Artificial Intelligence in the Microbiology Laboratory

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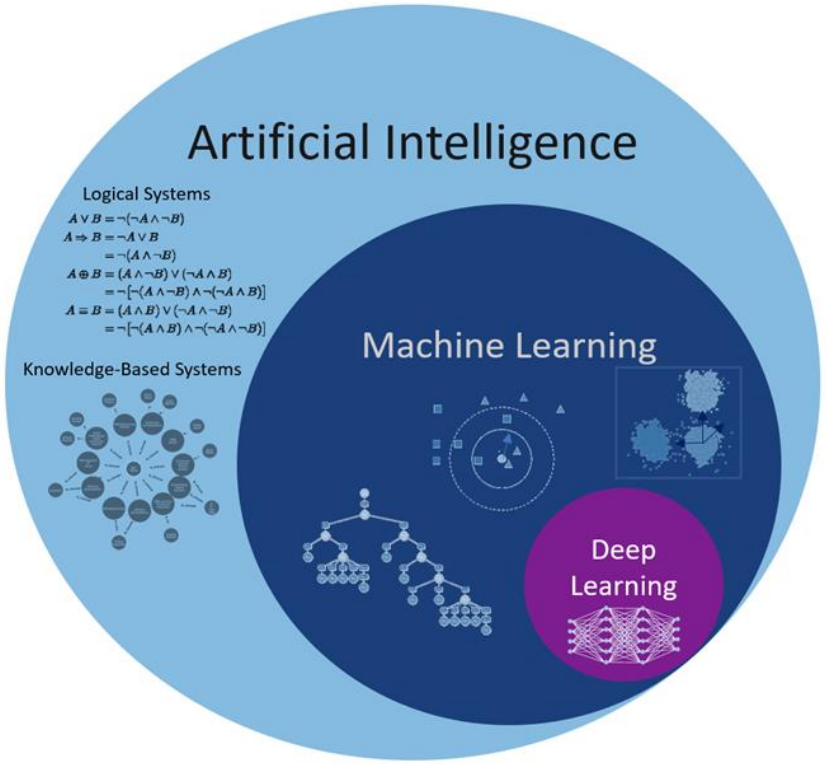
February 7, 2025

Disclosures

- Member of Copan Scientific Advisory Council

What is Artificial Intelligence?



- **Artificial Intelligence**: Computer algorithms that perform interpretation of data
- **Machine Learning**: Computer develops algorithms based on inferences it draws directly from the data
- **Neural Network**: Computing system inspired by the optic cortex of animal brains that use a collection of nodes loosely modeled on neurons and their numerous interconnections. Multiple inputs can influence the output of a node, and the output of a node can act as an input for multiple other nodes
- **Deep Learning**: A type of machine learning that uses multiple layers of nodes in its neural network.

https://www.vrogue.co/post/artificial-intelligence-ai-machine-learning-ml-in-supply-chain

Burns, B., Rhoads, D., Misra, A. "The Use of Machine Learning for Image Analysis Artificial Intelligence in Clinical Microbiology." Journal of Clinical Microbiology 3 July 2023, https://journals.asm.org/doi/10.1128/jcm.02336-21.

Is the microbiology lab ready for AI?

- Advances in full microbiology automation and digital microscopy provide the tools needed to leverage AI/Machine Learning algorithms
- The systems allow high-definition images of plates/slides, which serve as the data set for “training” algorithms
- The systems have image reproducibility (images taken same way every time)

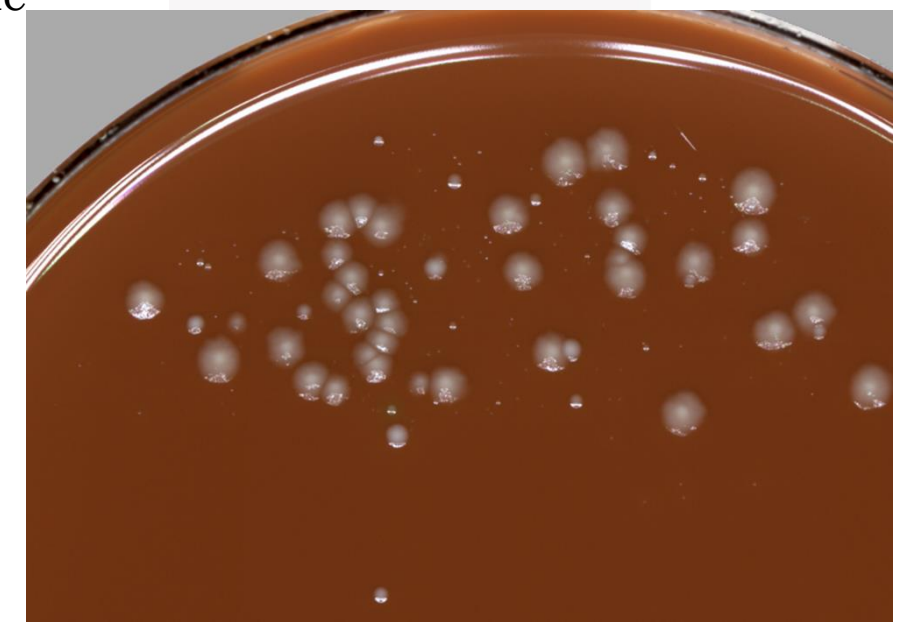
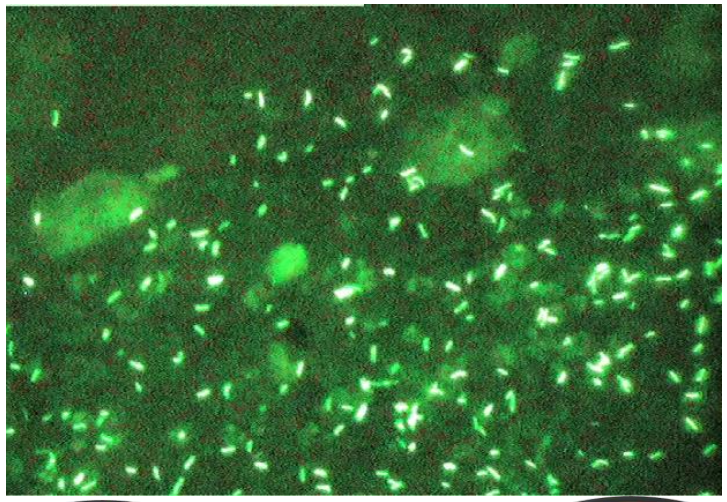
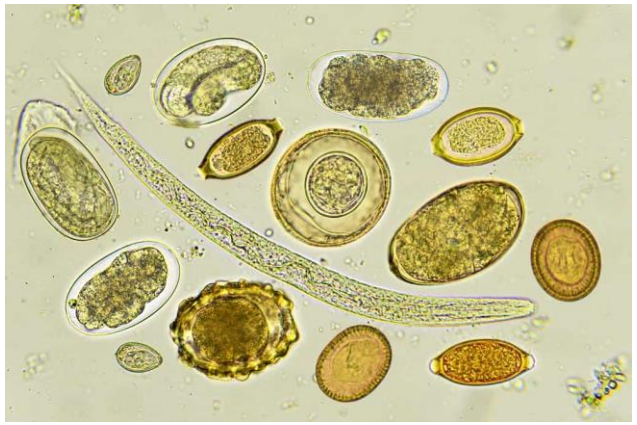
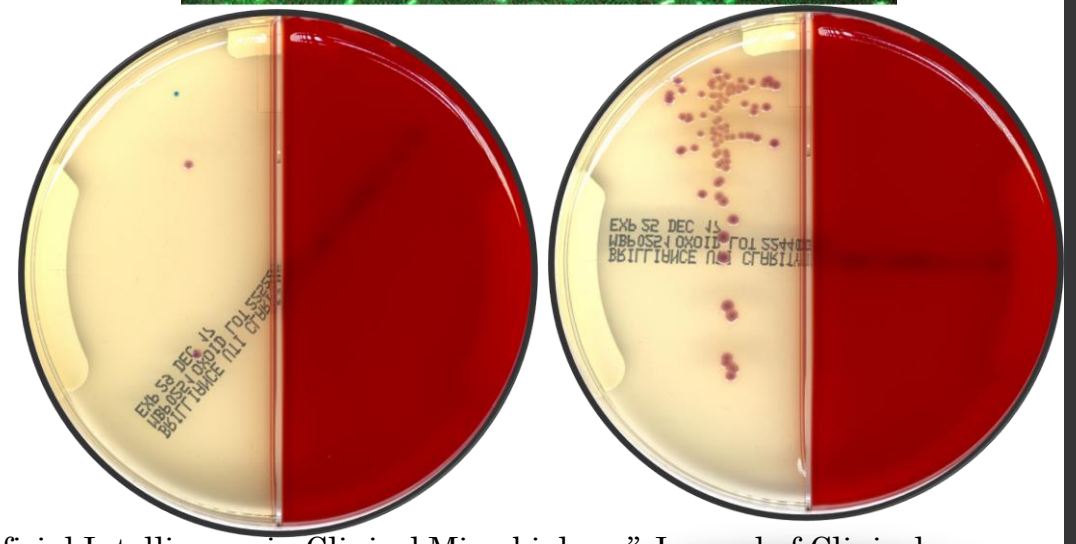


