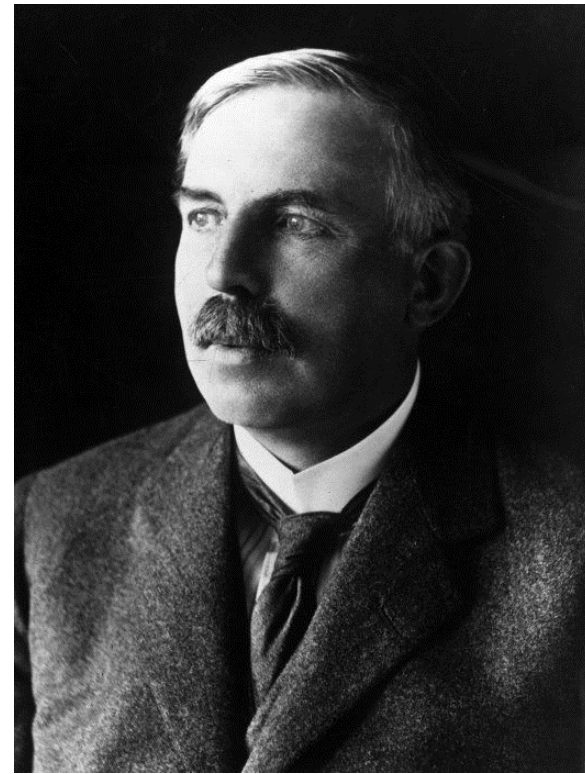# Orbital Diagnostics:
Rapid antibiotic sensitivity determination

Dr Robert J H Hammond

Lord Rutherford

"You can plan research….

…you cannot plan discovery"

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The reality of clinical bacteriology diagnostics

```
Is there and infection?  →  No!  →  No antibiotic
Is there and infection?  →  Yes  →  e.g., Virus  →  No antibiotic
                                Yes  →  Bacterium  →  Susceptibility?
```

0 hr   24 hr   48 hr

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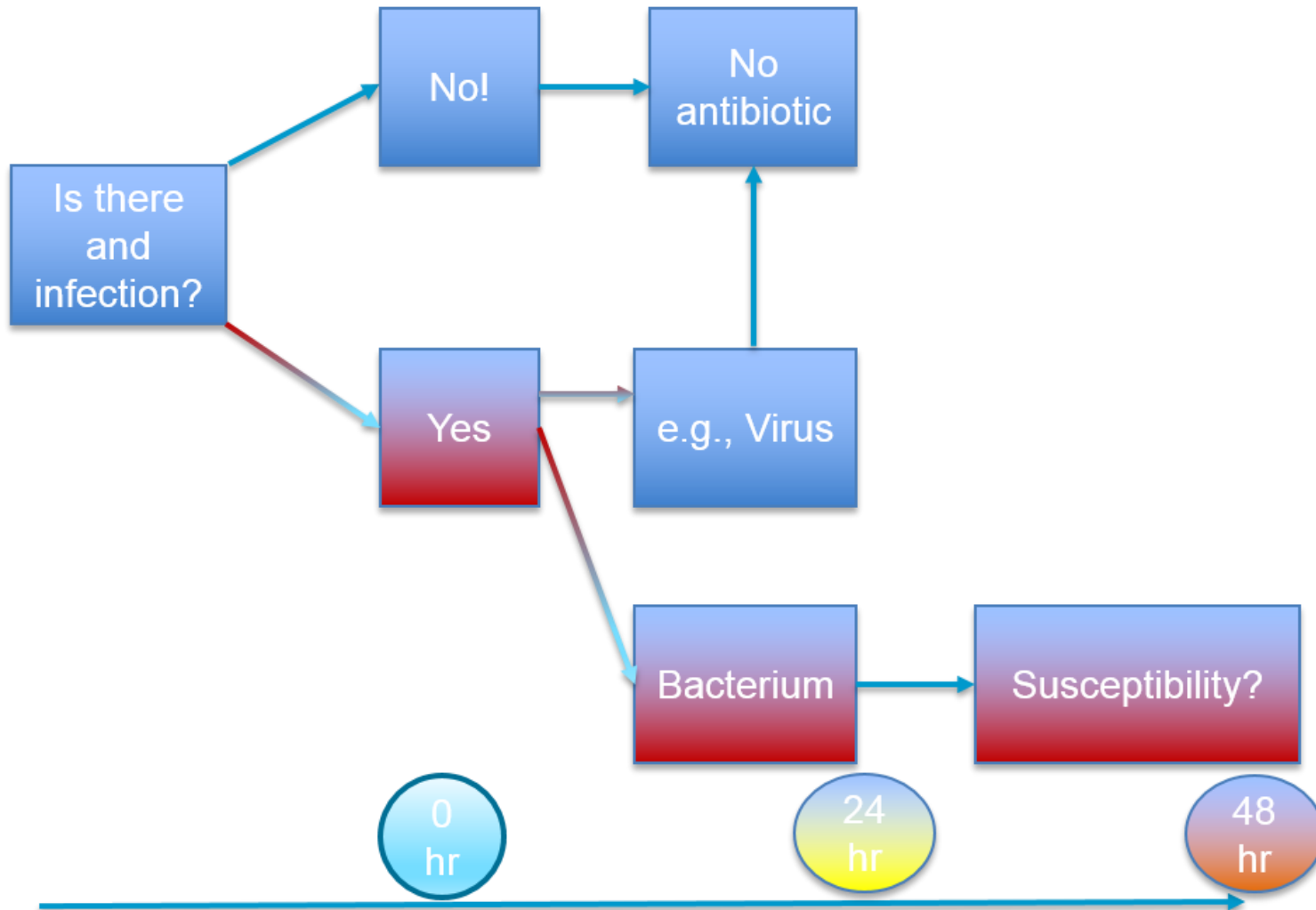
How long does it currently take?

