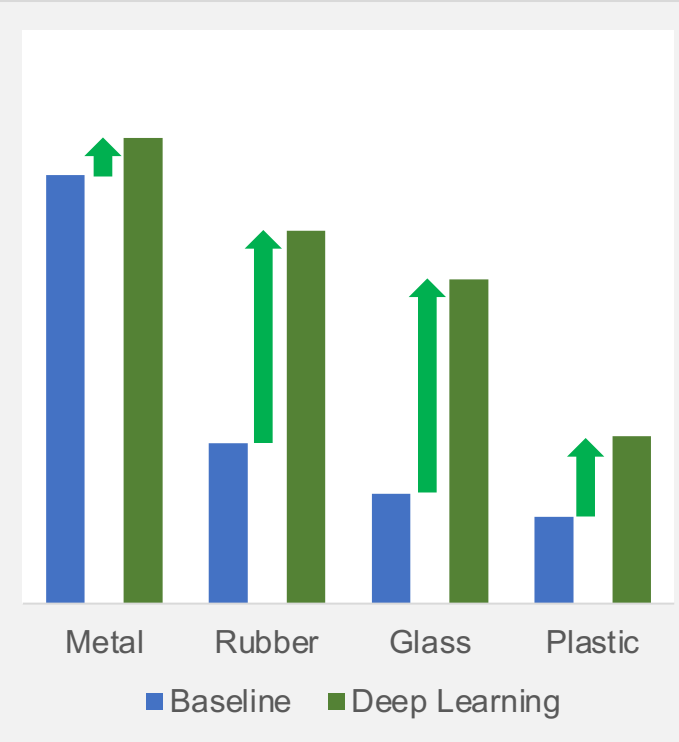
Studies have shown an increase in detectability of particles in syringes

Region Inspected By Other Stations

Inspection Region

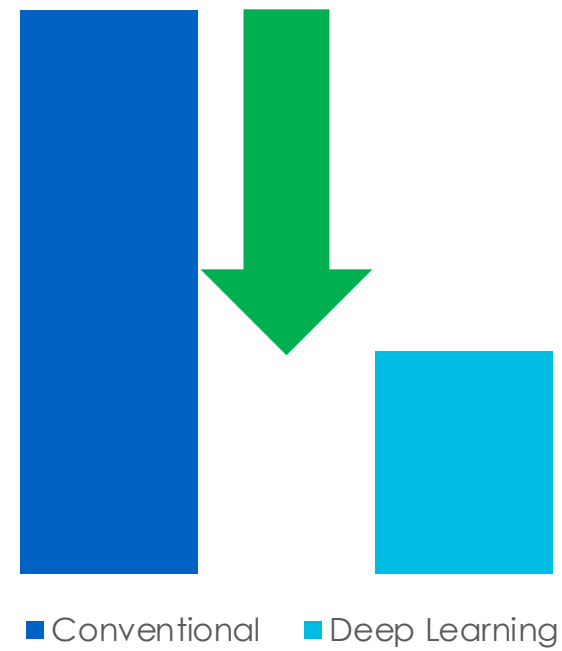




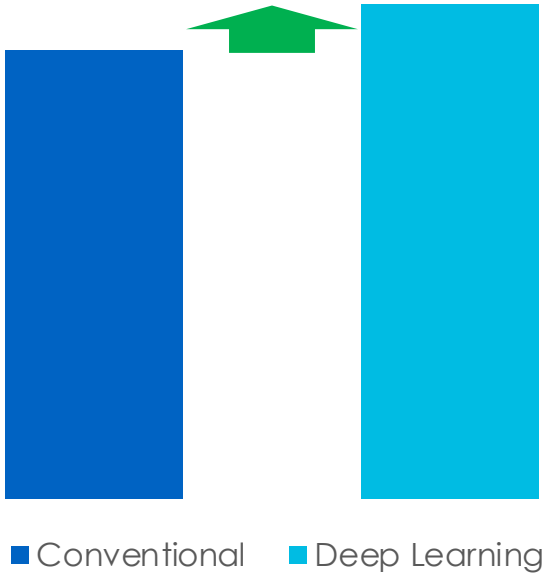


Machine vision is the integration of hardware and software technologies used to capture, process and analyze images