Image Analysis AI (IAAI)

- This can use any on of the modes of AI previously seen (deep learning, neural network, ect.)
- There are 2 classifications of IAAI
  - **Rare event classification/detection**-usually used for screening purposes
  - **Score Based/Categorical Classification**- used for AI plate/slide reading



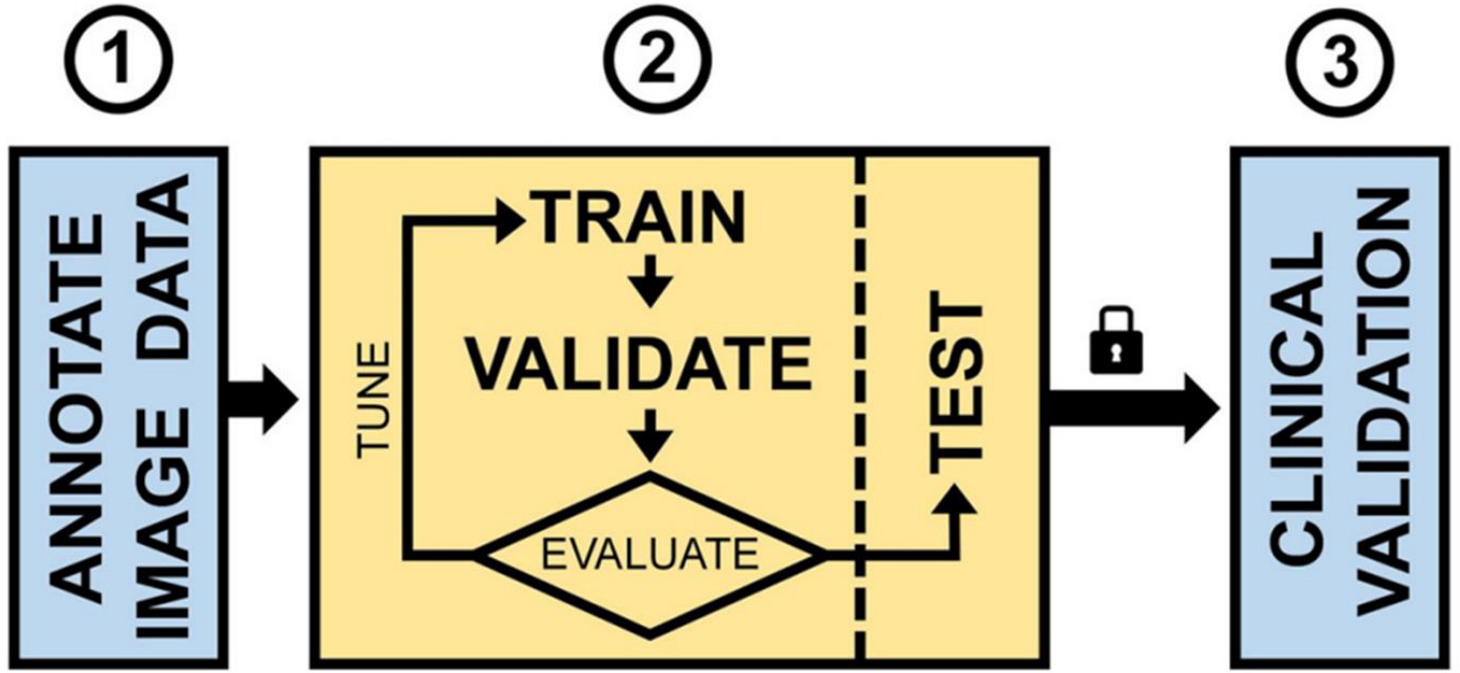




Burns, B., Rhoads, D., Misra, A. "The Use of Machine Learning for Image Analysis Artificial Intelligence in Clinical Microbiology." Journal of Clinical Microbiology 3 July 2023, https://journals.asm.org/doi/10.1128/jcm.02336-21.

What are the current AI algorithms doing?

- Most of the current algorithms are using machine learning
  - Use annotated data set done by a human
  - These data sets are usually large data but must be annotated the same way (little variation)
  - Used to train the AI
  - Once enough training is done a new set of data is used to validate the algorithm



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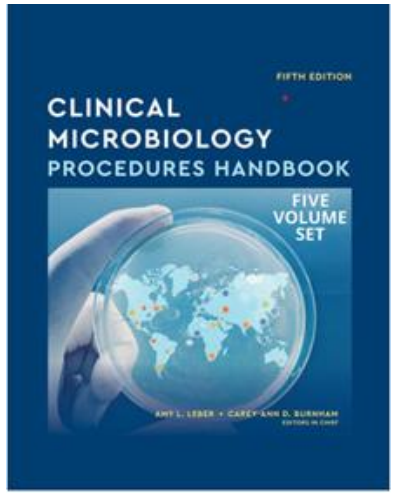
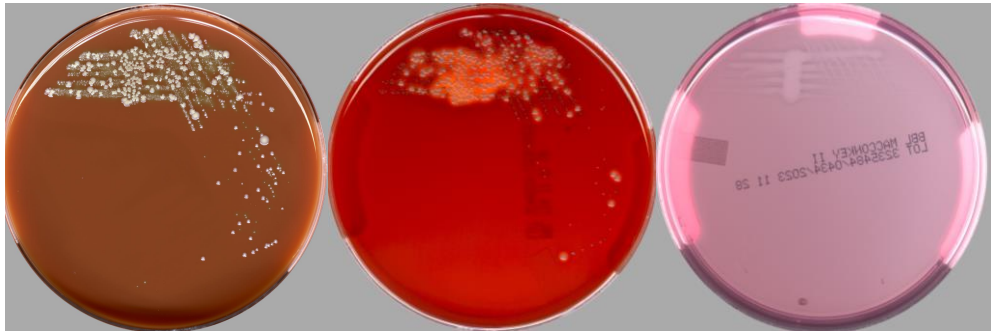
What Makes Developing Microbiology AI Algorithms Challenging?

