

The Rise of the Machines: Artificial Intelligence and Reading Algorithms in Microbiology

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We Practice What We Teach

What is Automation?



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Why Automate?

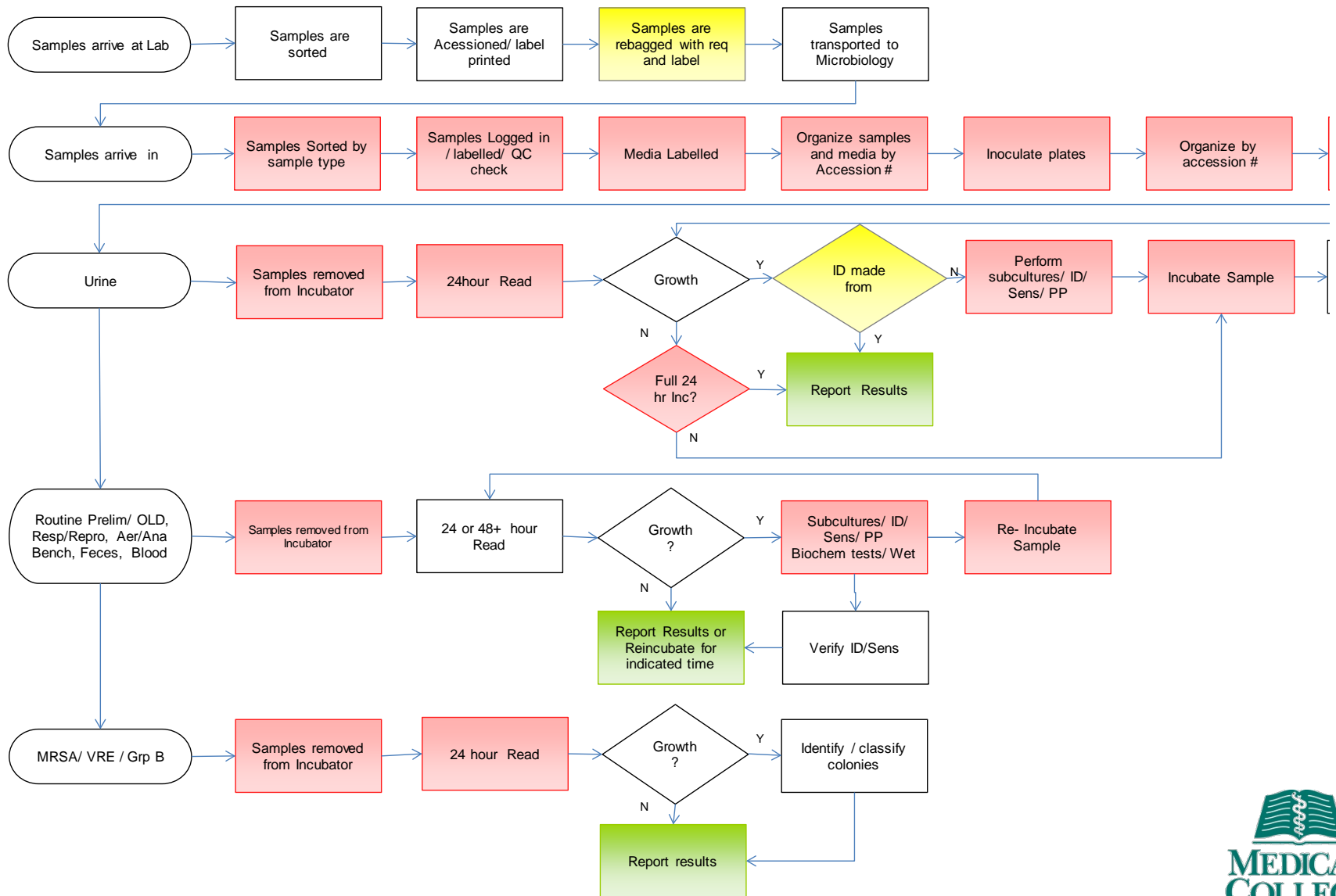
- Potential answer to shrinking workforce –
 - Need to staff when plates are to be read, not just 9-5
- Answer to ergonomic realities
 - Quality of life issues/cost to organization
- Labs are consolidating – can do more potentially with less – but perhaps larger
- Better **quality product** – consistent plating
- Pressure for decreased TAT from receipt to results
 - Pressure to be open 24/7
- Increased standardization of transport media – ie liquid transport media (eSwab)

Why Automate ?

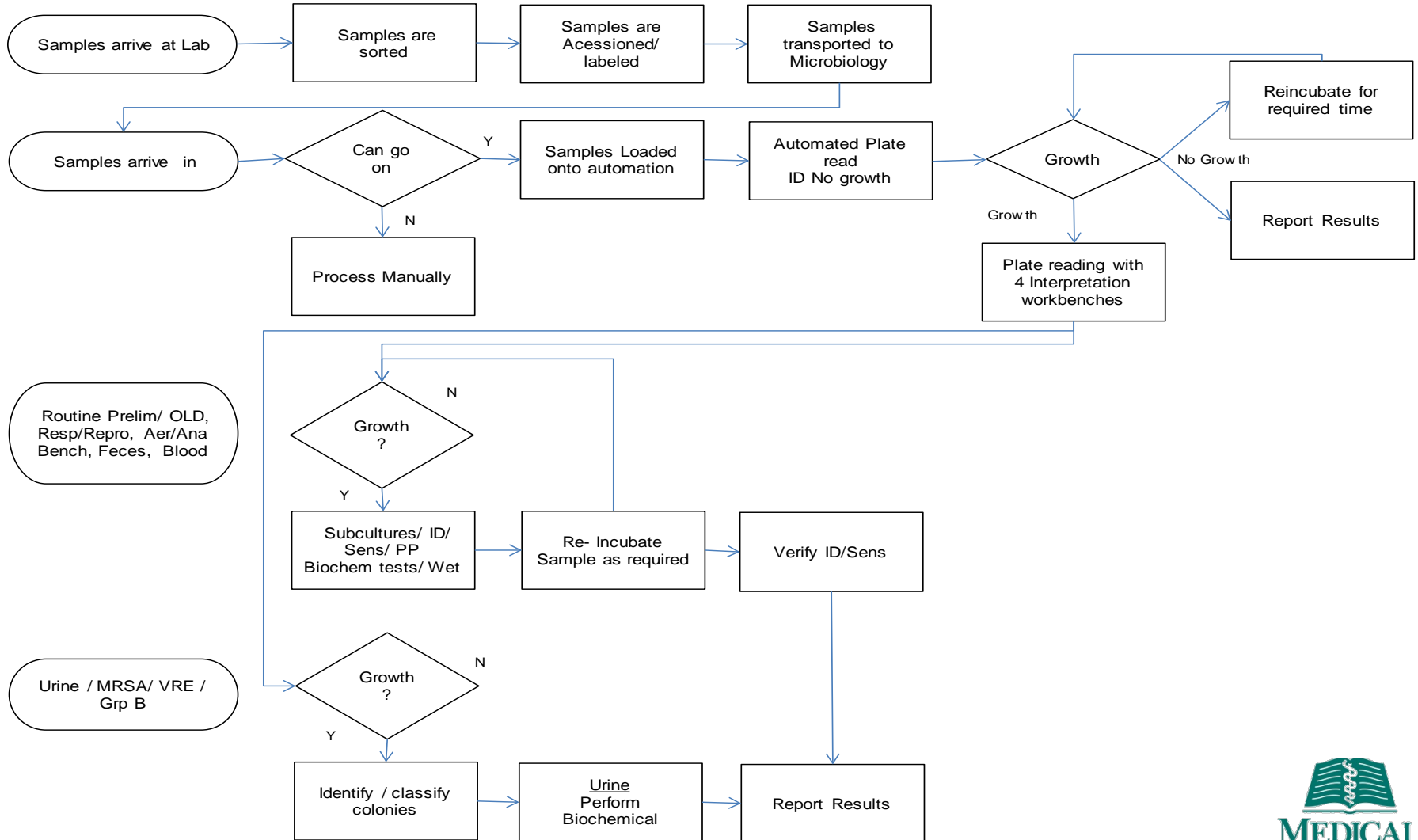
- Pre-analytical processing of specimens reduces time to incubation – increased quality, consistency in plating
- Digital Microbiology – imaging analysis to aid the CLS
 - Useful for training/Documentation
 - Quality Assurance
 - Remote locations – less skilled CLS