Name of Laboratory test	Target TAT	Actual (Average) TAT – July 2013
Routine Microbiology	**Time we aim to issue result by**	**From arrival in laboratory to first issued report**
Acid fast bacilli	Within 48 hours	22 hours
TB culture	7-12 weeks	6.5 weeks
Blood cultures (negatives)	48 hours	42 hours
Blood cultures (positives)	72 – 96 hours	79 hours
Urine culture and sensitivity	Within 48 hours of receipt	24 hours
Paediatric blood cultures	36 hours	42 hours*

Too long!

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What does clinical microbiology do?

- Identify the infecting organism - Diagnosis

- Susceptibility testing, treatment and response monitoring - Optimise treatment

- Identify clustered organisms over-represented in the community- Infection Control

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The problem & opportunity

- Antibiotic resistance is a pressing problem
- It is caused by excessive or inappropriate antibiotic use
- The speed of progression of infection is much faster than the time taken to generate lab results (we are too slow)
- Costs of equipment & testing is high

- ODx has a rapid, cost effective solution that addresses this global market

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The Problem- solved?

- The capacity to detect small quantities of bacteria in relatively massive volumes of liquid

- Specifically the minimum possible detection time for both slow and rapidly growing organisms

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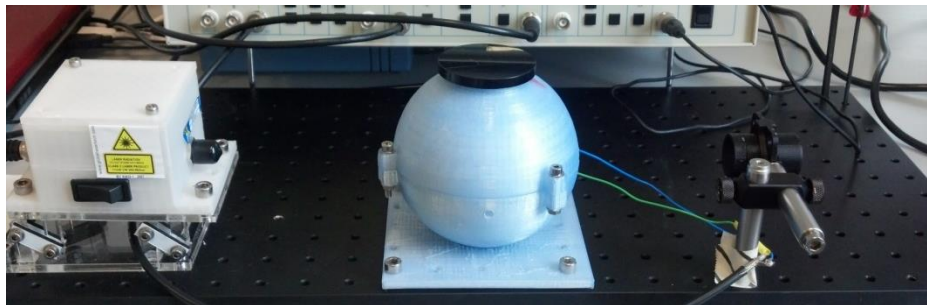St Andrews

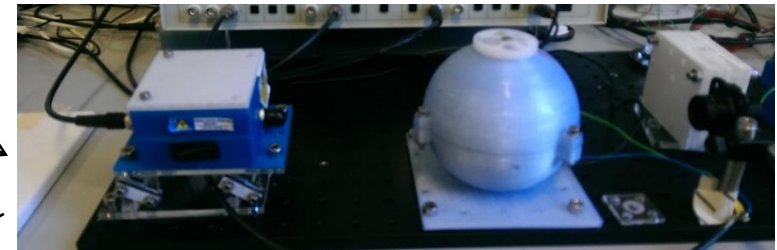# SLIC Prototype development

1. Modelling foam
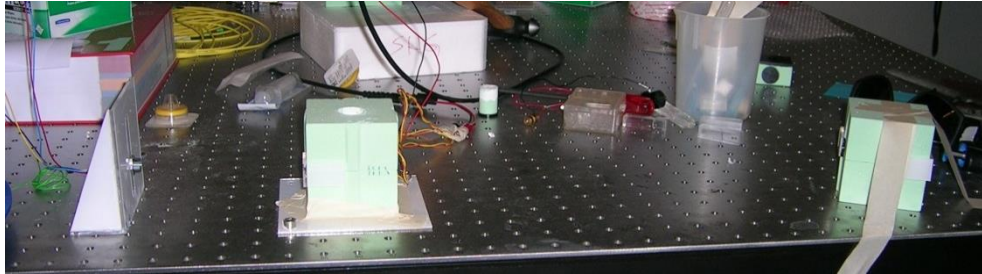
2. 3D print
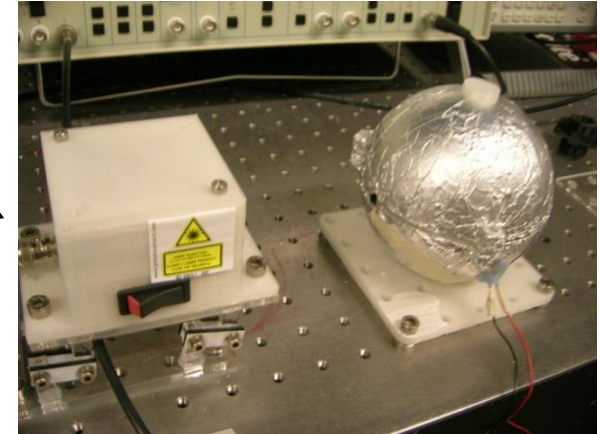
3.1. 3D print, internals modified