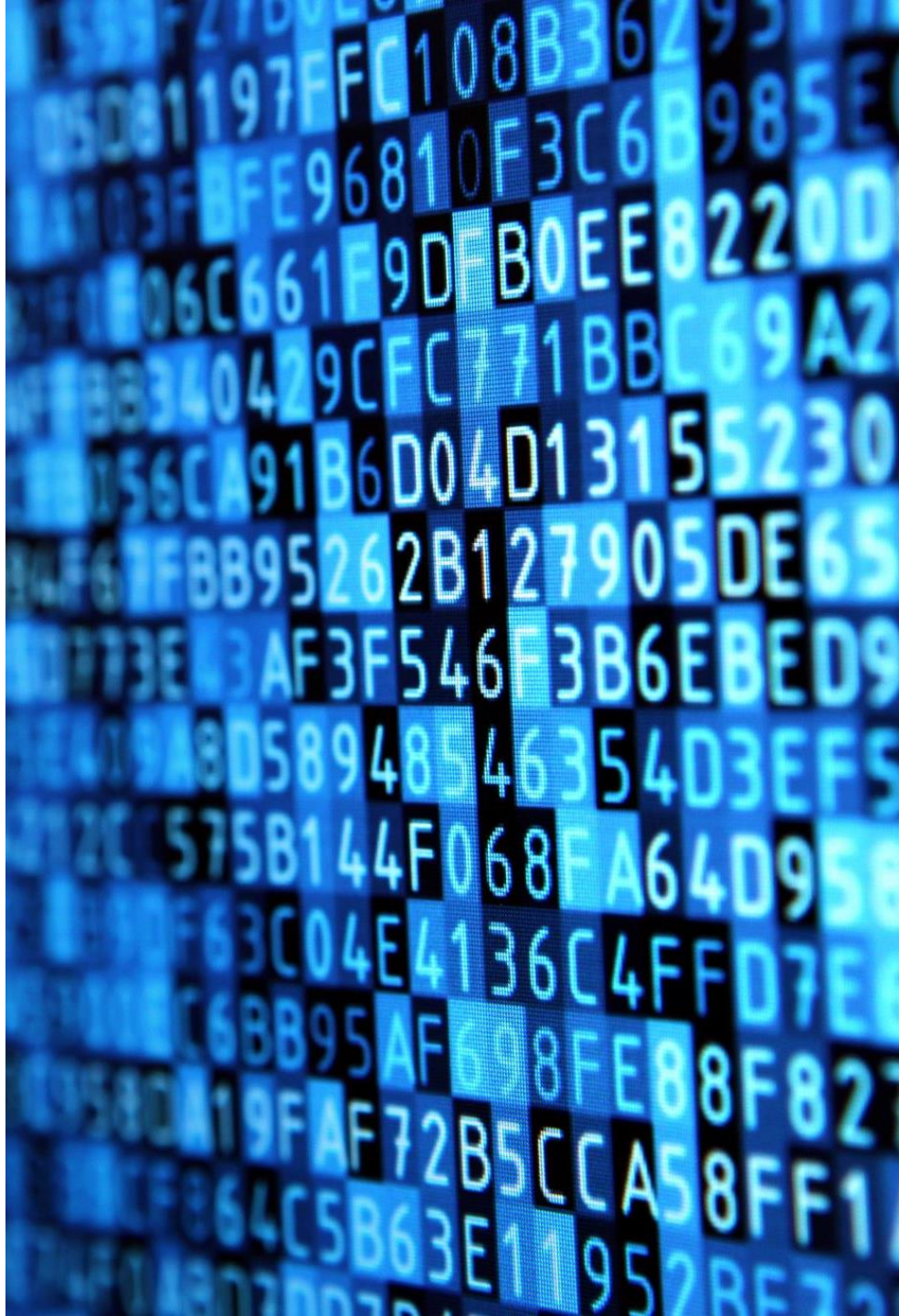
- Every lab works cultures up a bit differently (makes having universal algorithms hard)
- Many specimens are polymicrobial due to normal microbiomes and everyone's microbiome is different
- Vast array of specimen types that are cultured in the microbiology lab (each type needs its own algorithm)
- Many pathogens have multiple phenotypes on plates. Example some strains of *S. aureus* can be very β-hemolytic others only slightly or not at all
- Effects of antibiotics on organisms
- The need to use multiple plates and gram stains to understand what's going on in the culture
- Positive specimens are rare especially true for parasitology (need a scan of the whole slide at multiple levels)





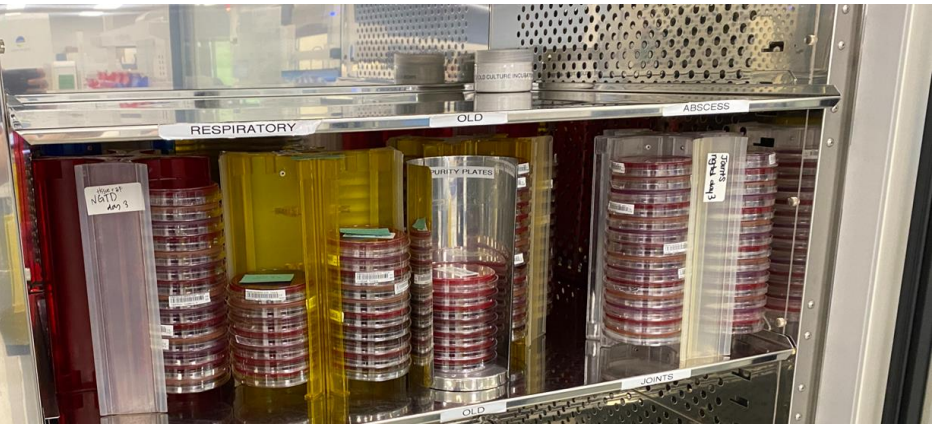
What type of AI/Machine Learning algorithms are available now?

- Growth/No Growth Sorting
- Chromogenic Agar Sorting
- Urine Quantitation with Chromogenic Sorting
- Ability of Algorithms to Choose Colonies for MALDI-TOF and Susceptibility Setup
- β-hemolytic Screening
- Kirby-Bauer Disk Reading
- Parasitology (O&P and Blood Parasites)
- Gram Stain and Fluorescent AFB smears



AI Plate Reading

What do we mean by AI plate reading?