Automation is NOT as Simple
as Installing New Hardware –
Laboratory Workflow is Critical

Laboratory Process Current

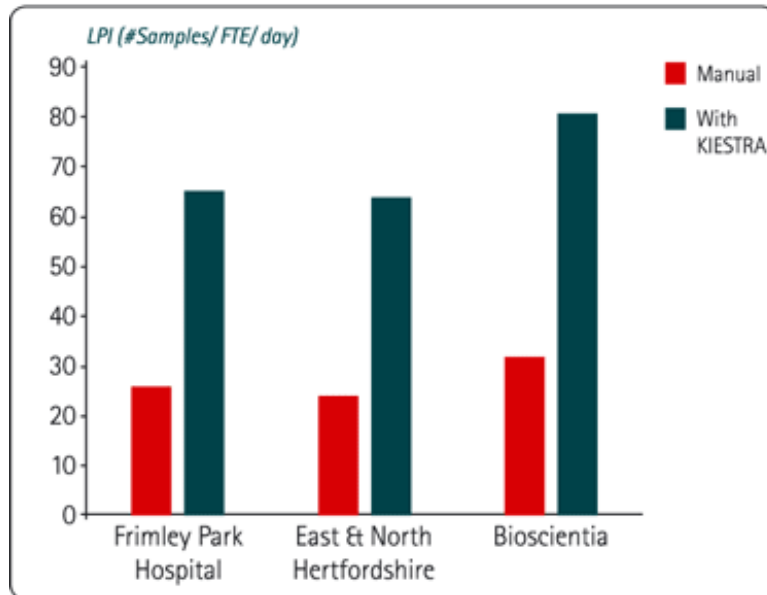


Laboratory Process-Post Automation



The future of diagnostic bacteriology

Productivity Increase



The Facts

- Productivity Frimley: 2.5 times higher
- Productivity Lister: 2.7 times higher
- Productivity Bioscientia: 2.5 times higher

Dr Ian Fry, Director of Pathology PPS Frimley Park:



"The efficiency of the system has been proven by far better management of samples both in terms of archiving and analysing. We had planned our staff reductions as we went through the procurement to full implementation and were successfully able to reduce our staff by 12 WT. This involved no compulsory redundancies as this was carefully planned part of our implementation. We did achieve what we set out to do in the Quick Scan. We were able to cope with 40% increase in workload and still make savings to the original staffing base. Much of this has been worked through using the Quick Scan approach"

Comparison of recovery rates of enteropathogens from stool cultures for a one-and two-year-period before and after introduction of automatic inoculation using Automation

Organism	N (%) of recovery at each half-year period								P value	
	With manual inoculation				With Previ Isola				1 yr pre	2 yr pre
	Aug 07-Jan 08 (n = 1,331)	Feb 08-Jul 08 (n = 1,238)	Aug 08-Jan 09 (n = 1,210)	Feb 09-Jul 09 (n = 1,361)	Aug 09-Jan 10 (n = 1,369)	Feb 10-Jul 10 (n = 1,487)	Aug 10-Jan 11 (n = 1,432)	Feb 11-Jul 11 (n = 1,596)	vs. 1 yr after	vs. 2 yr after
<i>Salmonella</i>	35 (2.6)	10 (0.8)	8 (0.7)	13 (1.0)	17 (1.2)	17 (1.1)	15 (1.0)	16 (1.0)	NS	NS
<i>Shigella</i>	0	3 (0.2)	1 (0.1)	1 (0.1)	3 (0.2)	0	0	2 (0.1)	NS	NS
<i>Yersinia</i>	2 (0.2)	0	1 (0.1)	0	0	0	2 (0.1)	0	NS	NS
<i>Campylobacter</i>	13 (1.0)	6 (0.5)	6 (0.5)	4 (0.3)	17 (1.2)	15 (1.0)	19 (1.3)	13 (0.8)	0.002	0.003
Total	50 (3.8)	19 (1.5)	16 (1.3)	18 (1.3)	37 (2.7)	32 (2.2)	36 (2.5)	31 (1.9)		

VALIDATION OF URINE SPECIMENS

- 92 urine specimens were processed on the WASPLab, images were captured at 0, 18, and 24 hours. Plate images were initially viewed on-screen after 18 h incubation.
 - Negative cultures were automatically unloaded, negative result confirmed and discarded
 - Positive cultures designated as “pathogens requiring further workup”, “fecal contaminated”, “pathogens <10,000 cfu/mL”, or “normal skin flora”.
 - The plates were extracted from the WASPLab incubator and sent to the specified canister, manually read, and compared to the on-screen image.
- 76 of the 92 cultures were designated as positive
 - 100% concordance between manual read and WASPLab interpretation for 16 negative cultures
 - Of the 76 positive cultures, 78% concordance between manual interpretation and WASPLab. 17 cultures (22%) where the on-screen image and manual plate reading interpretations did not match.
 - 13 were due to overcalling a potential *Enterococcus* species on-screen, when the colony was actually a normal skin flora
 - Corrected through technologist education
 - 4 were due to missing a pathogen in heavily mixed cultures on the manual read
- **Turnaround was reduced by ~18 hours**

Recovered Species

B Recovered species correlation

WASP 1 μ l Manual	0	1	2	3	4	≥ 5
0	55	8	4			
1	1	33	6			
2		5	6			
3		1	1	1		
4						
≥ 5						

WASP 10 μ l Manual	0	1	2	3	4	≥ 5
0	161	35	5			
1	8	91	24	1		
2	4	9	30		1	
3		1	3	5		
4						
≥ 5				1		

Alphabet, DeepMind and AI

“Fears about computers run amok are the stuff of movies, I worry about inequality but there’s no evidence the stuff we do creates a permanent underclass. However, for many tasks it seems humans are just not very good”

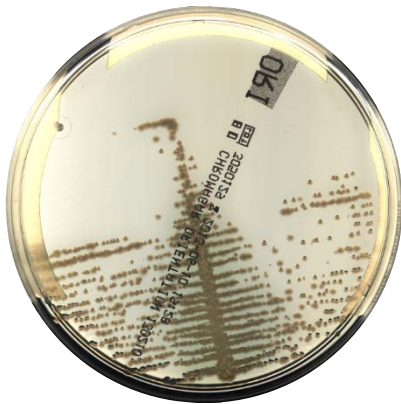


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How can we use these images for automation