3.2

4.0

6.0

Opening for LIA access

6x signal inputs

6x outputs

1x Sig Gen input

LaserMod   DetOP
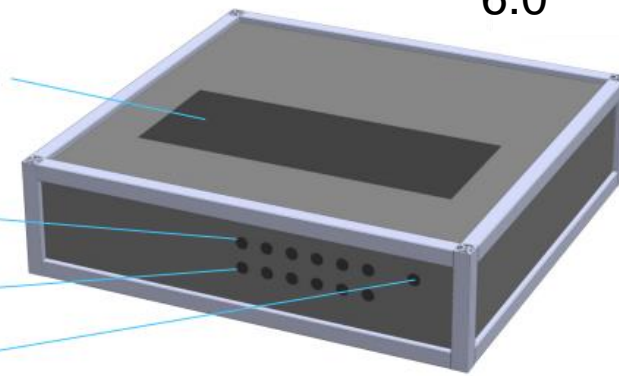
Laser scattering technology
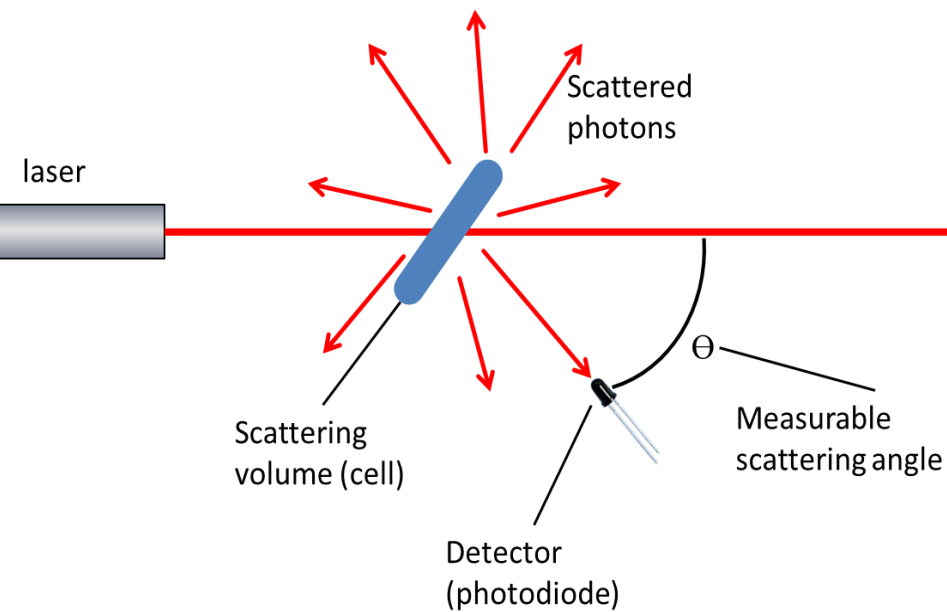
Scattered **L**ight **I**ntegrating **C**ollector

- What is it?

- The rapid and inexpensive ability to generate information about particles in a liquid non-invasively
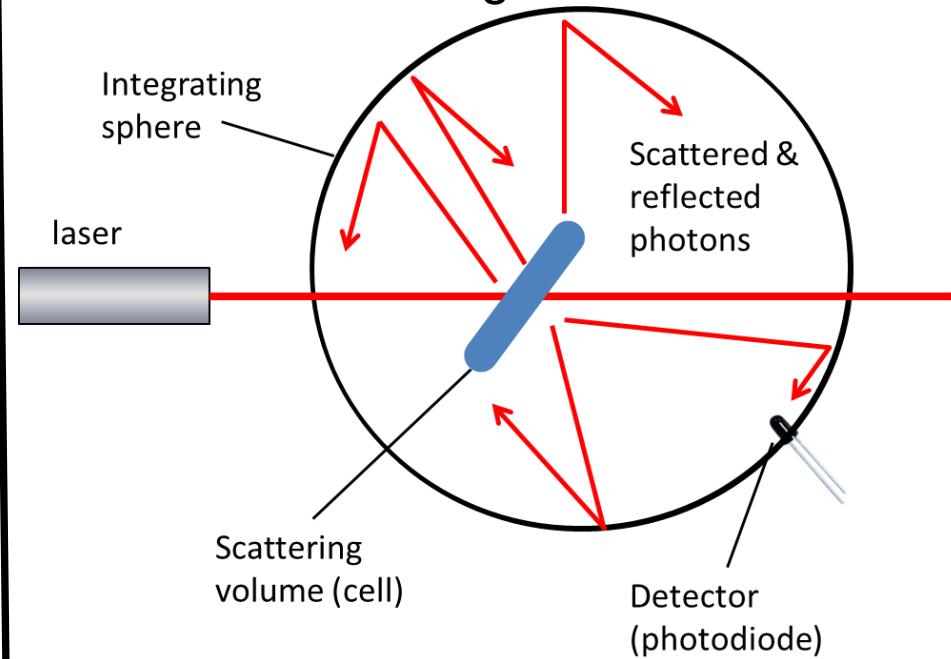

SLIC v4.0

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Laser scattering technology

Classic Scattering

- Scattered photons
- laser
- Scattering volume (cell)
- Detector (photodiode)
- Θ
- Measurable scattering angle

SLIC Scattering

- Integrating sphere
- Scattered & reflected photons
- laser
- Scattering volume (cell)
- Detector (photodiode)