Algorithms Sort Plates into Groups

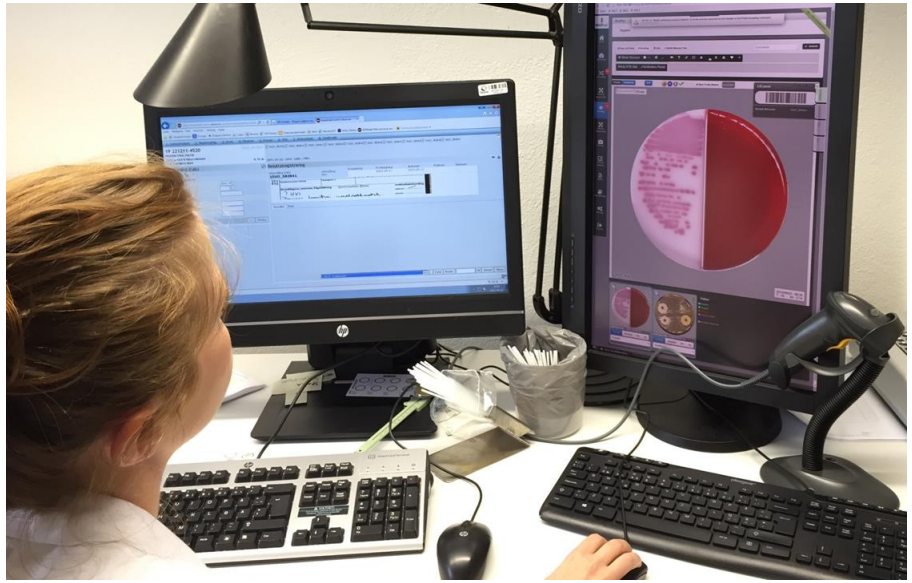
No Growth

Normal Flora

β-hemolytic

Sig. Growth

Batch Report

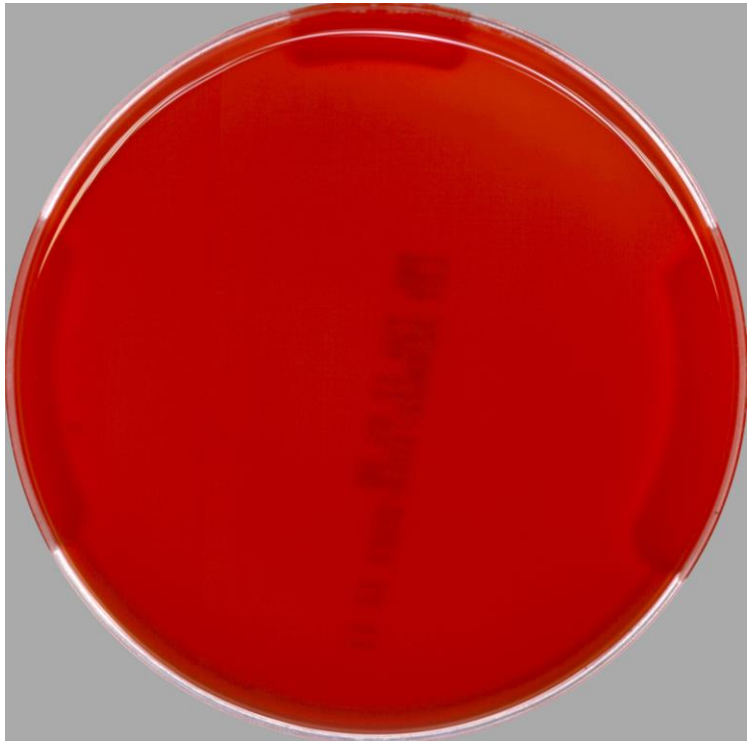


Growth/No Growth Sorting

- Looks at the time 0 image and compares to later images looking appearance of colonies
- These types of screens are very useful for culture types where any growth is considered significant
- Great time saving for technologists only really have to deal with positive cultures
- Can batch out no growths easily

Algorithm:
Is something there compared to time zero picture?

0 hours



14 hours

Chromogenic Agar Sorting

- Chromogenic agars are available for screening MRSA, VRE, CRE, Candida, GBS, GAS
- Great time saving for technologists they can batch the positives and negatives from many of these chromagars

Algorithm:
Is something there compared to time zero picture?
And
Is it the right color?

Urine Quantitation with Chromogenic Sorting

- Urine cultures can be sorted by quantitation, such as No growth, No significant growth, significant growth with quantitation (10,000-25,000 cfu/mL, etc.)
- If using Chromogenic urine agar, cultures can be sorted by organisms such as *E. coli*, GBS, enterics other than *E. coli*.
- These sorted cultures can be quickly batch reported

Algorithm:

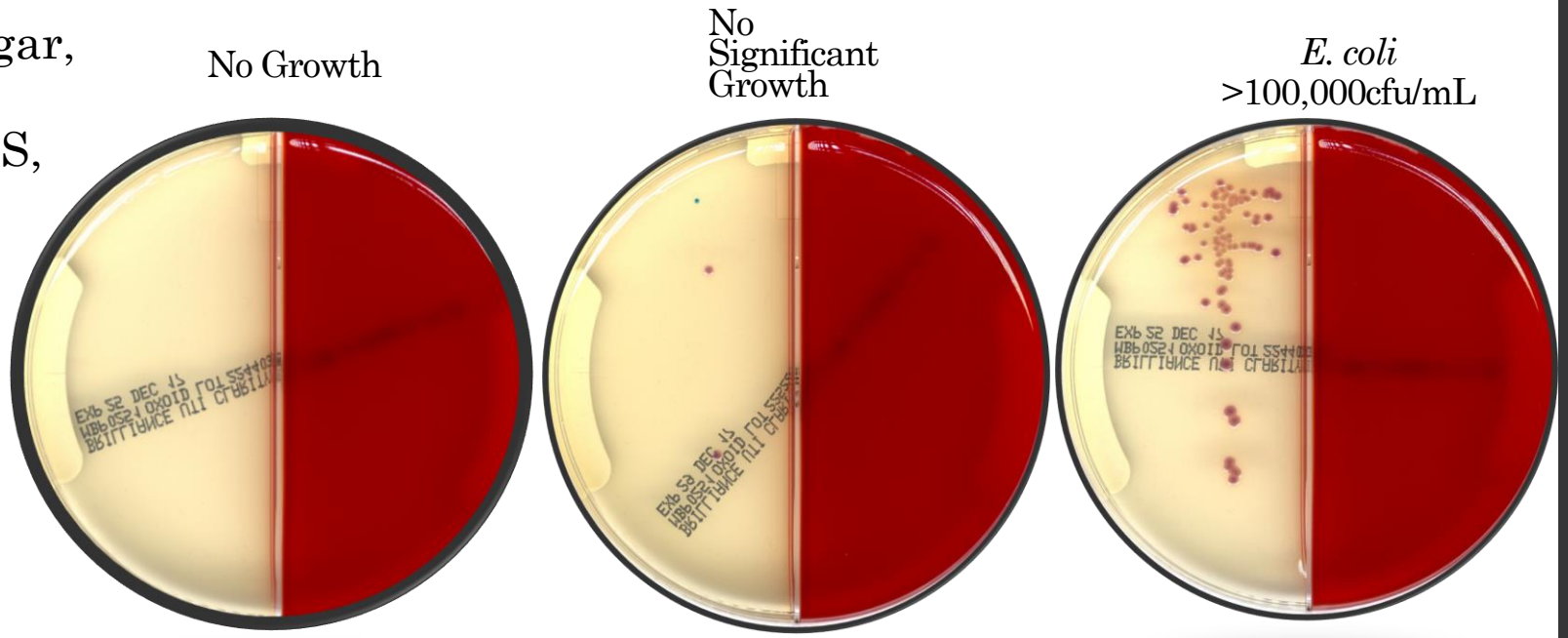
Is something there compared to time zero picture?

And

Is it the right color?

And

How much of each colony type is present?



β-hemolytic Screening

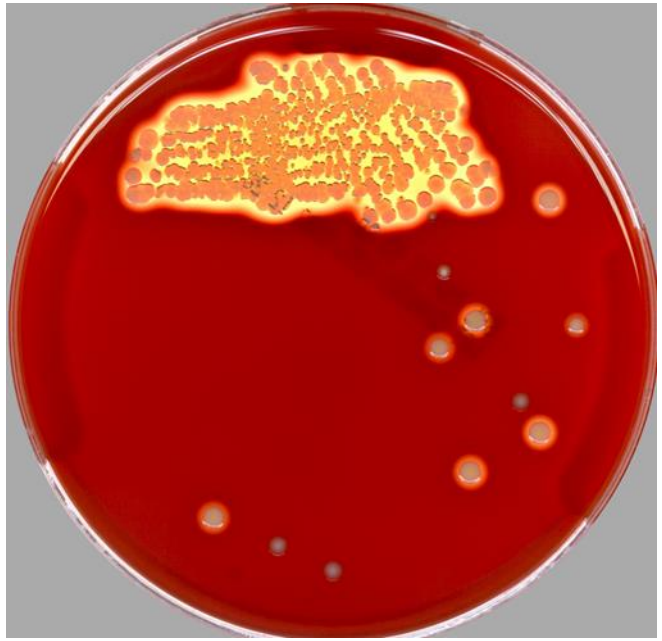
- This sorting allows wounds to be easily categorized since many significant pathogens in wounds are β-hemolytic.
- It can also be used for throat cultures looking for β-hemolytic streptococci

Algorithm:

Is something there compared to time zero picture?