- Software analysis - Image differentials

Time = 24
hours



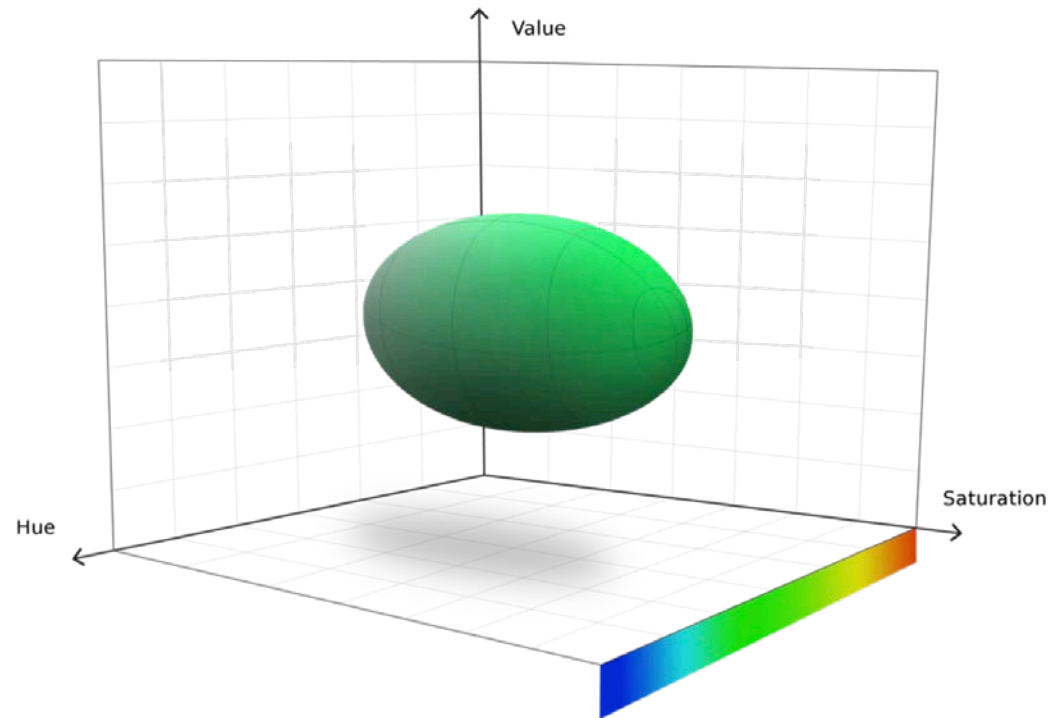
Time = 0
hours



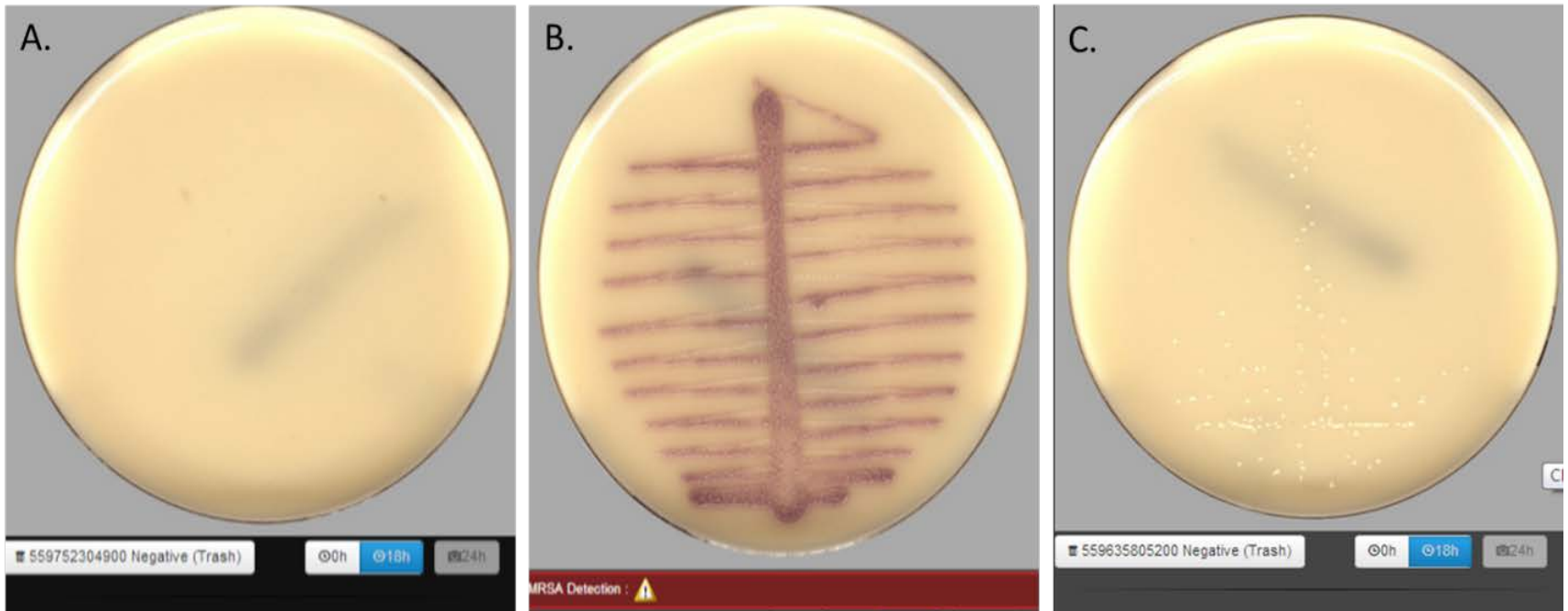
Differential



The Algorithm



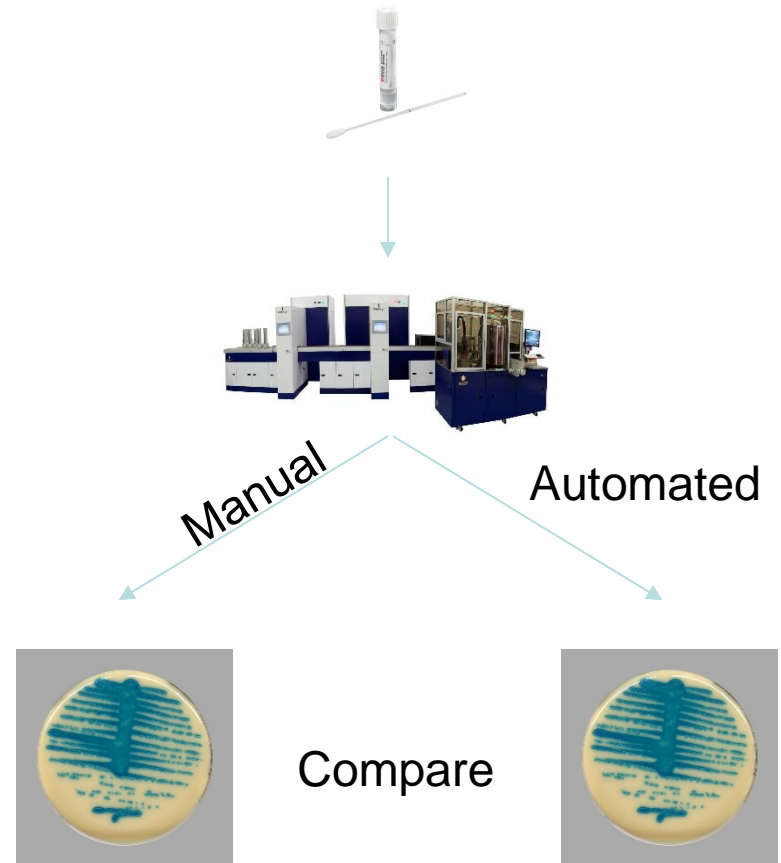
How it Works



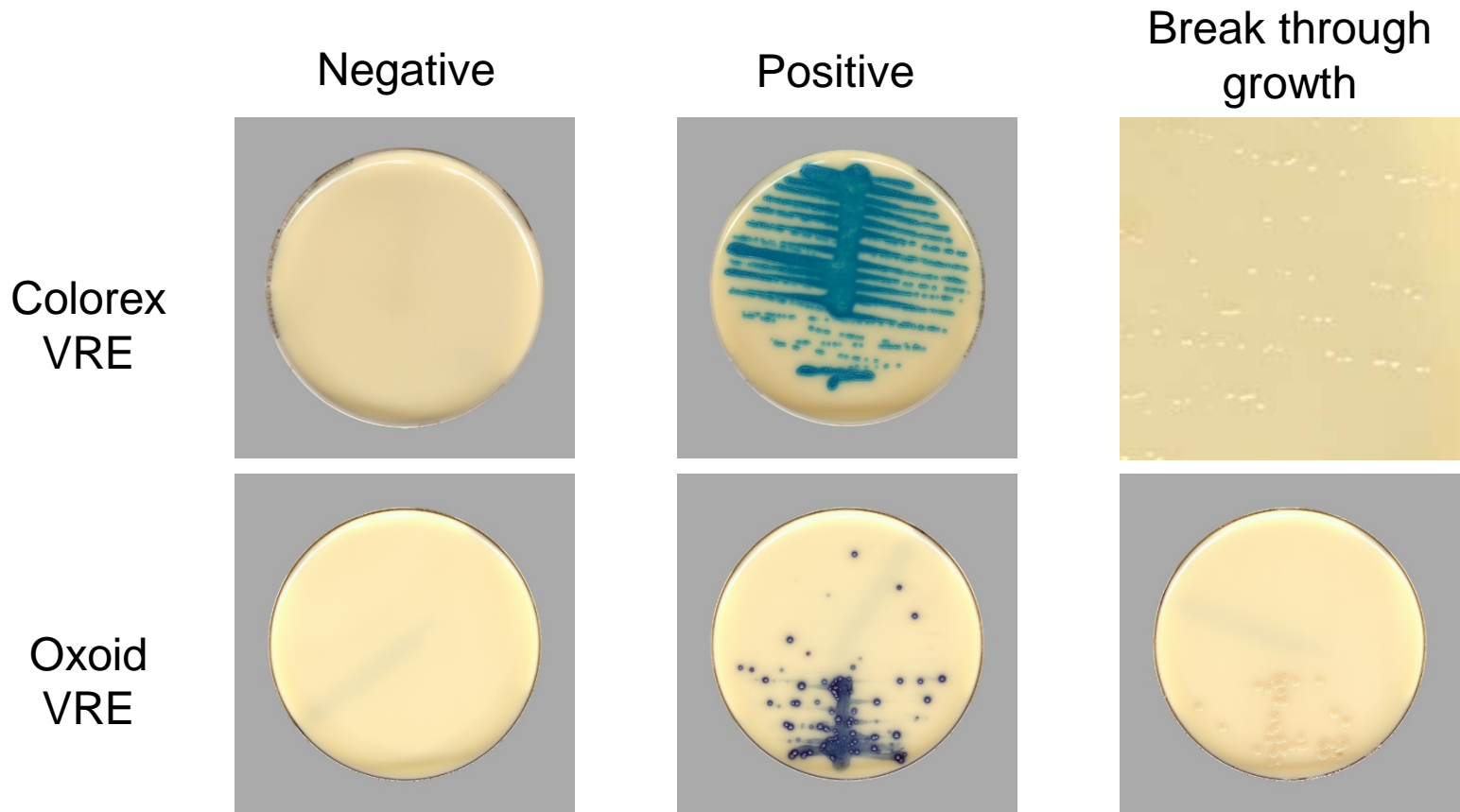
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Can we use this software for VRE screening?

- 3 sites
- Specimens (n=104,730)
 - Rectal Eswabs™
- Media (n=2)
 - Colorex VRE (BioMed Diagnostics)
 - Oxoid VRE (Thermo Fisher Scientific)
- Reference method
 - Manual reading
- Discrepant analysis
 - Images reviewed by supervisor



Representative Images



Results

Performance of WASPLab™ digital imaging of VRE plates compared to manual reading

Clinical test site	No. of specimens tested	Results (no.) ^a				Performance (% [95% CI]) ^b		PPV ^c (%)	NPV ^c (%)	Prevalence
		MP/AP	MN/AN	MN/AP	MP/AN	Sensitivity	Specificity			
1	11,438	1,474	9,129	835	0	100 (99-100)	91.6 (91-92)	64	100	12.9%
2	75,518	2,822	64,535	8,161	0	100 (99-100)	88.8 (88-89)	26	100	3.7%
3	17,774	2,107	14,315	1,352	0	100 (99-100)	91.4 (91-92)	61	100	11.8%
Total	104,730	6,403	87,979	10,348	0	100 (99-100)	89.5 (89-90)	38	100	6.1%

