Everything You Need to Consider When Considering Automation of Microbiology

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WHY WE AUTOMATE

Trends to Automation?

- The Industry is Changing
  - Specimens increasing on average 10-15% per year
  - Laboratory consolidation
  - Reimbursement
- Workforce
  - Less students choose Medical Technology: reduction of 30-50%
  - Pay for technologists is substandard
- Quality
  - Physicians are demanding more services, in less time
  - Traceability

Manual Processing

- Microbiology too complex to automate
  - Specimen Diversity
  - Collection Device Diversity
  - Diversity of Techniques
  - Diversity of Media
- The human element
  - Technologists are faster than machines
  - Humans are capable of thinking, machines are not
  - Humans are flexible
- Automation considered too Expensive
- Small volumes
  - Only the large labs can automate
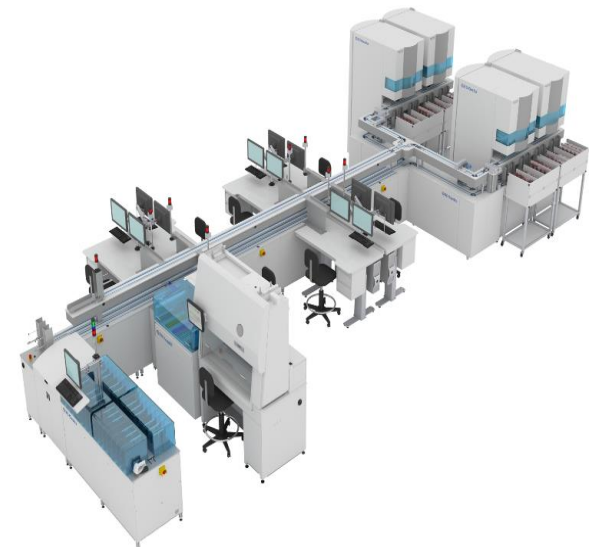
And Don't Forget:
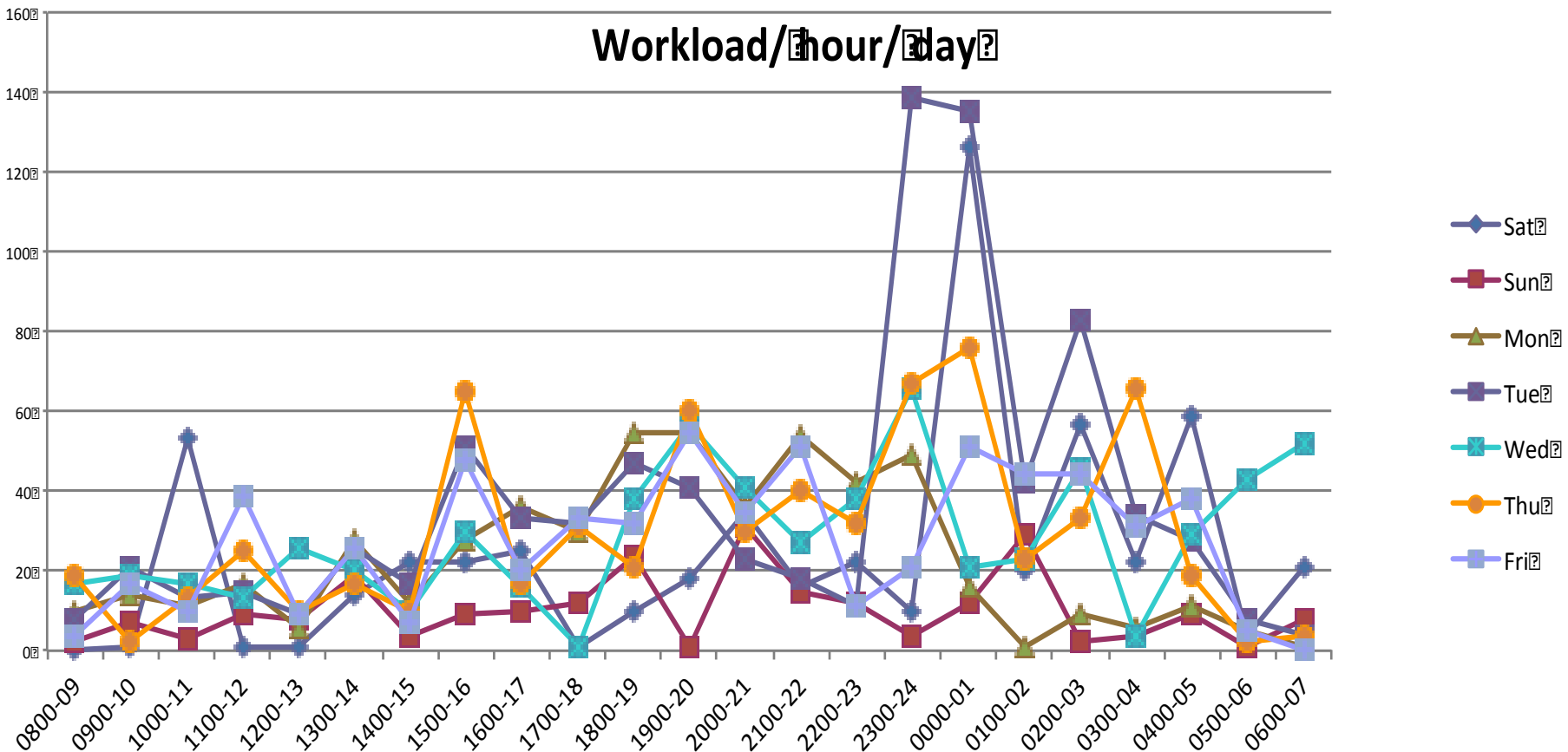
Laboratory Automation Systems