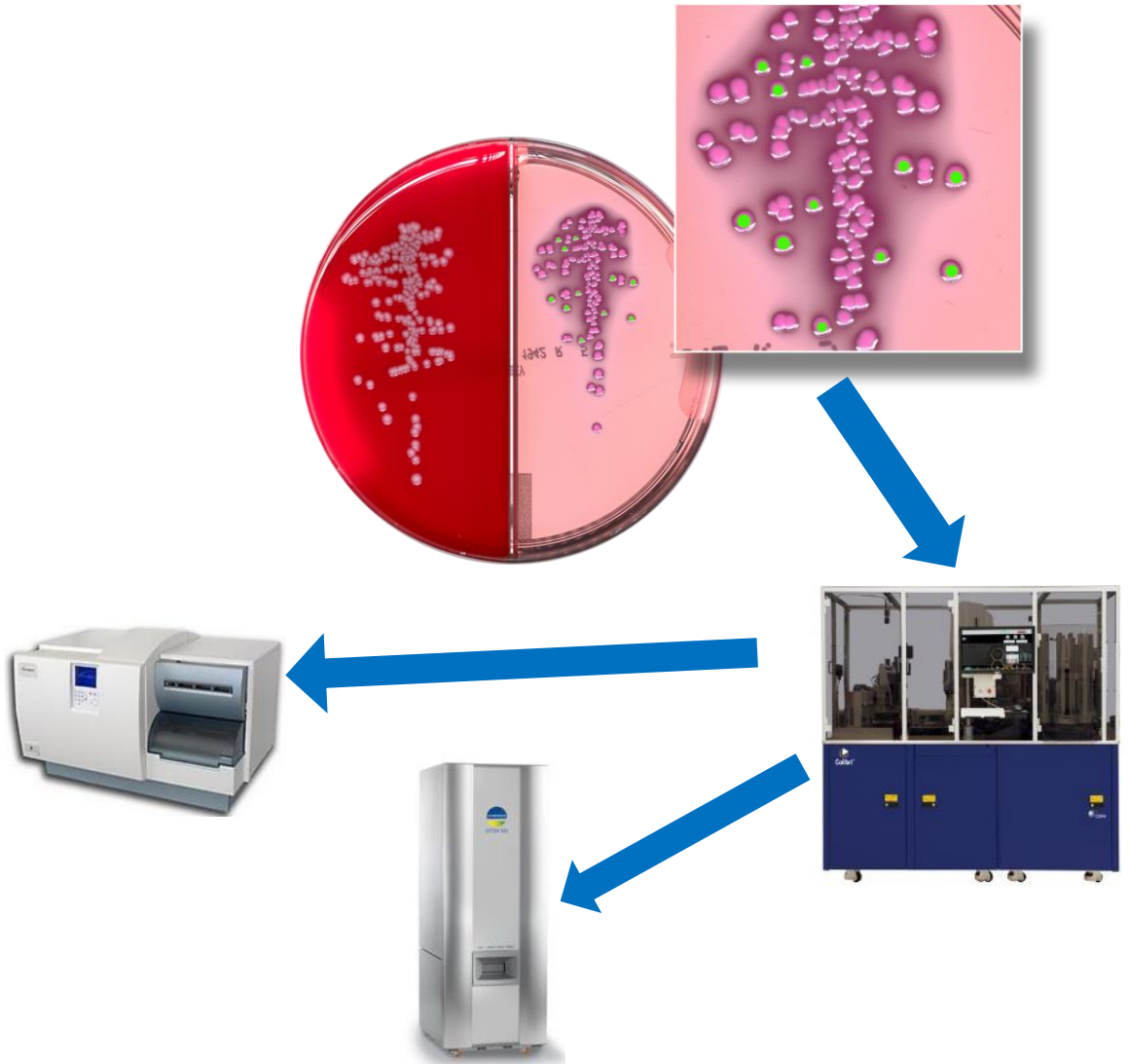
And

Is it the β-hemolytic?



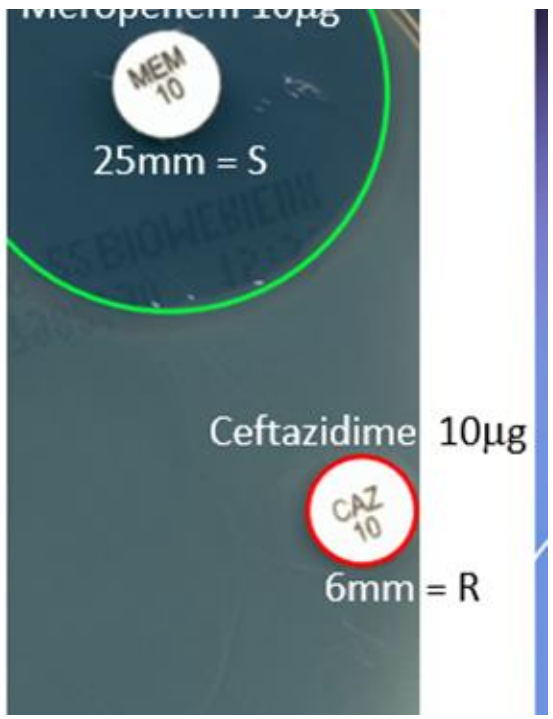
Ability of Algorithms to choose colonies for MALDI-TOF and Susceptibility setup

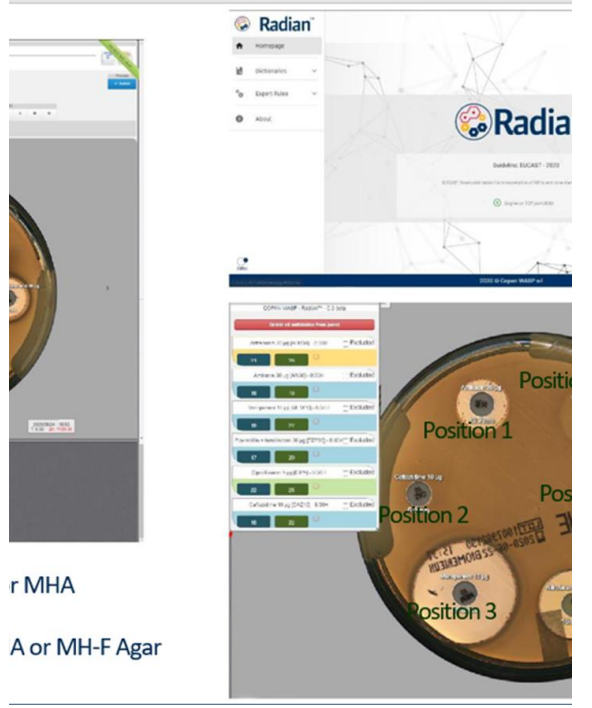
- Algorithm picks colonies that look alike for MALDI-TOF and McFarland standard setup. Technologist reviews the picked colonies and accepts them
- This allows the automation to handle all parts of the workup with very little technologist intervention, saving time

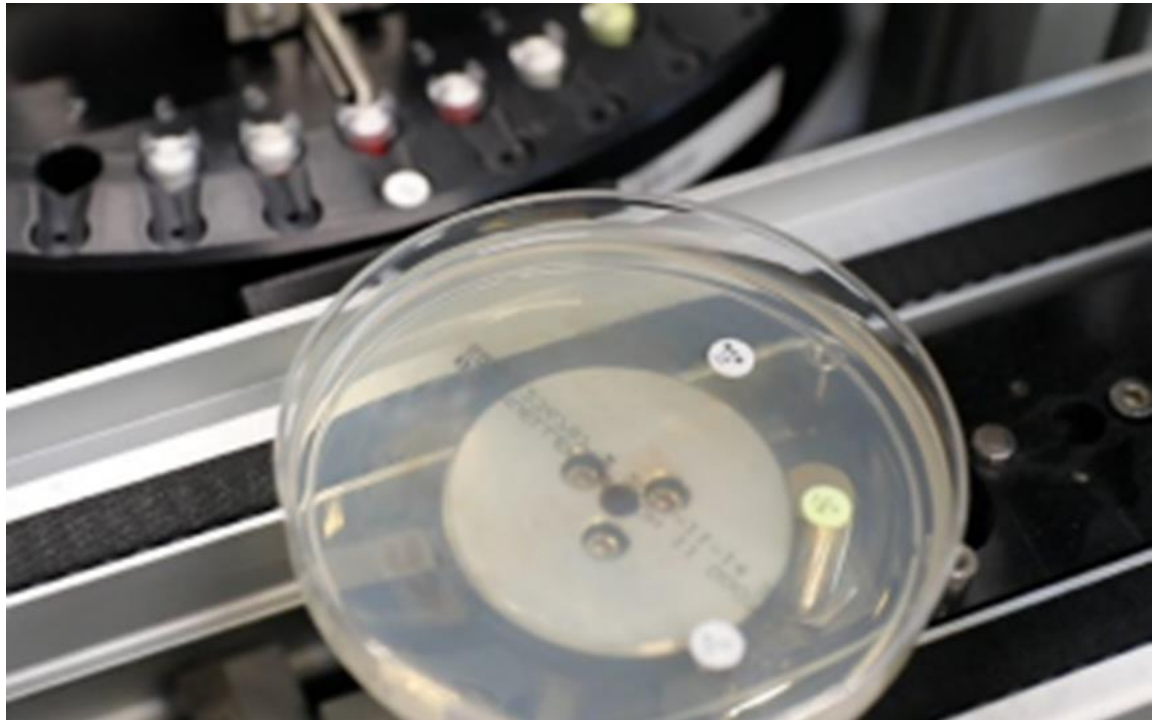


Kirby-Bauer Disk Reading Algorithms

- Algorithms can see zone clearing and measure the zone size.
- Can interpret the zone sizes using a susceptibility program with expert rules
- Allows easy reading of KB results







Where is Plate Reading AI Heading?