^aMP/AP, manual Pos automation Pos; MN/AN, manual Neg/automation Neg; MN/AP, manual Neg/automation pos; MP/AN, manual Pos/automation Neg.

^b CI, confidence interval.

^cPPV, Positive Predictive Value; NPV. Negative Predictive Value

Discrepant analysis

Discrepant analysis of Manual Negative/Automation Positive Plates

Discrepant Category	MN/AP ^a	Automation Positive 2 nd Manual Positive	Residual Matrix/Yeast	Borderline Colors
Total number of plates	10,348	499	8,234	1,616
Colorex VRE	8996	432	7684	881
Oxiod VRE	1352	67	550	735

^a Manual Negative/Automation Positive

Comparison of agars

Comparison of 2 Chromogenic Agars for the detection of VRE using automated scoring							
Chromogenic media	No. of specimens tested	Results (no.) ^a				Performance (% [95% CI]) ^b	
		MP/AP	MN/AN	MN/AP	MP/AN	Sensitivity	Specificity
Colorex VRE	86,956	4,296	73,664	8,996	0	100 (99-100)	89.1 (89-89)
Oxoid VRE	17,774	2,107	14,315	1,352	0	100 (99-100)	91.4 (91-92)

^aMP/AP, manual Pos/automation Pos; MN/AN, manual Neg/automation Neg; MN/AP, manual Neg/automation Pos; MP/AN, manual Pos/automation Neg.
^b CI, confidence interval.
^cPPV, Positive Predictive Value; NPV. Negative Predictive Value

Technologist Labor is
\$40.00/hour
(w/benefits)