- Specimen inoculation/processing unit
- Incubation system
- High-resolution digital imaging system
- +/- track system for moving plates
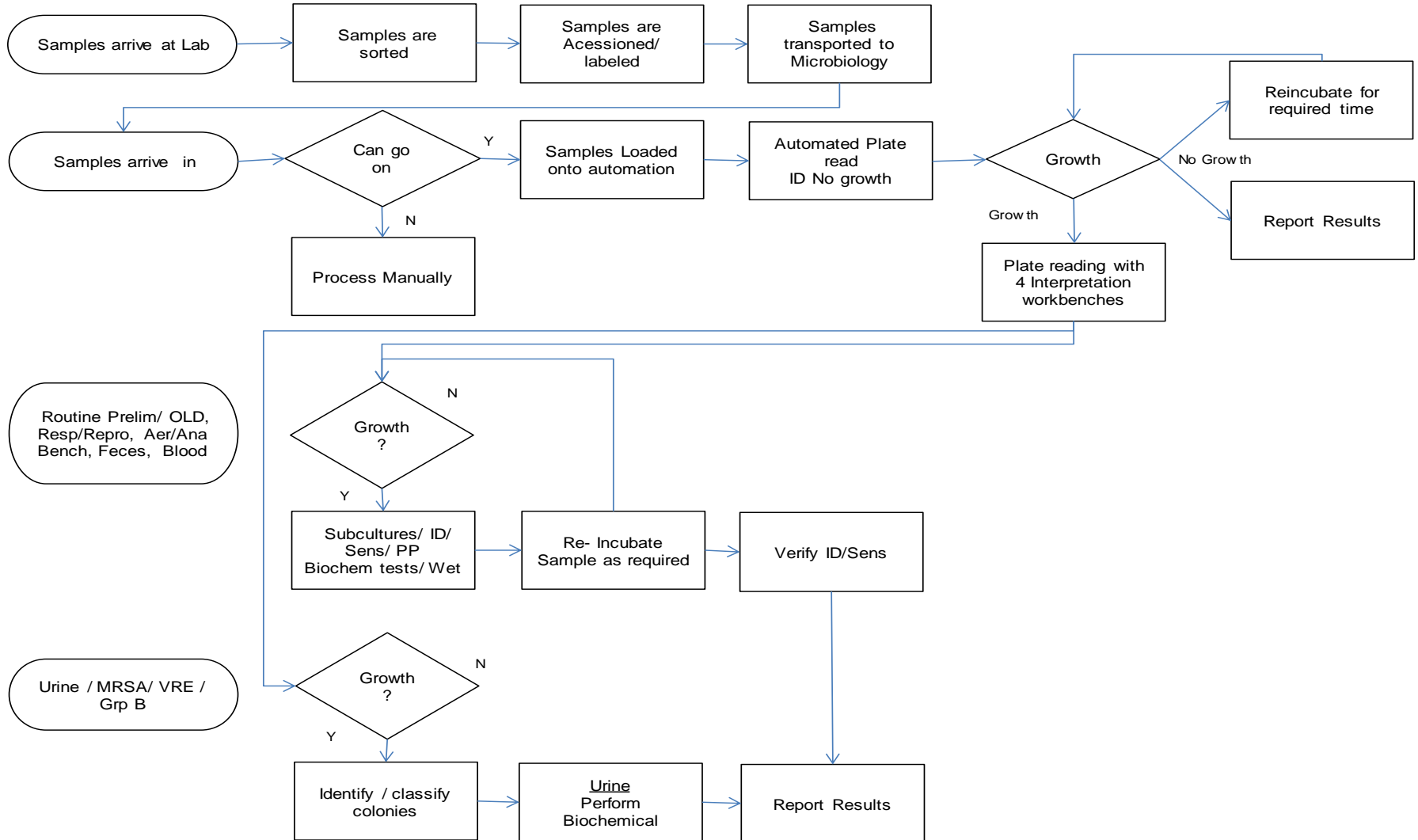- Workstations