SLIC - sensitivity

CFU = 2.6 x 10^8
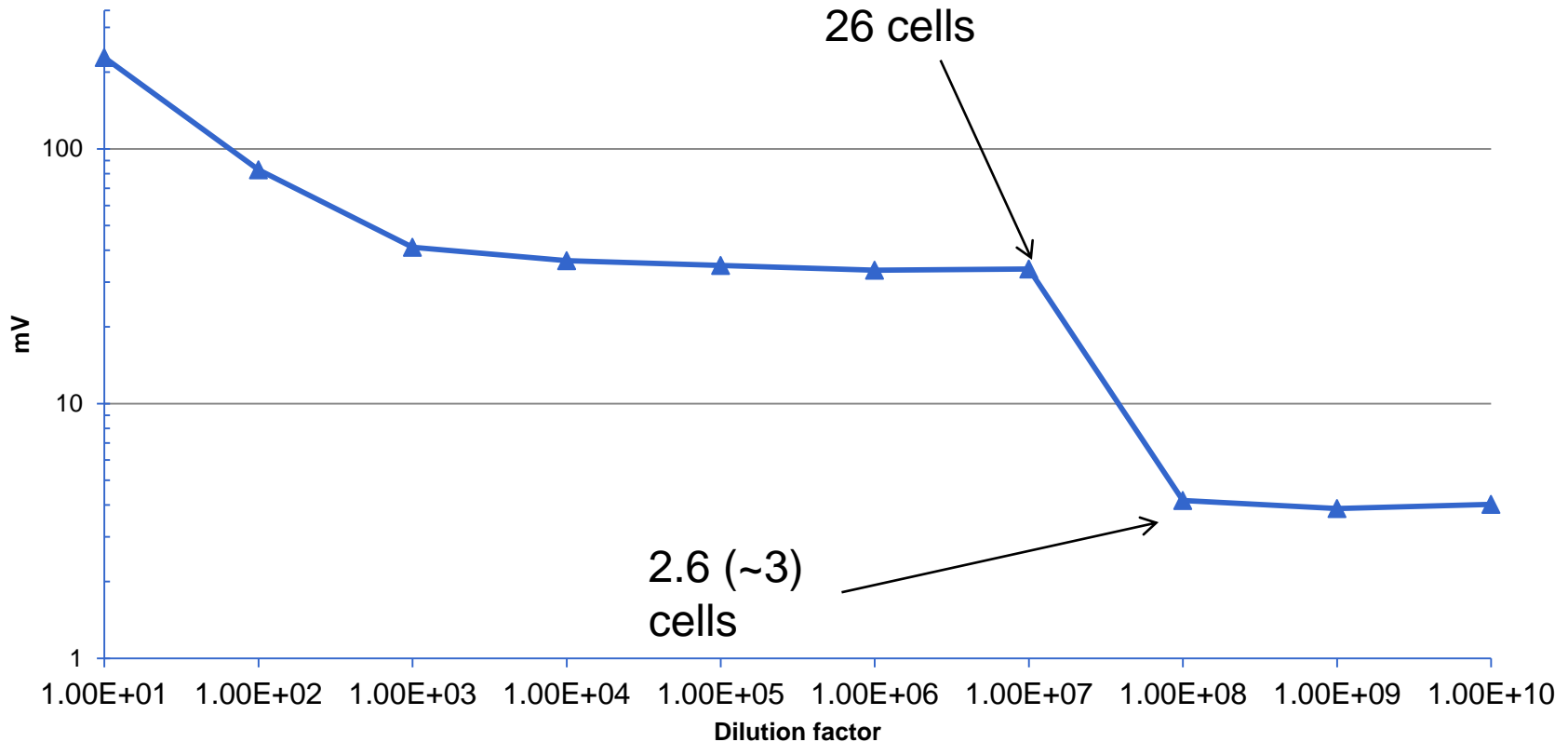
SLIC can 'see' concentrations of cells down to ~10 cells/ml, the abrupt drop in signal is indication that the limit of detection has been reached. The 'blank' reading that is taken at the beginning and end of every experiment must equal the lowest