Manual Processing

9.6 min/negative
specimen^a

\$6.40 in
labor/negative
specimen

\$563,065.60 in labor

Automated Processing

~2 min/negative
specimen

\$1.33 in
labor/negative
specimen

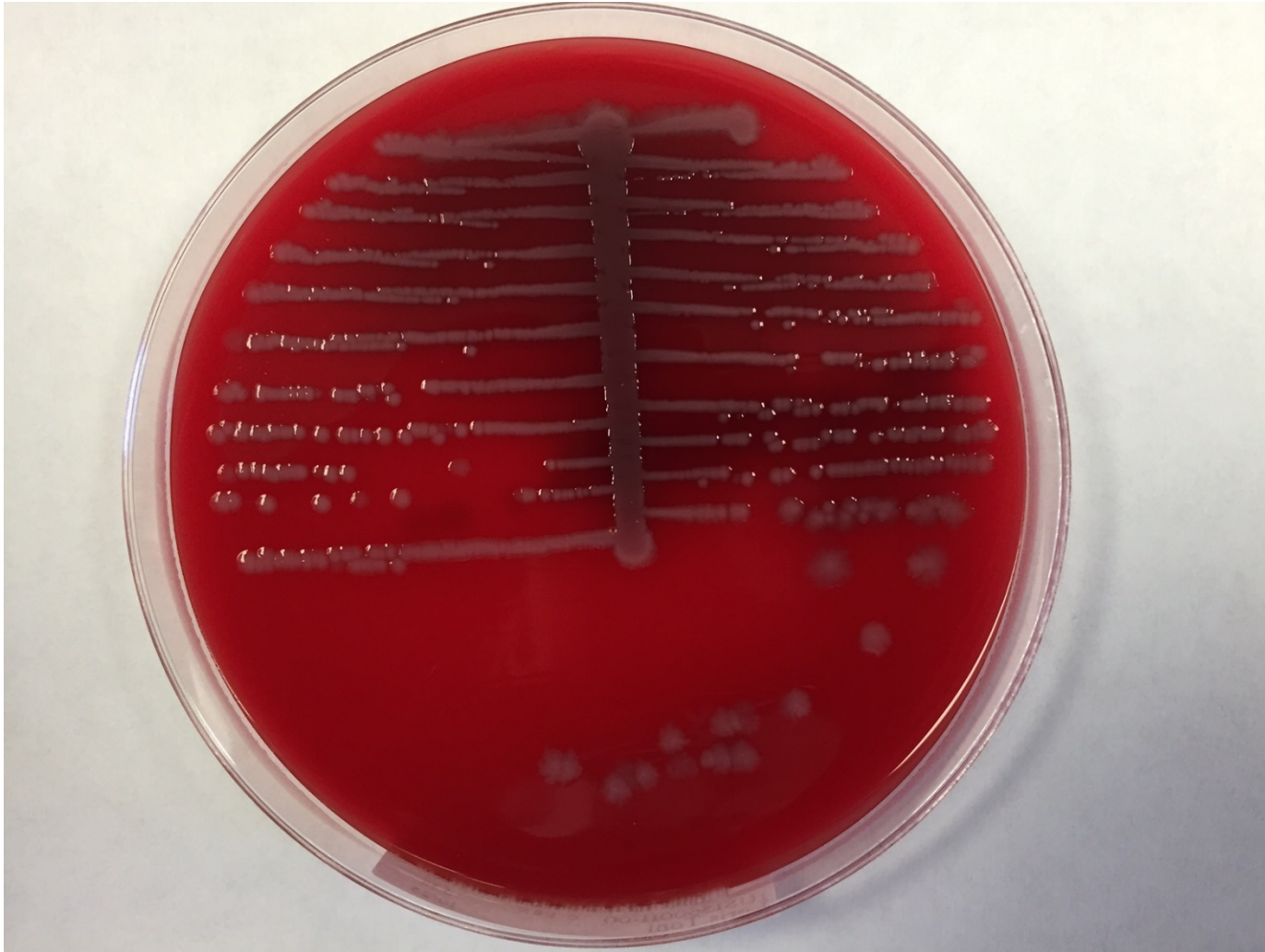
\$117,305.33 in labor

Cost of negative workup for
the study (n = 87,979)

Savings = \$445,760.27

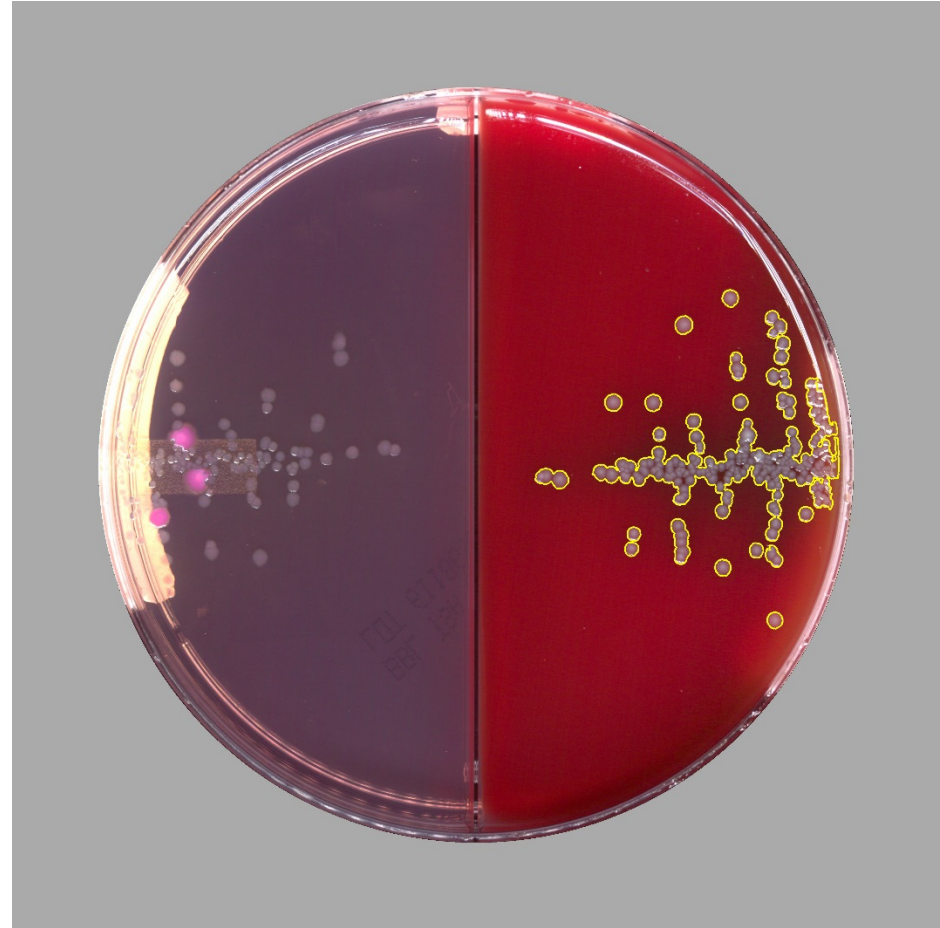
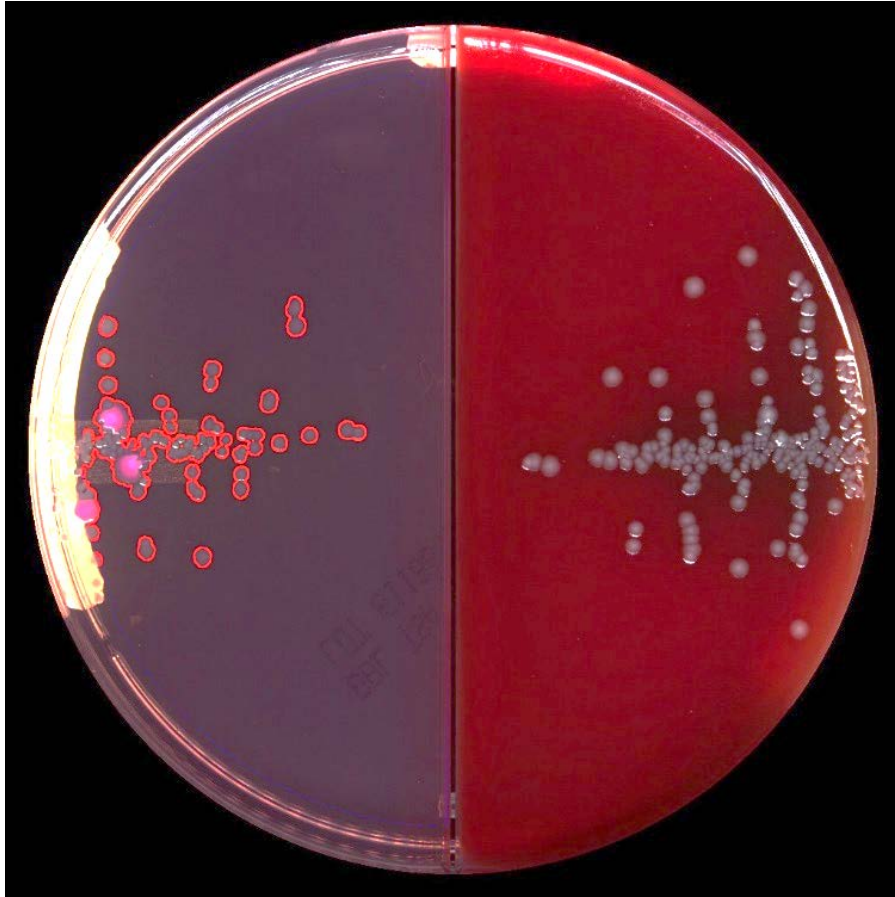
^a. Shadel *et al.* Surveillance for vancomycin-resistant enterococci: type, rates, costs, and implications.