Available Models:

- WASPLab
- BD Kiestra™ TLA

Hourly Workload

Workload/ hour/ day

Laboratory Process - Post Automation

Impact on productivity

Productivity Index = #samples / #FTEs worked

Productivity for hours worked	# FTE/d	Productivity Index
Current FTE	22	23.0
Future FTE	15	34.8

Productivity - Increased by 51%

A Traditional Workflow Problem: "Time Out"

How significant of a problem is this?

We followed >200 blood cultures to find out…

Take All Plates Out in AM…

AM ——————————————————→ PM

Time spent at inappropriate temperature and atmosphere

Return All Plates in PM…

Slide Courtesy of Neil Anderson, MD

Results: Time Out

	Day 1 n=232	Day 2 n=232	Day 3 n=147	Day 4 n=35
Plate age (range)	1h51min-25h37min	26h29m-50h2m	51h5min-75h17min	78h22m-96h50m
Cumulative time outside incubator (average)	26m	2h9m	5h48m	9h58m
Cumulative time outside incubator (range)	2m-2h1m	52m-7h20m	3h3m-11h57m	6h22m-18h27m

Plates as young as 26 hours may have spent as much as 7 hours outside of the incubator

Slide Courtesy of Neil Anderson, MD

Recovery of Multiple Organisms Enhance

TABLE 2 Differences and percentages of change in the recovery of uropathogens reported in urine cultures pre- and post-TLA[a]

Organism	No. of times organism reported per 1,000 urine cultures		% change	P value
	Pre-TLA	Post-TLA		
Escherichia coli	79.4	101.2	+27	<0.0001
Klebsiella spp.	22.9	24.0	+5	0.24
Streptococcus agalactiae	22.2	36.7	+66	<0.0001
Aerococcus urinae	2.2	4.4	+103	<0.0001
Staphylococcus saprophyticus	1.0	2.3	+126	<0.0001
Neisseria gonorrhoeae	0.2	1.0	+371	<0.0001
Actinotignum schaalii	0.1	0.13	+33	0.77
Streptococcus pneumoniae	0.02	0.1	+312	0.27
Alloscardovia omnicolens	0.0	0.06	NA	0.30

[a]TLA, total laboratory automation; NA, not applicable.

LainhartW,BurnhamC-AD.2018. Enhanced recovery of fastidious organisms from urine culture in the setting of total laboratory automation.JClinMicrobiol56:e00546-18. https://doi.org/10.1128/JCM.00546-18.

How can we use these images for automation

- Software analysis - Image differentials
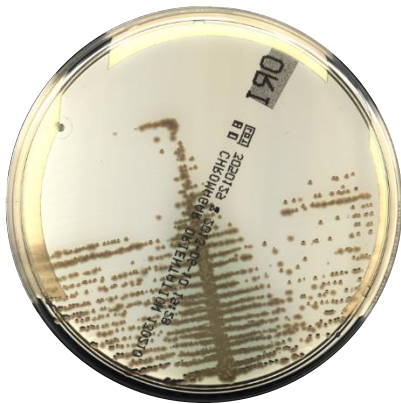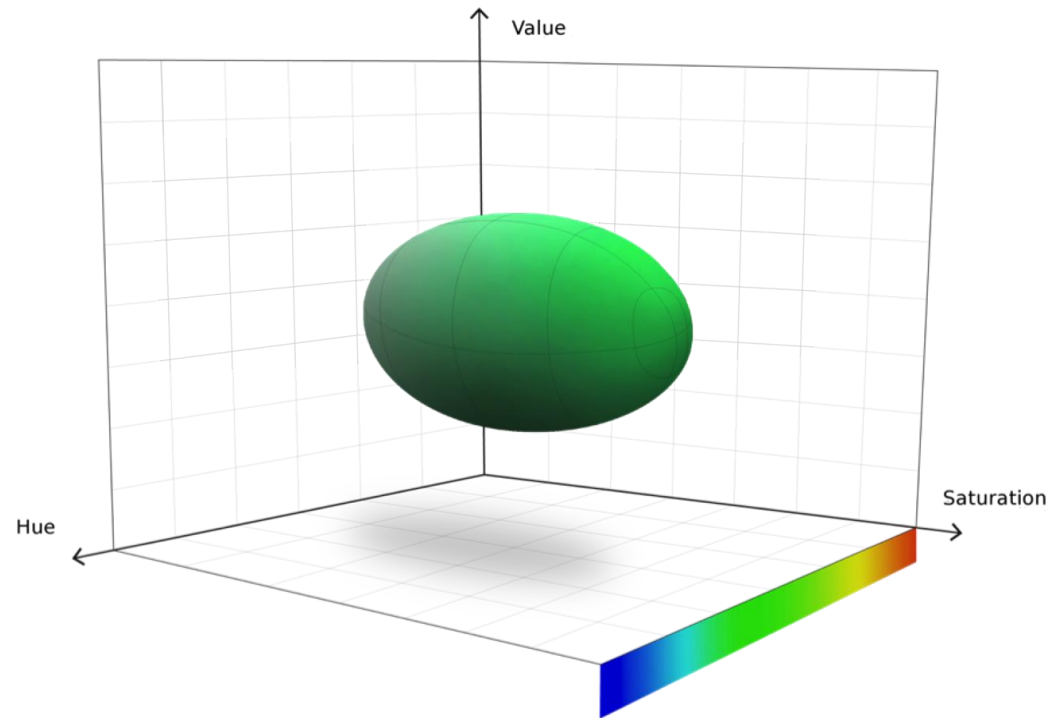