recording in order for the experiment to be declared valid
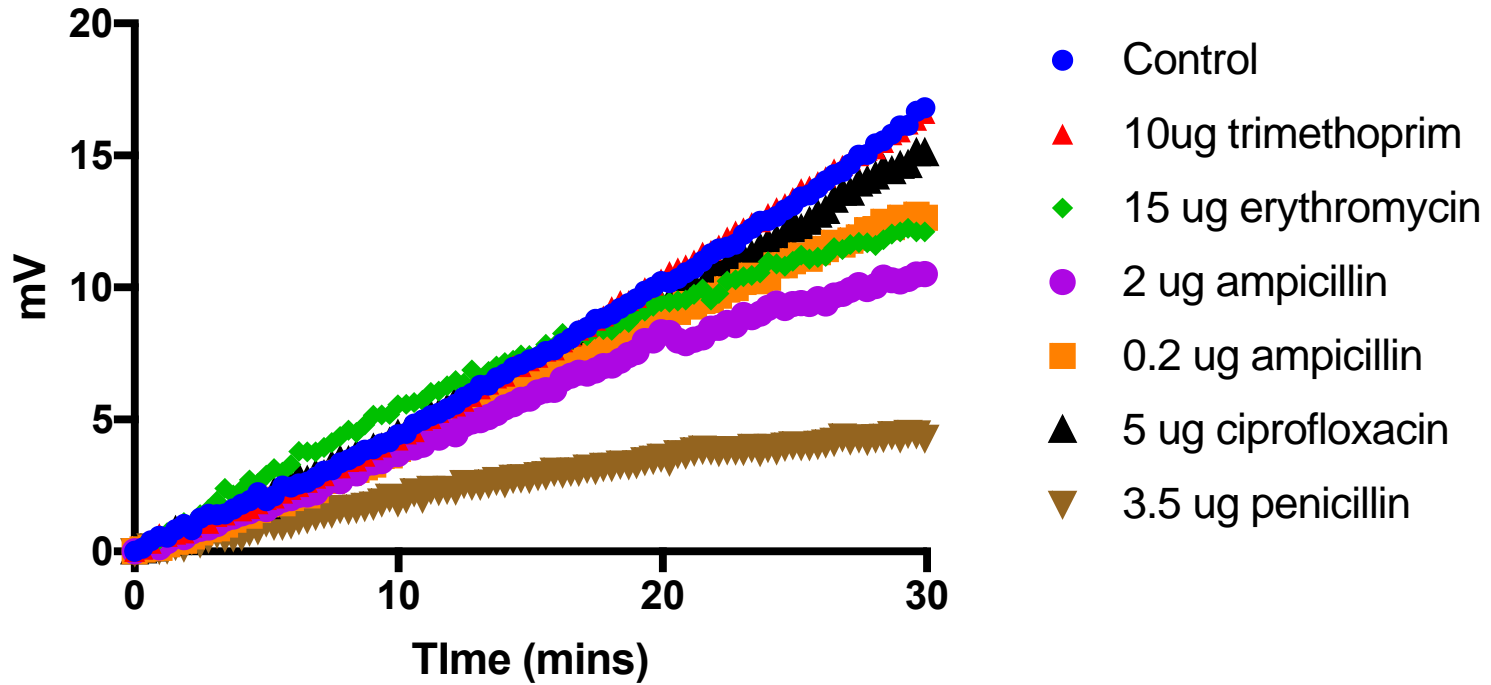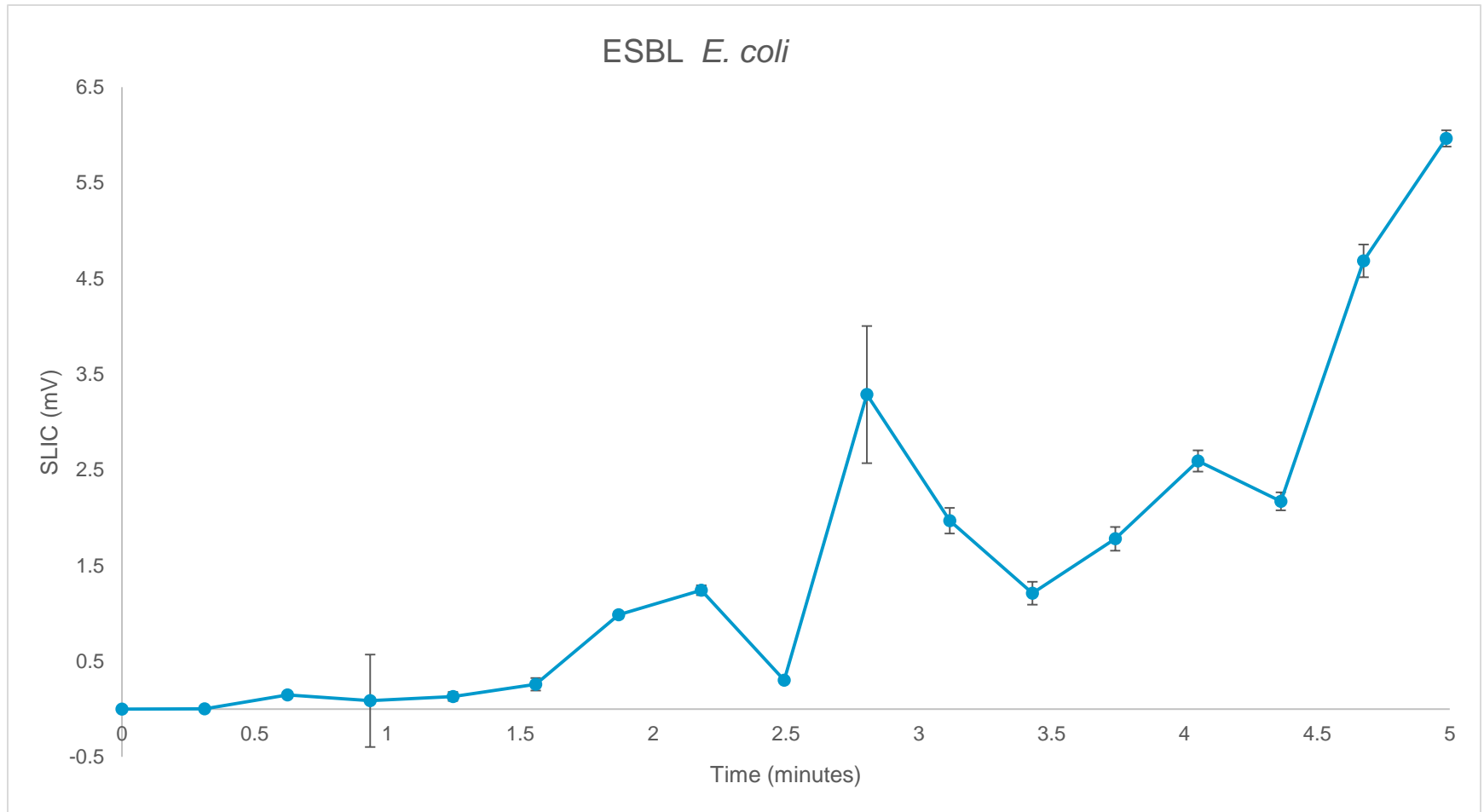
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SLIC- real-time monitoring
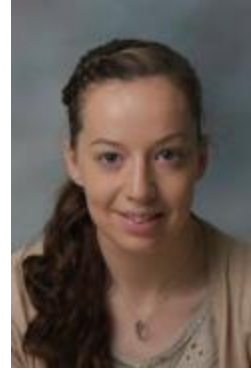
Monitoring *H. influenzae* growth and susceptibility on SLIC