Can it Quantitate?



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Yes, IT CAN!!



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Can we quantitate colonies?

- The Chromogenic Detection Module looks for color changes at a pixel level, but can we train the software to differentiate colonies?
- Similar methodology differential analysis
- Recognition of patterns

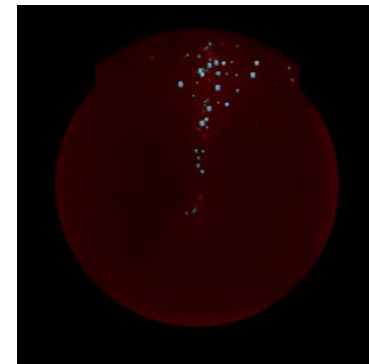
Time = 24
hours



Time = 0
hours

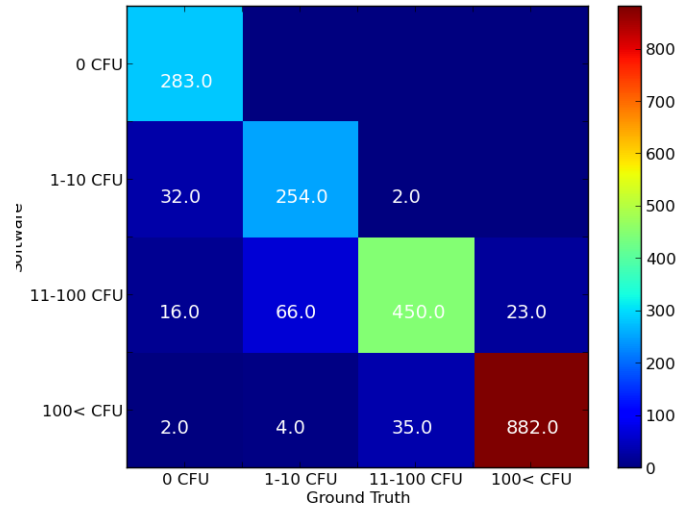
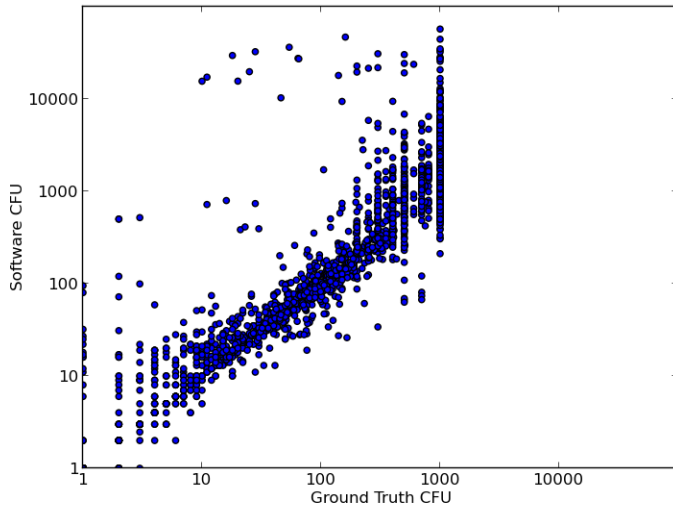


Differential



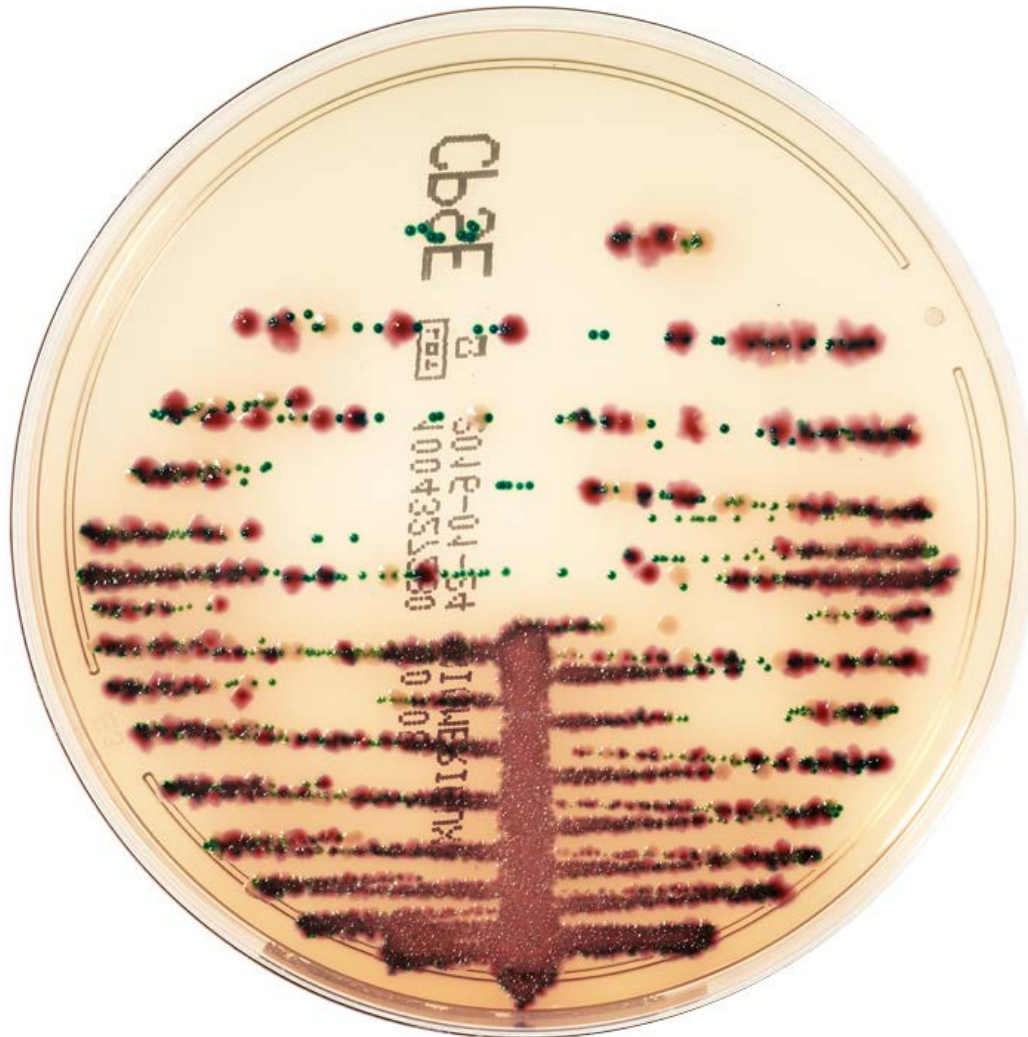
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Scatter plot/Heat map of Manual VS. Automated Quantification