Time = 24 hours — Time = 0 hours = Differential

The Algorithm

Applying Algorithms to GAS

- Evaluated 250 throat swabs submitted from single center

- Specimens tested by: PCR, BAP, Colorex Strep A

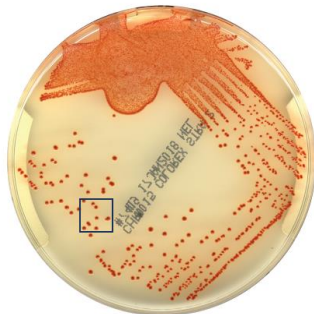- Compared results of manual read to automated read; compared BAP to chromogenic agar

Table 1. Manual examination of Colorex Strep A Agar after 24 hours incubation with secondary manual review

		Orange Colony	
		Pos	Neg
CHROMagar at 24 hours (visual)	Pos	55	0
	Neg	2	193
		Sensitivity: 55/55+2 = **96.5%**	Specificity: 193/193+0 = **100.0%**

PPV = 55/55 + 0 = 100% ; NPV = 193/193+2 = 98.9%

Table 2. WASPLab examination of Colorex Strep A agar after 24 hours incubation using CDM software with secondary manual review

		Orange Colony	
		Pos	Neg
CHROMagar at 24 hours (CDM algorithm)	Pos	57	7
	Neg	0	186
		Sensitivity: 57/57 + 0 = **100%**	Specificity: 186/186 + 7 = **96.4%**

PPV = 57/57 + 7 = 89.1%: NPV = 186/186 + 0 = 100%

Table 3. Comparison of manual examination of BAP versus Colorex Strep A Agar (with secondary manual review)

		Orange Colony	
		Pos	Neg
Beta Hemolysis Present on BAP	Pos	45	51
	Neg	12	142
		Sensitivity: 45/45 +12 = **78.9%**	Specificity: 142/142 + 51 = **73.6%**

Dien Bard J, *et al.* ECCMID 2018.

What about GBS?

- 254 vaginal/rectal swabs
- All swabs were initially incubated in LIM for 18-24h at 35-37 degrees C
- Compared ChromID GBS to Carrot Broth
  - Equivalent performance
- Compared WASPLab segregartion software to CLS read
- Have subsequently increase n to >4000 specimens enrolled
- Multi-Center Study comparing with CDC method and PCR currently enrolling