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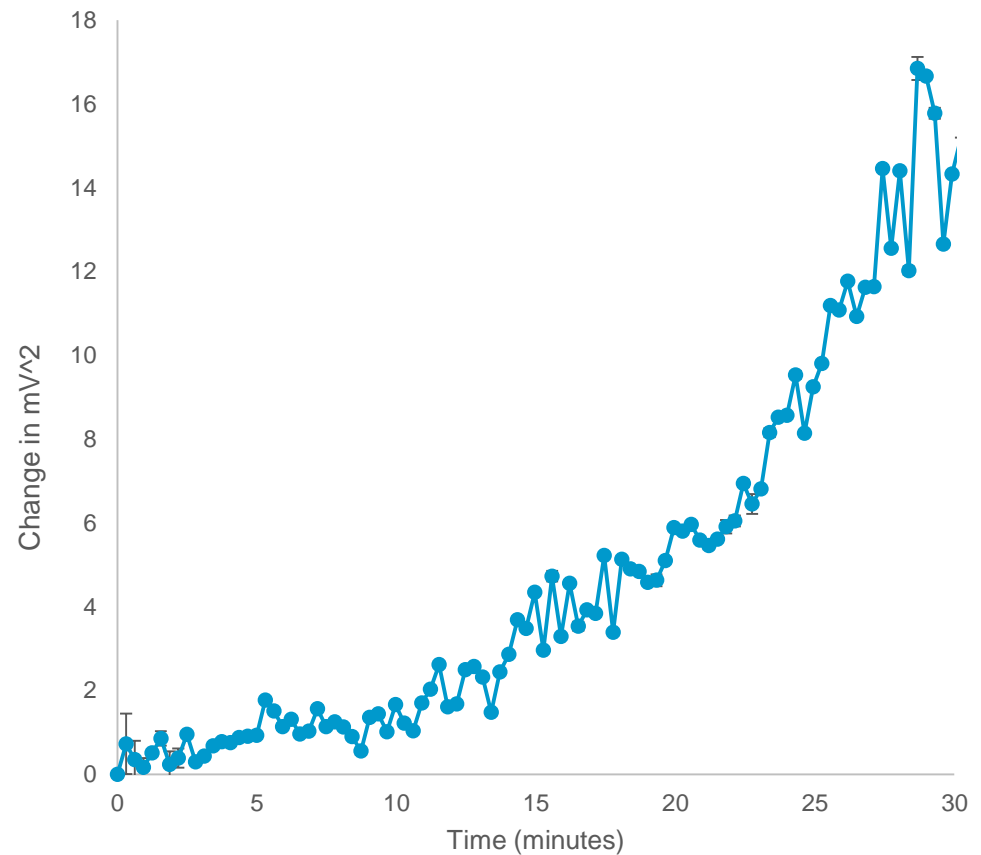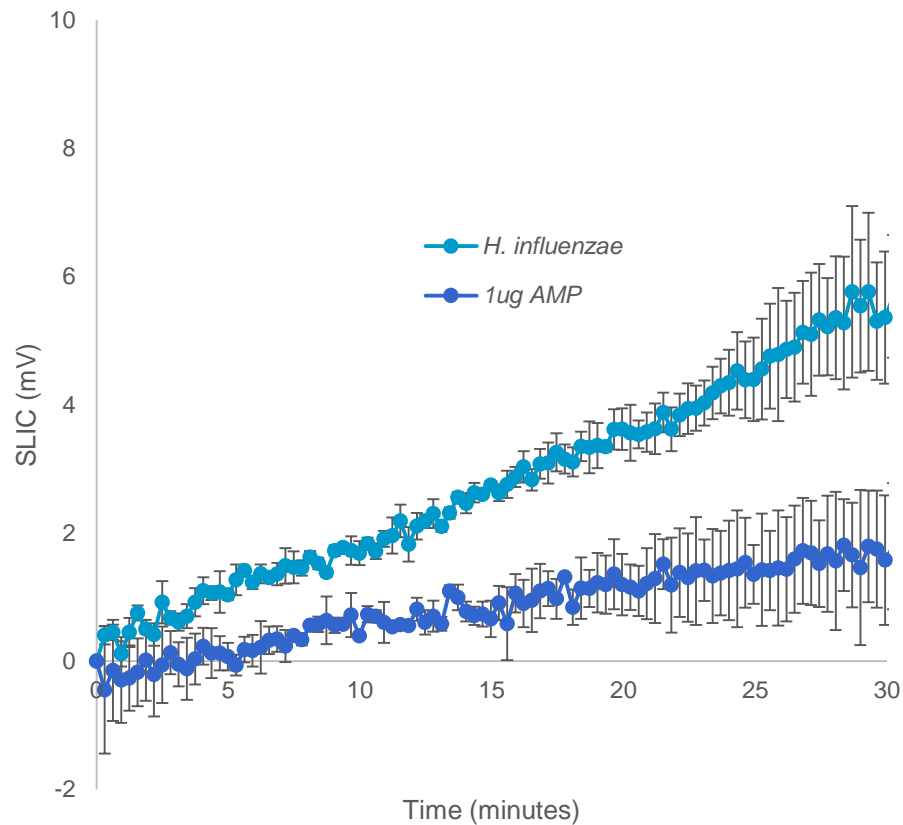
S. agalactiae