Automatic Releasing of Results with No Technologist Intervention

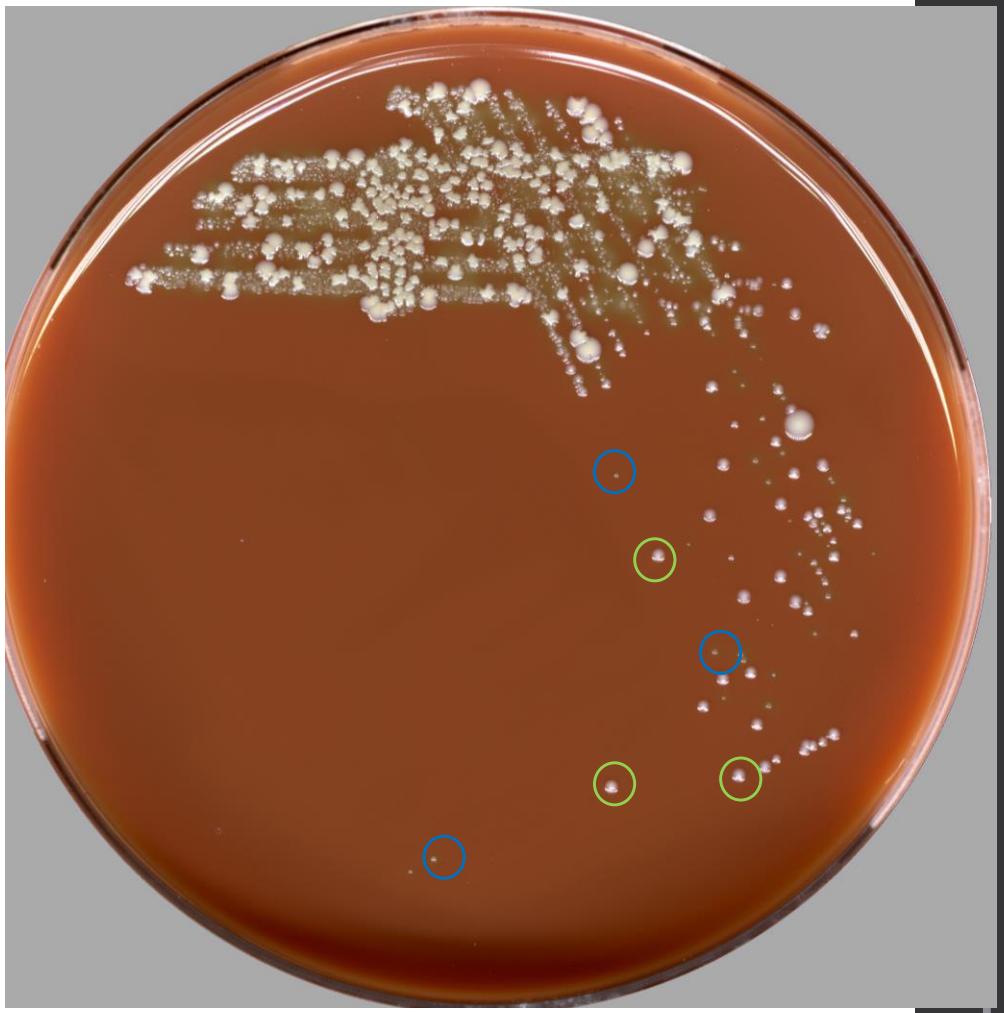
- Many of the previously discussed algorithms could release some results without any intervention. Similar to how chemistry results are released
- This would make results expedite results and require less technologist time
- Allow microbiology cultures to be resulted when ready

Algorithms Sort Plates into Groups

Auto report to Chart

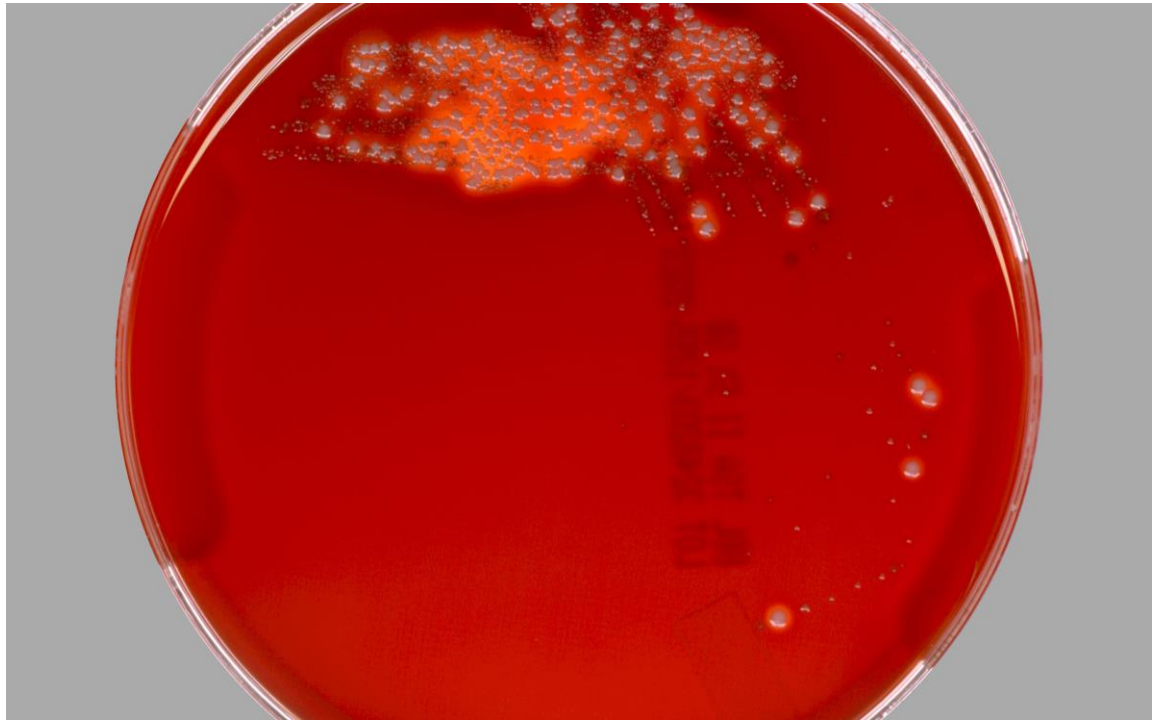
AI could choose colonies for further workup in complex cultures

- AI could look at all colony morphologies and find the predominate morphologies and tag for further workup
- This helps the technologist see the different morphologies
- These colonies could automatically be sent to instruments that spot MALDI-TOF slides
- So, when the technologist sees the culture the first time predominate morphologies already identified