		SSW	
		Negative	Positive
Visual Exam.	Negative	124	32
	Positive	0	89

Pham and VanHorn, ASM Abstract. 2018

Incorporating into the laboratory

- Negative Specimens
  - Batch viewing 40 images/page
  - Batch report
- Non-negative Specimens
  - Still requires Technologist
  - View on HD monitor
    - Positive vs Matrix or Yeast
  - Standard of care
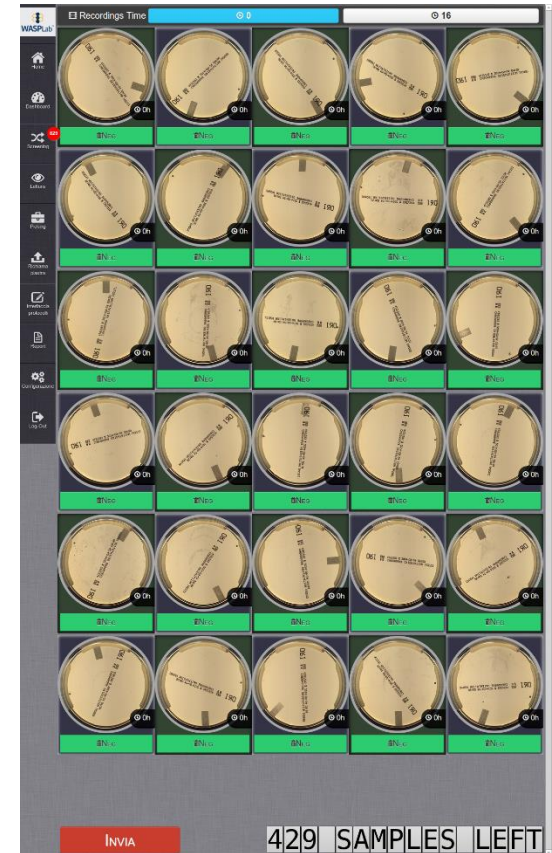
Technologist Labor is
$40.00/hour
(w/benefits)

Manual Processing

Automated Processing

9.6 min/negative
specimen[a]

~2 min/negative
specimen

$6.40 in
labor/negative
specimen

$1.33 in
labor/negative
specimen

Cost of negative workup for
the study (n = 87,979)
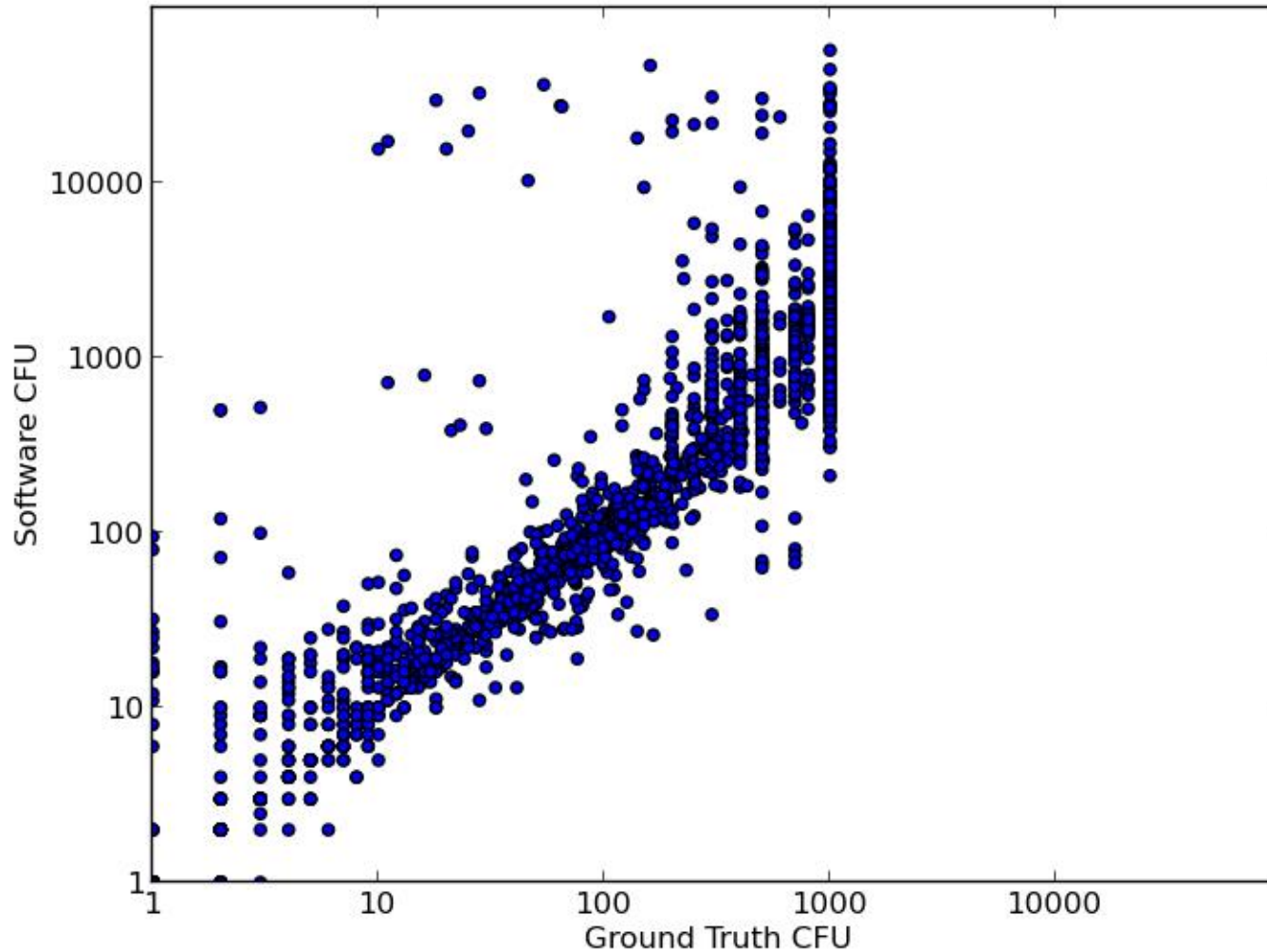
$563,065.60 in labor