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Can Computers Quantitate and Identify Organisms?



We Practice What We Teach

Performance of the WASPLab digital imaging of CPSe plates compared to manual reading

		Manual result	
		Negative	Positive
Software result	Negative	2906	40
	Positive	654	1651

Positive Percent Agreement = 97.6%
Negative Percent Agreement = 81.6%

Breakdown of results based on software colony count

Count Software	Negative (manual)	Contaminated (>3 colony types)	Positive (manual)
0	1514	0	0
1-10	1431	1	40
11-100	459	41	429
>100	23	131	1222
Total	3387	173	1691

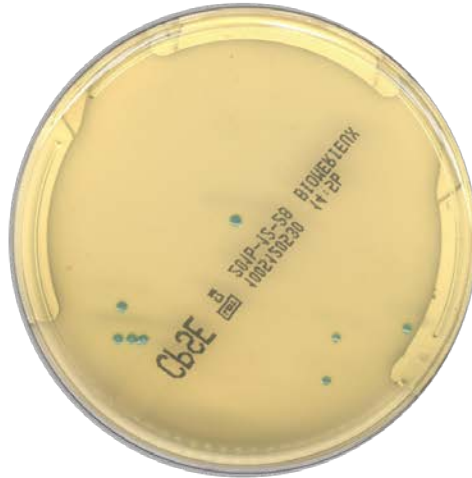
Re-evaluation of discrepant results

		Manual result	
		Negative	Positive
Software result	Negative	2946	0
	Positive	654	1651

Positive Percent Agreement = 100%
Negative Percent Agreement = 81.6%

Image examples of discrepant specimens

Manual Positive, Automation Negative



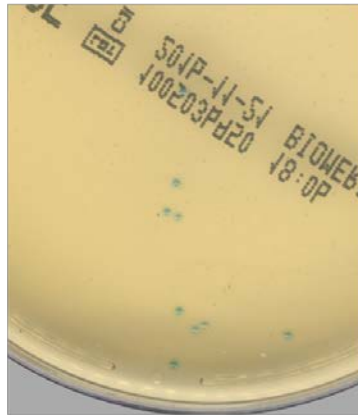
9 colonies



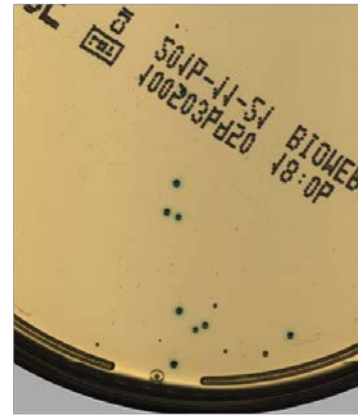
8 colonies

Image examples of discrepant specimens

Manual Negative,
Automation Positive



White light

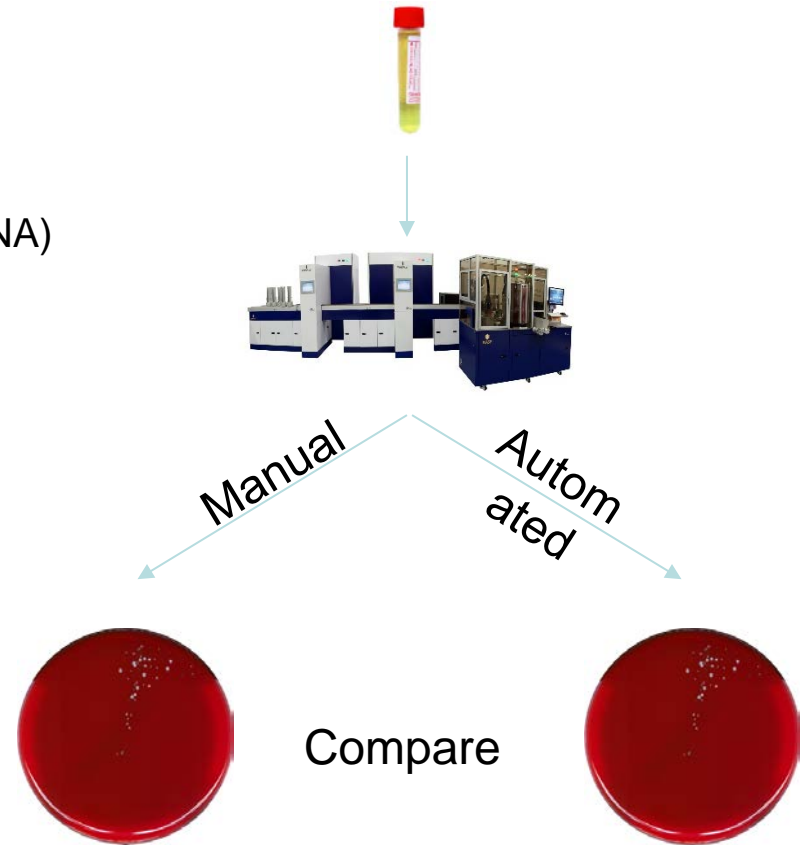


Backlight

8 colonies white light 13 colonies backlight

Can we use this software to Analyze Urine Using Non-Chromogenic Plates?

- 3 sites
- Specimens (n=13,465)
 - Urines (Plated Blood, MacConkey, CNA)
- Algorithm results
 - POS >10 colonies on any plate
 - Neg \leq 10 colonies in all 3 agars
- Reference method
 - Manual reading
 - Site specific procedures for results
- Discrepant analysis
 - Images reviewed by supervisor



How well does it work?