Results Obtained After Millions of Units Processed with Deep Learning for the Inspection of Pre-Filled Syringes



False Fails Reduction



Overall Equipment Efficiency Increase

0

AQL Failures

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Deep Learning models require a significant number of images which brings several challenges

- Line time required for image gathering
- Cost of test material and components
- Availability of test material and components
- Resources time for image labeling

Many of these challenges can be overcome with technology

AMGEN

Work have been done to augment images using Generative Adversarial Networks

Deep Learning Image Augmentation using Inpainting with Partial Convolution and GANs

by **Aik Jun Tan**

Submitted to the Sloan School of Management and Department of Electrical Engineering and Computer Science in partial fulfilment of the requirements for the degree of

Master of Business Administration and **Master of Science in Electrical Engineering and Computer Science** in conjunction with the Leaders in Global Operations (LGO) program at the

MASSACHUSETTS INSTITUTE OF TECHNOLOGY

June 2021

This tool can be used to provide a baseline model that can be further fine tunned

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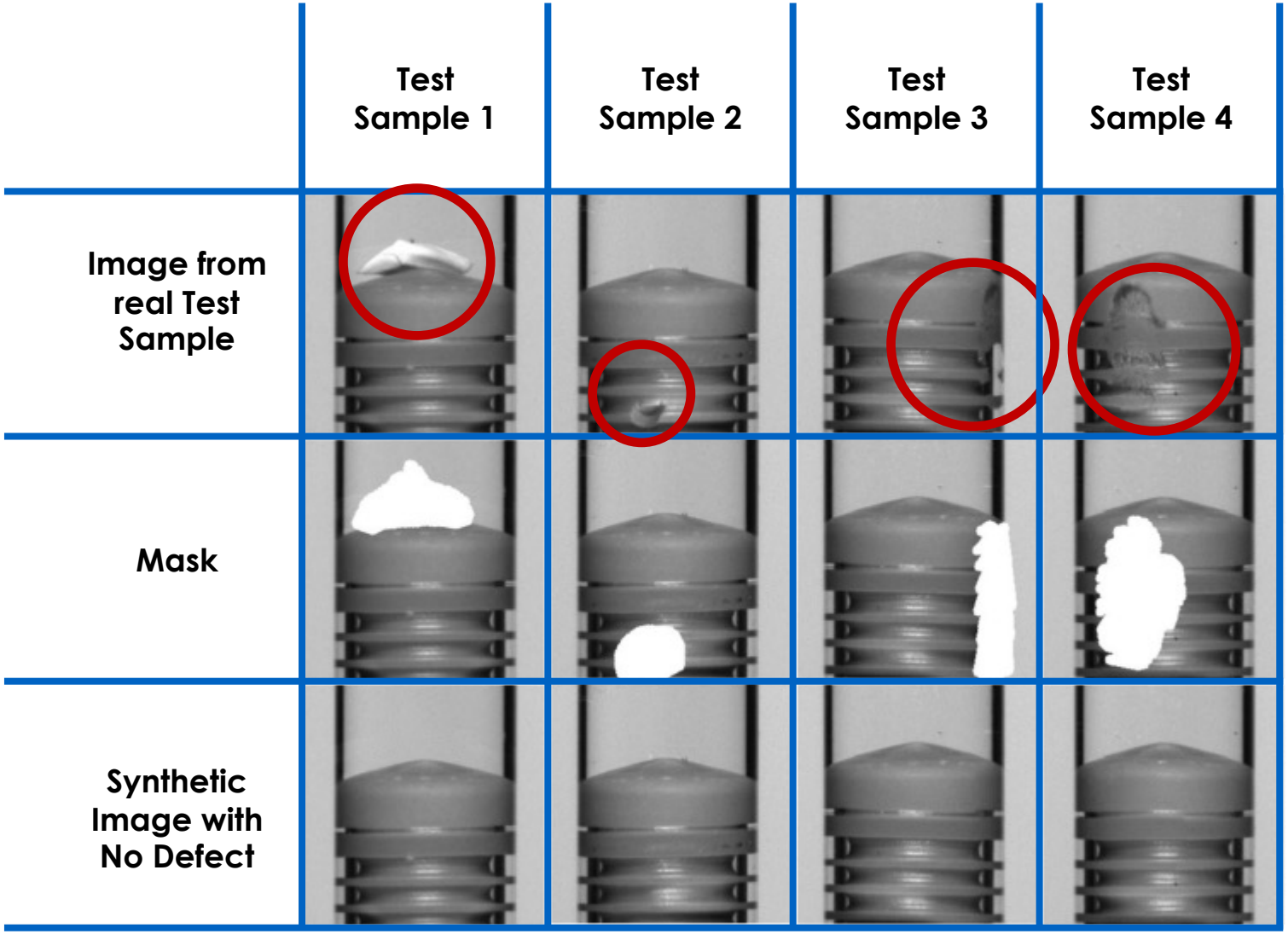
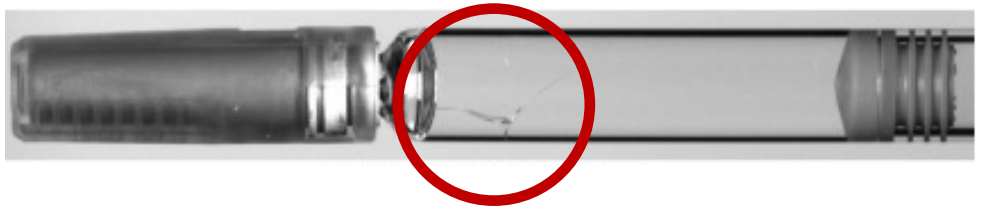
Stopper Defects Removed