$117,305.33 in labor

Savings = $445,760.27

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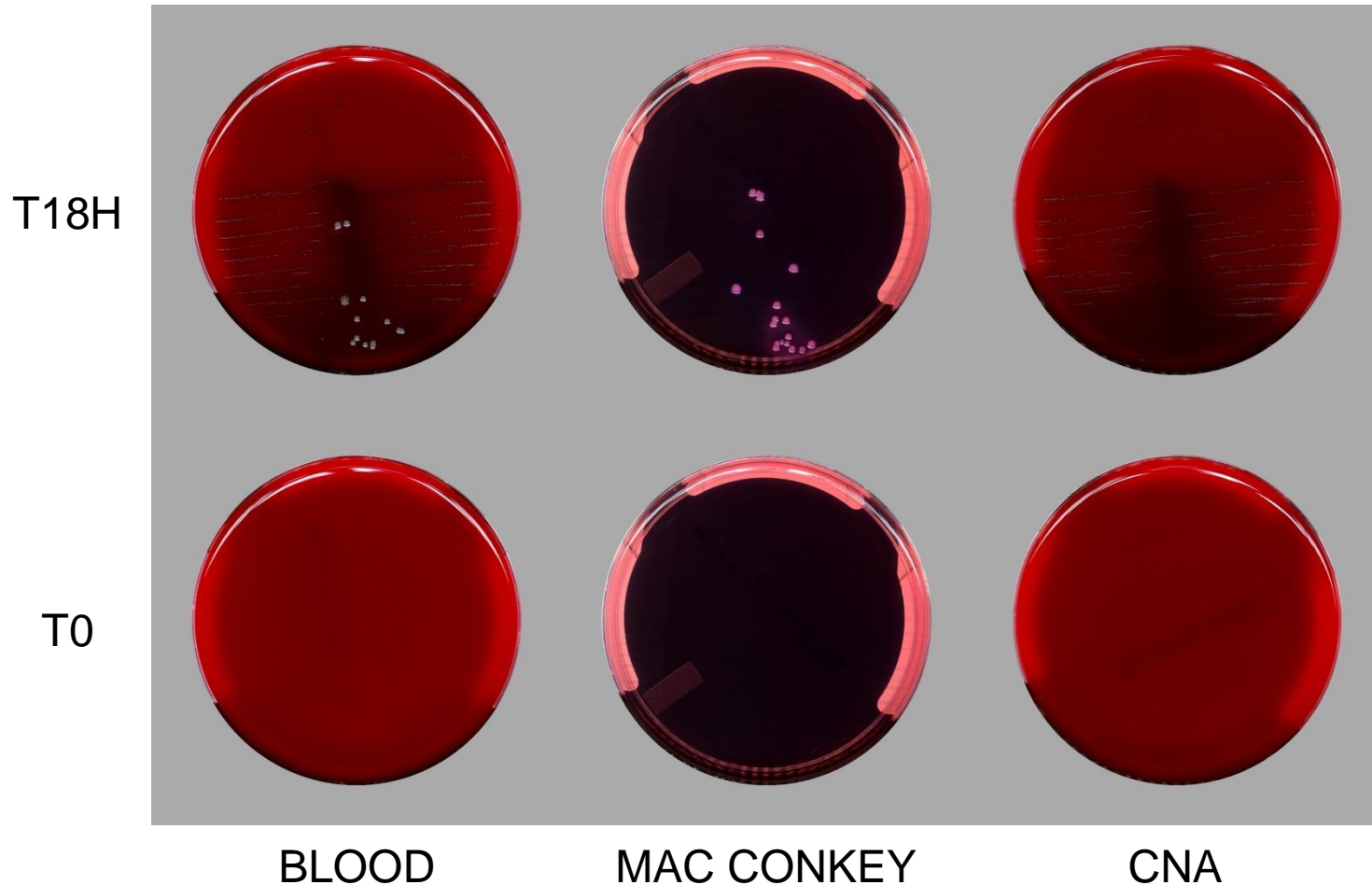implications.