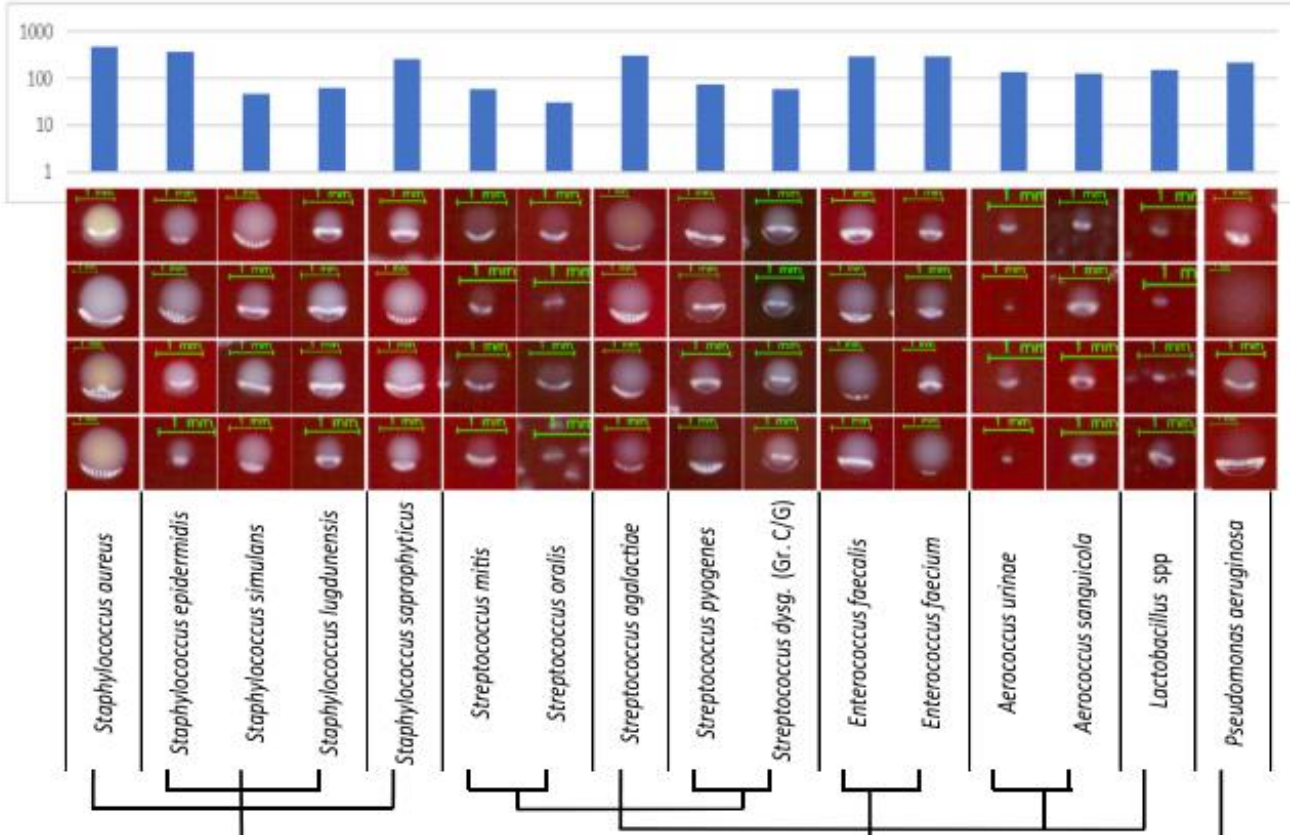
AI workup of complex cultures that use multiple plates

- The algorithm could analyze data from multiple plates to decide what needs to be worked up
- AI could notice growth on Chocolate and not on blood indicative of *Haemophilus*.
- AI could alert technologists to organisms that are slowly growing only on Chocolate agar (*Francisella*, *Brucella* etc.)



AI can ID organisms by colony morphology

- Many bacteria have distinct morphologies on plates. AI can be trained to recognize and ID them directly from a picture This means less use of MALDI-TOF or other ID methods
- Eventually whole cultures can be reported with no technologist intervention (more like chemistry results)

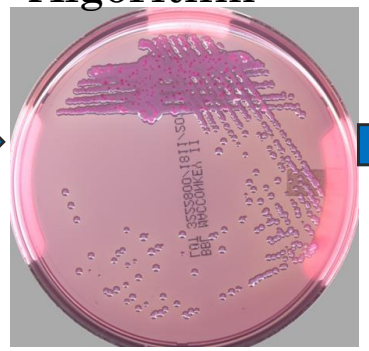


Signoroni, A., Ferrari, A., Lombardi, S. *et al.* Hierarchical AI enables global interpretation of culture plates in the era of digital microbiology. *Nat Commun* **14**, 6874 (2023). https://doi.org/10.1038/s41467-023-42563-1

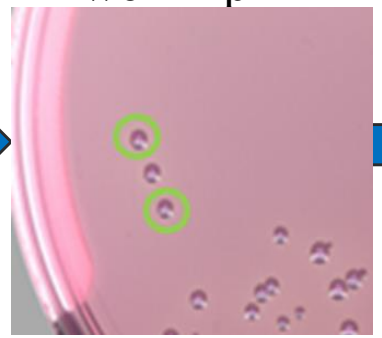
Future Clinical Micro Lab with AI Fully Integrated Plate Reading

Culture loaded to full automation system

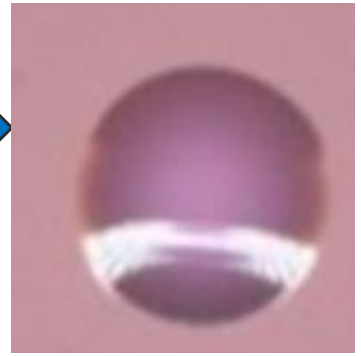
Plate Images Analyzed by AI Algorithm

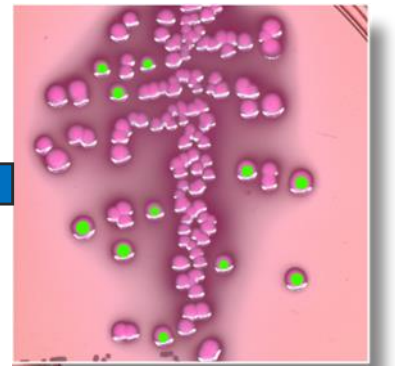


AI chooses colonies to workup



AI Identifies colony by morphology





AI selects colonies for AST

Instrument picks colonies and makes McFarland

Instrument sets up AST and AI interprets

Results post to chart with no technologist interaction

What Does Our Incubator Shelf Look Like with AI?