SLIC- susceptibility

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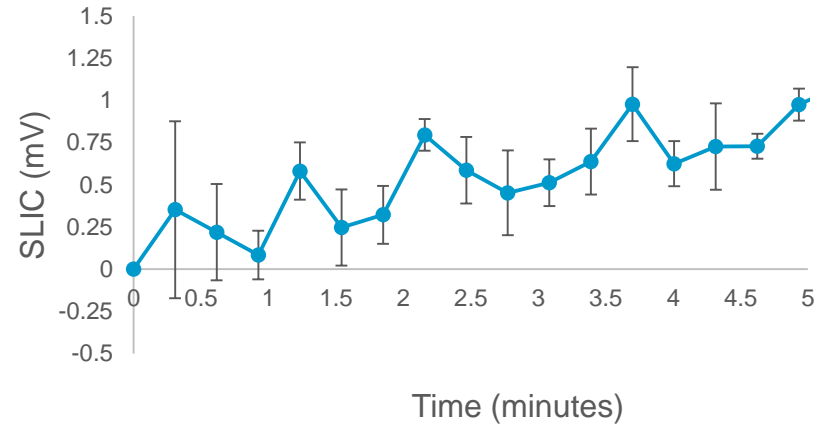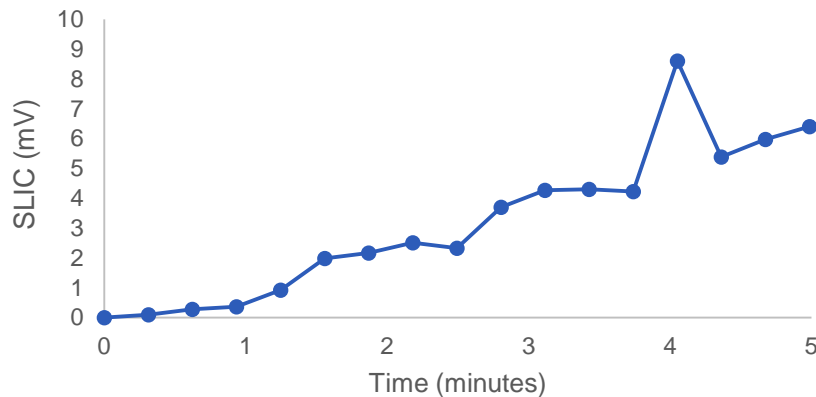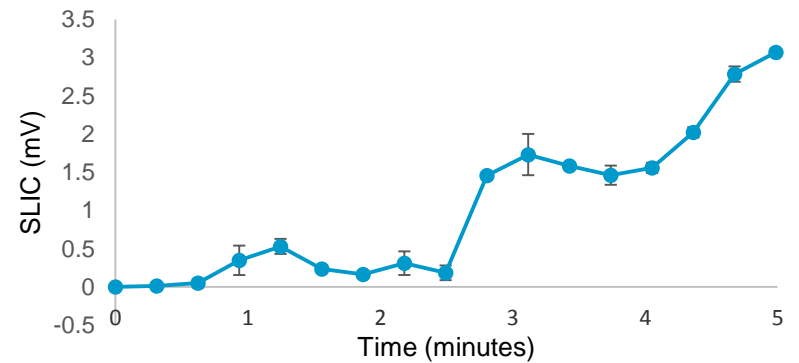
SLIC- susceptibility