Can it Quantitate?
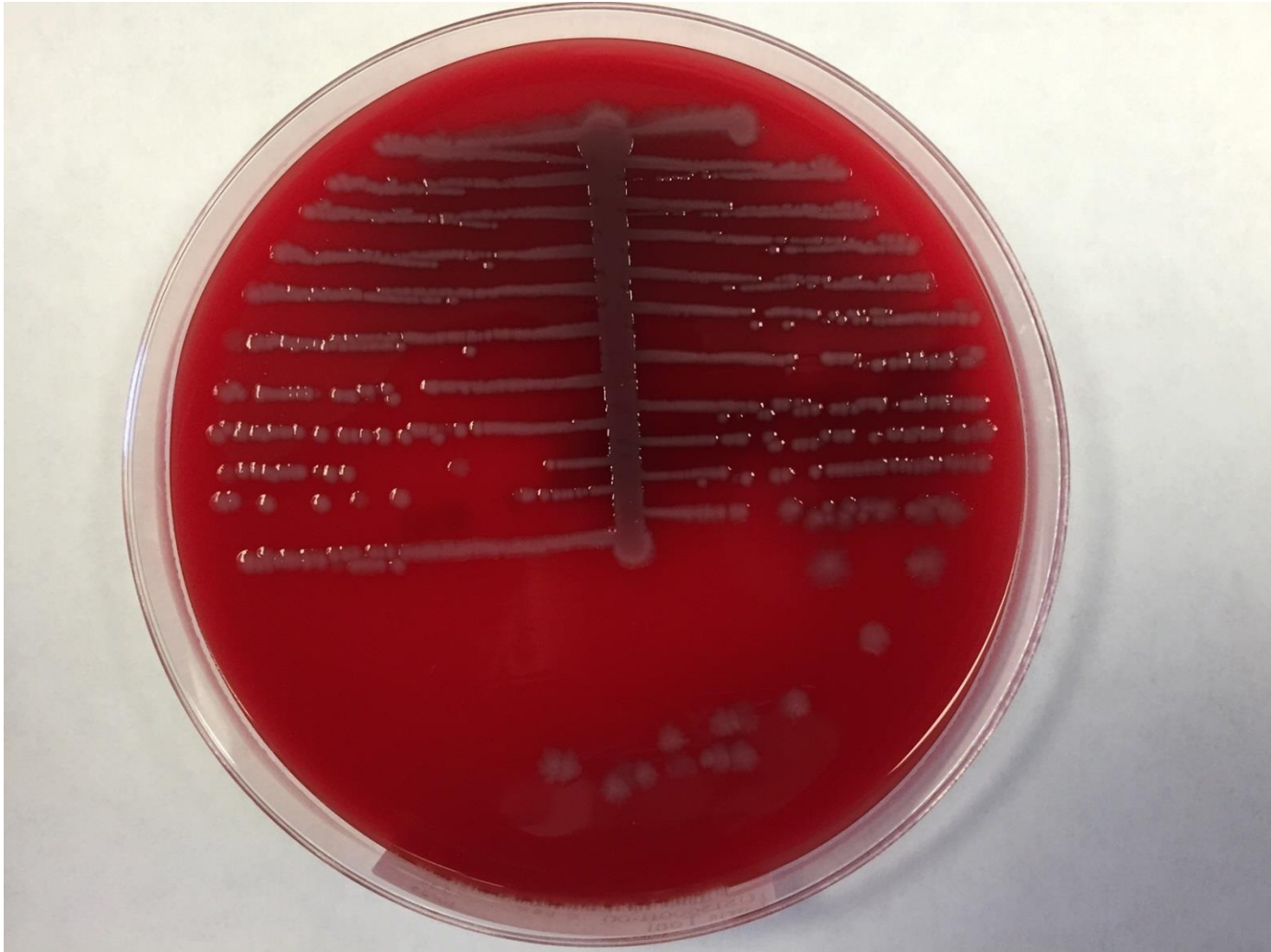
Blood Plate Reading

False Positive Example
SW POS, human NSG

T18H

T0

BLOOD   MAC CONKEY   CNA

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 ≤ 10 colonies in all 3 agars
- Reference method
  - Manual reading
  - Site specific procedures for results
- Discrepant analysis
  - Images reviewed by supervisor