Syringe Defects Removed

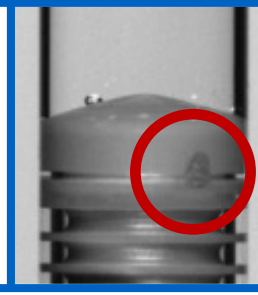
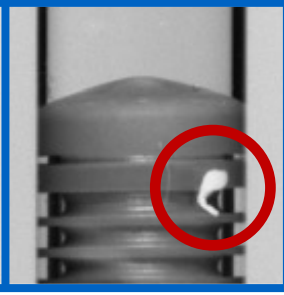
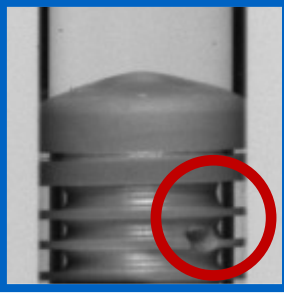
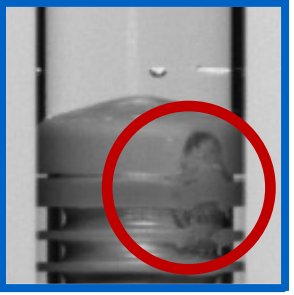
	Test Sample 1	Test Sample 2
Image from real Test Sample		
Synthetic Image with No Defect		

Syringe Defects Removed

	Test Sample 3	Test Sample 4
Image from real Test Sample		
Synthetic Image with No Defect		

AMGEN

Stopper Defects Added

	Test Sample 1	Test Sample 2	Test Sample 3	Test Sample 4
Image from real Test Sample				
Mask				
Synthetic Image with No Defect				

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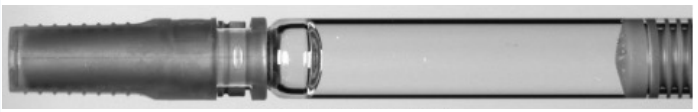
Syringe Defects Added

	Test Sample 1	Test Sample 2	Test Sample 3
Image from real Test Sample			
Synthetic Image with No Defect			

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Possibilities in the Future of AVI

- Increased use of Deep Learning for the inspection of parenteral drug product
- Image augmentation will reduce development time and implementation cost
- Image gathering will allow for continuous improvements with periodic fine tuning of deep learning models
- Vendors will provide machines with little to no need for development
- AVI will be feasible for High Mix Low Volume products
- Technology will allow more inspections at earliest stages of the process, detecting weak signals while processing a batch
- AVI systems will have the capability to classify particle types, facilitating the identification of potential root causes and their resolution

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THANK YOU