Algorithms Sort Plates into Groups

No Growth

Normal Flora

β-hemolytic

Sig. Growth

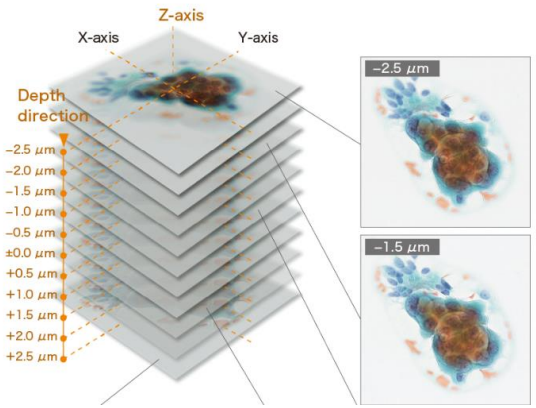
Cultures not fitting an Algorithm

Auto report to Chart

AI Slide Reading

Steps for Digital Microscopy

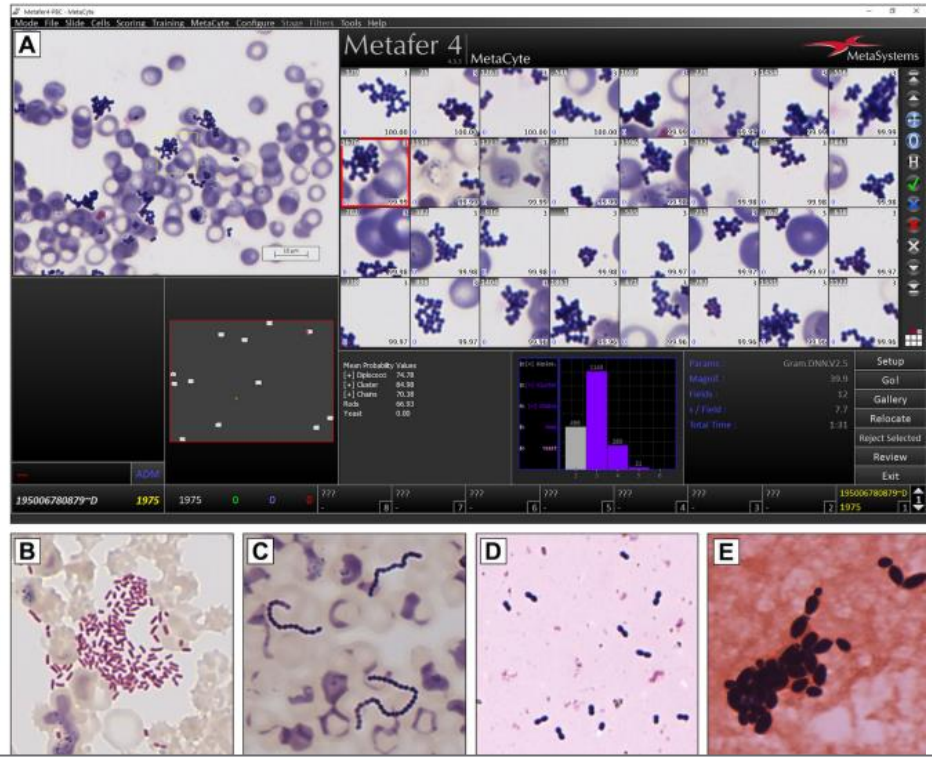
- Slides are made (fixed stained, dried, coversliped)
- Slides are inserted in whole slide imager
- Digital picture of the slide available
  - Most can do z stake (like focusing up and down)



Gram and AFB

Current Gram Stain Algorithms

- So far most are focused on blood culture gram stain results
- Scans slides and identifies organisms

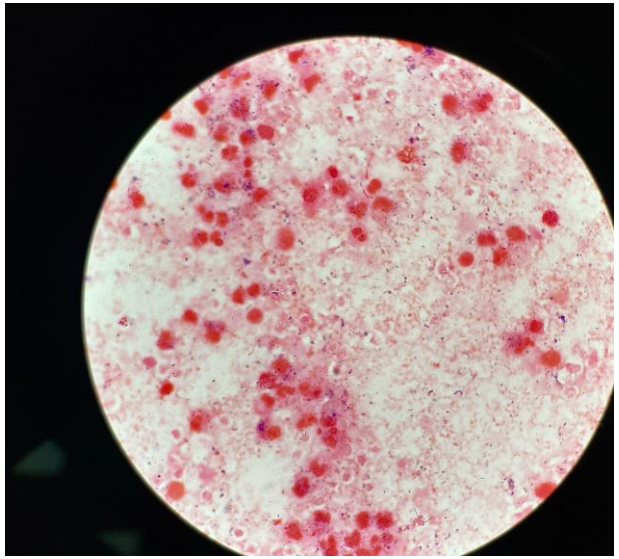


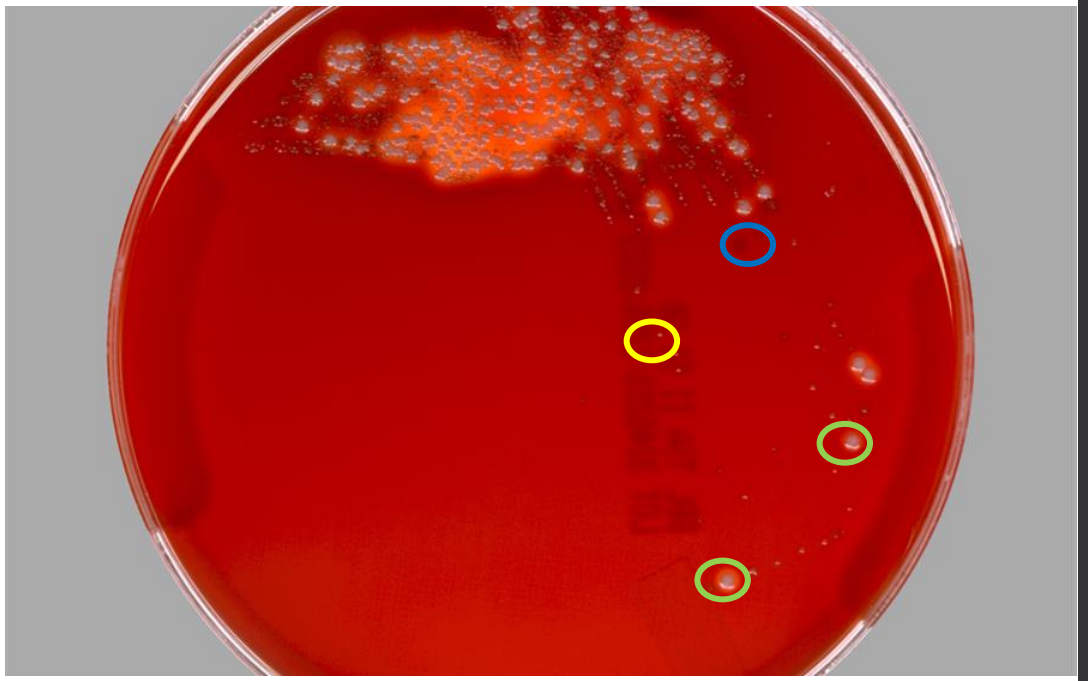
Comparison	Class	PPA (%)	95% CI	NPA (%)	95% CI
BCA-assisted interpretation to manual microscopy	GPCCL	95.8	93.8–97.1	98.0	96.8–98.6
	GPCP/GPCC	87.6	82.5–91.3	99.3	89.6–99.5
	RSB	97.4	95.9–98.4	97.8	96.6–98.5
	Yeasts	83.3	68.1–92.1	99.3	98.8–99.6
	Negative/false positive	87.0	77.0–93.0	98.5	97.7–99.0

Walter C, Weissert C, Gizewski E, Burckhardt I, Mannsperger H, Hänselmann S, Busch W, Zimmermann S, Nolte O.2024.Performance evaluation of machine-assisted interpretation of Gram stains from positive blood cultures. J Clin Microbiol62:e00876-23.https://doi.org/10.1128/jcm.00876-23

AI could use gram stain data to inform what to workup

- AI could be trained to use gram stain data to decide how many organisms to workup (Q345 scoring) and chose the most predominate colony types for workup
- AI could also correlate the gram stain results with culture results
- This could be an automated QA process for every culture





Parasitology

Challenges to AI Development in Microbiology

- Equipment is expensive
  - Currently each algorithm is lab specific so you must implement microbiology automation/slide scanning before you can start building AI algorithms
  - The time it takes to do this eats into the return on investment for the equipment
- No Consensus on how to work up cultures
  - Every lab has slightly different
  - No agreement on what is consider “normal flora”
  - No agreement on what is considered a pathogen in some sources

What's Needed to Speed Up the Development of AI in Microbiology?

- Greater adoption of full microbiology automation
  - more automation=more plate pictures
- Consensus protocols for working up cultures
  - Allows data from multiple institutions to be used to train the AI
- Multi-laboratory studies defining normal flora in cultures

AI Integrated Into Laboratory Information System

- AI could review previous results and perform delta checks (have the susceptibility patterns of an isolate changed over time)
- AI could correlate lab results from other sections (e.g., CSF sample results from chemistry or molecular results) and compare them with cultures

What Will AI Provide to Clinical Microbiology and in 10 Years?

- The future is now:
  - Full microbiology automation provides us with the high-definition images needed for AI development
  - Digital slide scanning provides high definition pictures that can be used to train algorithms
  - AI already exists for many common culture types enabling
  - AI can already provide efficiencies saving technologist time
- AI will continue revolutionize the way we do clinical microbiology
  - The integration of AI promises faster, more accurate result with reduced technologist intervention, including automatic result release and identification by colony morphology