Manual

Automated
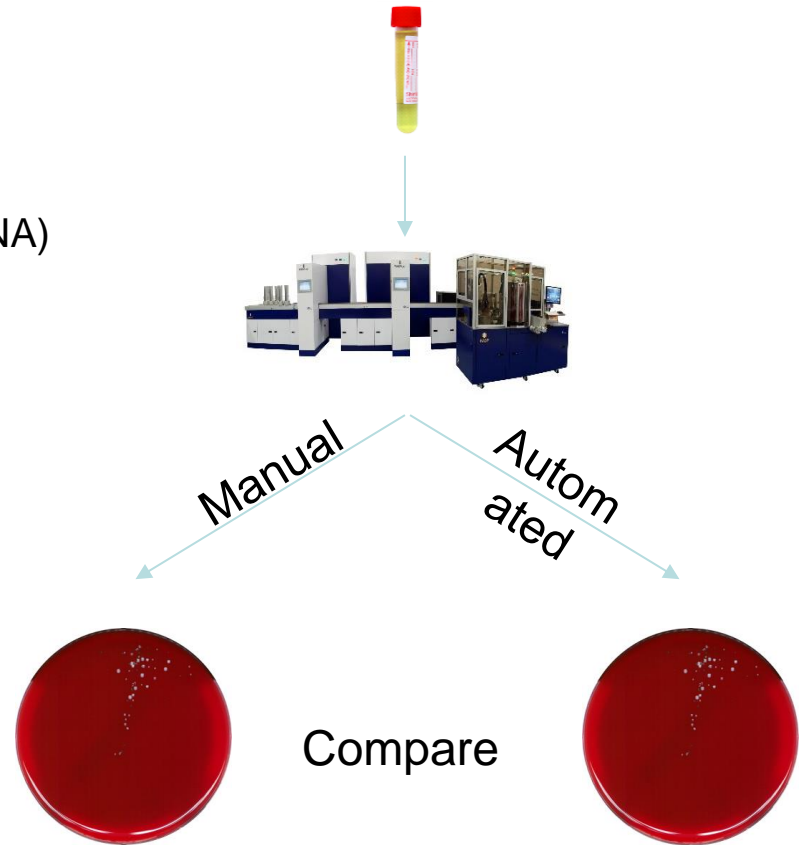
Compare

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)

[a]MP/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.
[c]PPA, Positive Percent Agreement; NPA, Negative Percent Agreement

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 } NEG
  - NFW: No Further Workup - ≥ 10 CFU, but >3 pathogens (fecal contamination)

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

Can AI Identify Organisms, Based on Morphology

Organism Classifications	n	Correct Classification	Percent	Unclassified	Percent	Misclassified	Percent	Correct Gram Classification	Percent
Staphylococcus species	28	24	86%	4	14%	0	0%	28	100%
Candida species	17	16	94%	0	0%	1	6%	17	100%
Streptococcus species	37	24	65%	5	14%	8	22%	37	100%
Enterobacteriacae	69	62	90%	6	9%	1	1%	69	100%
Pseudomonas aeruginosa	10	7	70%	3	30%	0	0%	10	100%
Enterococcus species	20	20	100%	0	0%	0	0%	20	100%

Timm and Culbreath, ECCMID 2017
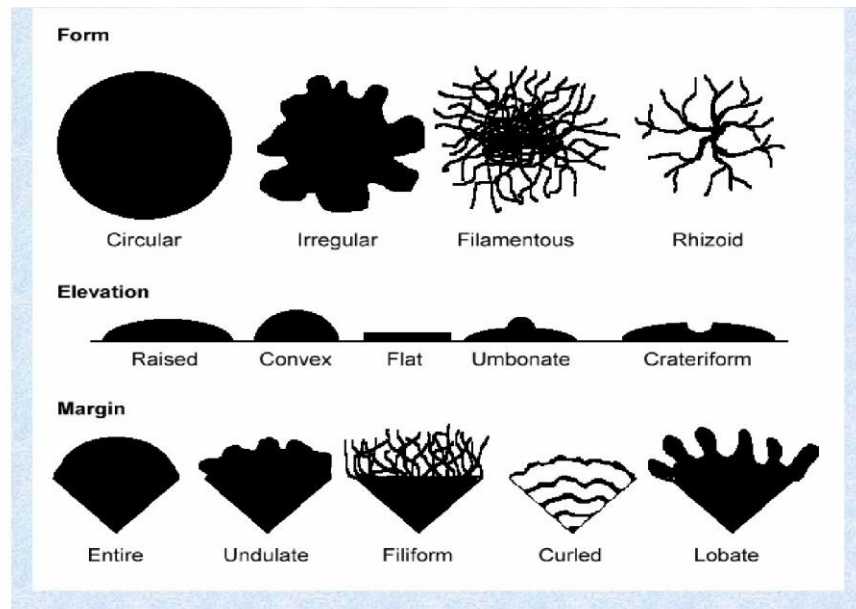
Summary, Where is the Field and Where are We Going?