Performance of WASPLab™ digital imaging software compared to manual reading of BAP, MAC and CNA

	No. of specimens tested	Results (no.) ^a				Performance (% [95% CI]) ^b	
		MP/AP	MN/AN	MN/AP	MP/AN	PPA ^c	NPA ^c
Site 1	5201	2960	1101	1099	41	98.6 (98-99)	50.0 (48-52)
Site 2	5513	1620	3392	500	1	99.9 (99-99)	87.2 (86-88)
Site 3	2751	1108	1184	393	66	94.4 (93-96)	75.1 (73-77)
Total	13465	5688	5677	1992	108	98.1 (97-98)	74.0 (73-75)

^aMP/AP, manual Pos automation Pos; MN/AN, manual Neg/automation Neg; MN/AP, manual Neg/automation pos; MP/AN, manual pos/automation Neg.

^b CI, confidence interval.

^cPPA, Positive Percent Agreement; NPA, Negative Percent Agreement



We Practice What We Teach

Urines are not all 1s and 0s

Consideration of manual negatives based on rules for interpretation MCW

Automation	Manual			
	No Growth	NFW ^a	NSG ^b	Positive
Negative	728	70	303	41
Positive	88	355	656	2960
Total				5201

^a No Further Workup: contains > 3 pathogens on the plate

^b No Significant Growth: Consistent with normal skin and urethra flora

Rules ~ 92% of all MN/AP specimens

- LAB results:

- POS: Positive ≥ 10 CFU, Catheter any growth, Urinary clinic any growth
- NG: No Growth
- NSG: No Significant Growth - ≥ 10 CFU but consistent with Normal skin flora
- NFW: No Further Workup - ≥ 10 CFU, but >3 pathogens (fecal contamination)

} NEG



Summary of 41 manual positive, automation negative specimens with lab report

- 6 specimen lab report negative
- 15 specimens (growth) were from catheters <10 cfu
- 5 specimens >10 colonies called at 48 hours
 - 4 GPR
 - 1 *S. anginosus*
- 12 from Urinary Clinic – policy similar to catheters
- 1 unspecified specimen from 16th street clinic (1 of many out patient facilities)
 - Policy states minimum ID on pathogens less than 100,000 CFU/mL
- 1 Pregnant patient
 - Growing GBS - reportable
- Only 1 image at 24 hours had >10 colonies after second review (non-lab report)

Evaluation of the 41 manual positive, automation negative specimens by source at MCW

Void	Catheter	Unspecified
12 ^{a,b}	17 ^{c,d,e}	12 ^{b,f}

^a 3 specimens were negative for growth by laboratory report

^b 2 specimens were positive after 48 hours

^c 1 specimen was negative for growth by laboratory report

^d 1 specimen was positive after 48 hours

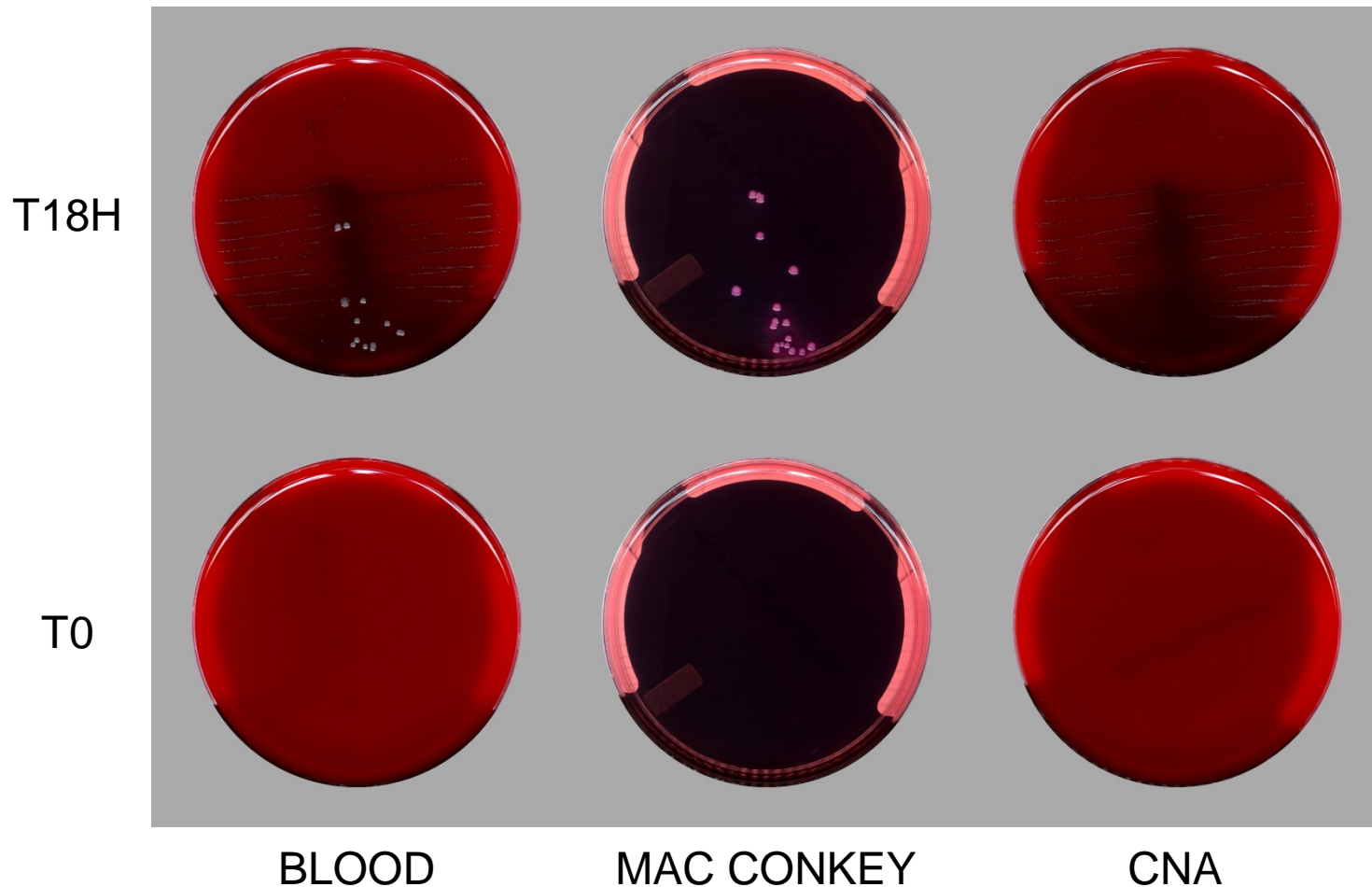
^e Policy states min ID for any growth from Catheter

^f 2 specimen was negative for growth by laboratory report



False Positive Example

SW POS, human NSG



Overall Performance based on colony count alone (>10 CFU) and re-evaluation of MP/AN specimens

Automation	Manual	
	Negative	Positive
Negative	5782	3
Positive	214	7466
Total	13465	
Positive Percent Agreement = 99.96%		
Negative Percent Agreement = 96.43%		

Is AI a Threat or a Friend?



“I think the development of full artificial intelligence could spell the end of the human race”

“AI is our biggest existential threat”



We Practice What We Teach

Is AI a Threat or a Friend?



“Fueled by science-fiction novels and movies, popular treatment of this topic far too often has created a false sense of conflict between humans and machines. “Intelligent machines” tend to be great at tasks that humans are not so good at, such as sifting through vast data. Conversely, machines are pretty bad at things that humans are excellent at, such as common-sense reasoning, asking brilliant questions and thinking out of the box. The combination of human and machine, which we consider the foundation of cognitive computing, is truly revolutionizing how we solve complex problems in every field.” Guruduth S. Banavar, IBM Watson