A. baumanii
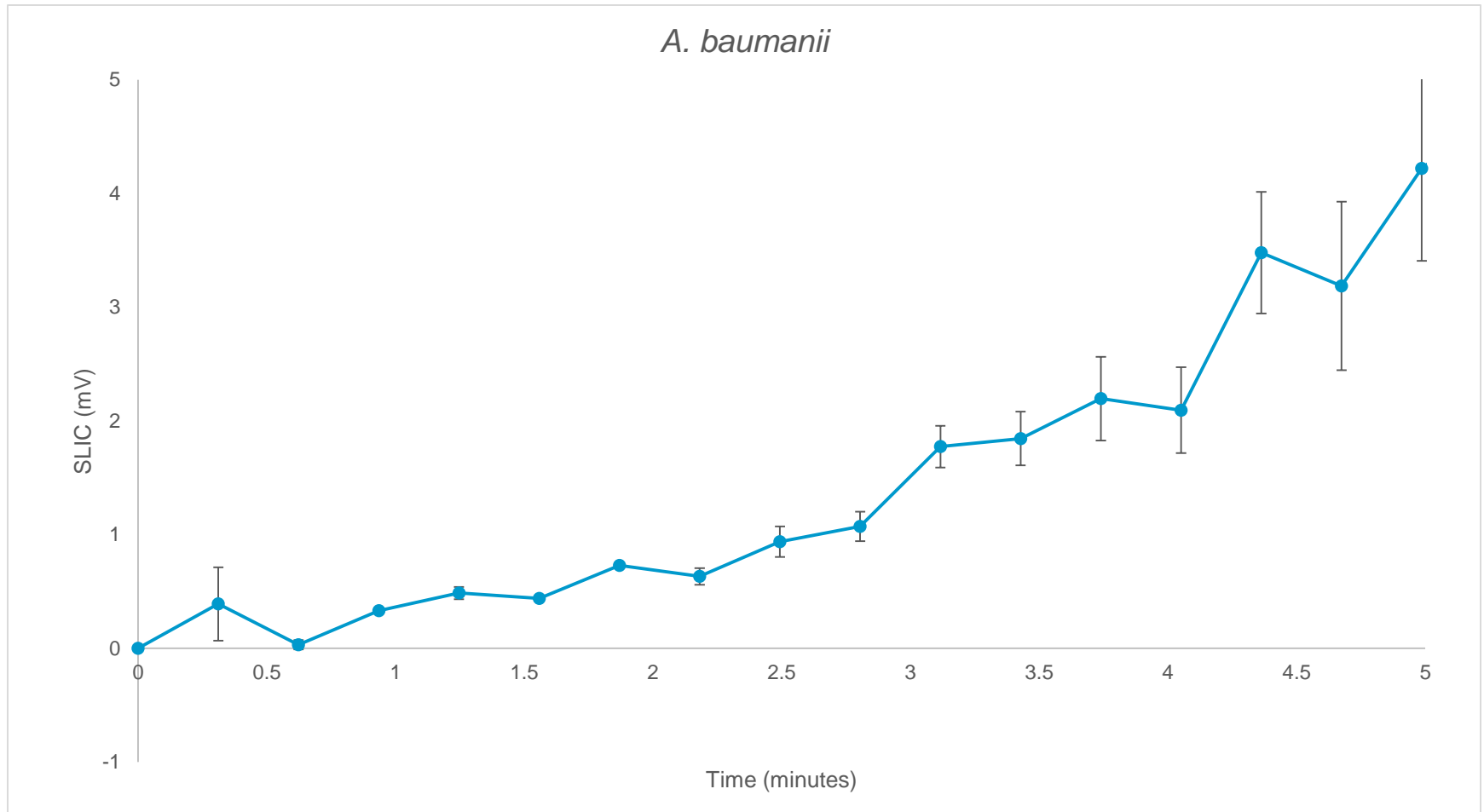
SLIC- susceptibility

C. albicans
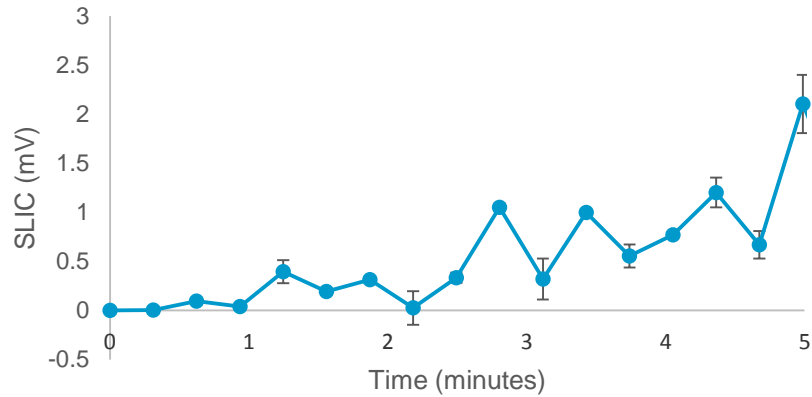
M. smegmatis

S. aureus (MRSA)

S. pyogenes

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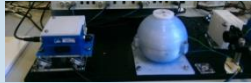
SLIC Vs. The Market (time to positive result)
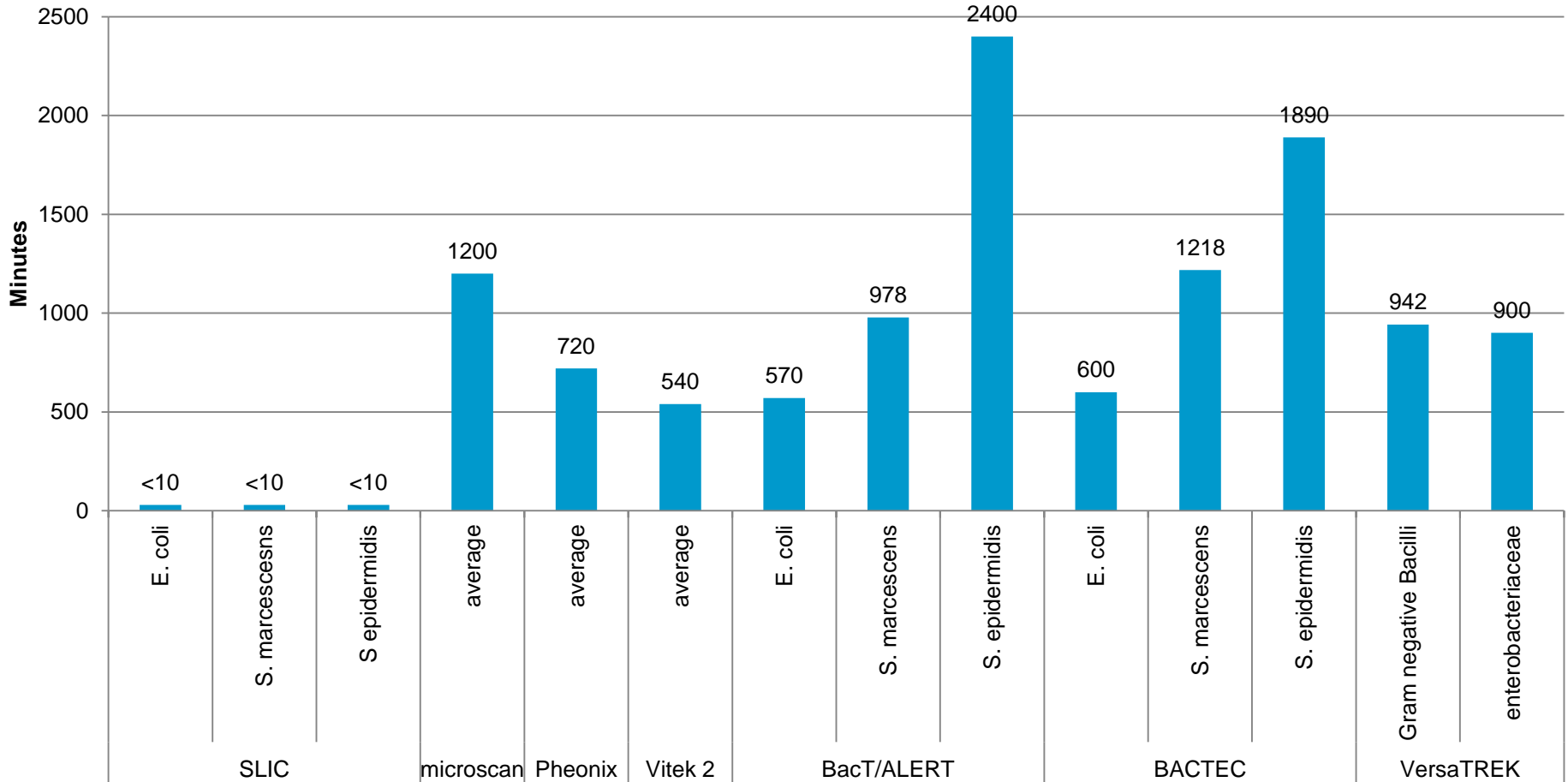
Comparison of the SLIC to other commercial products currently on the market for establishing bacterial number and their relative time to positivity (TTP) times in minutes for three rapidly dividing bacteria. TTP in this context is defined as the first time point at which a statistically significant difference can be found between an exponentially growing and a non-growing culture.

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SLIC Vs. The Market: Costs

Manufacturer	Equipment	Picture	Eqpt. Cost ($US)	Sample cost ($US)
Becton Dickinson	BACTEC MGIT		20-40k	50-200
Dade Behring	Microscan		20k	5-15
bioMérieux	Vitek Two		100-120k	Not known
bioMérieux	BacT/ALERT 3D		>20k	>100
Becton Dickinson	Phoenix		>20k	Not known
TREK diagnostic	VersaTREK		20k	100
Orbital Diagnostics	SLIC		5000 upwards (currently- in production much less)	<5

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SLIC Vs. The Market: Sensitivity

Bacterium	limit of detection (CFU/ml)	Time to significant result (TTP) – [mins]	Generation time [mins]
C. koseri	100	<5	22-37
E. coli	100	<1	20-38
E. faecium	100	<5	48
K. pneumoniae	100	<2	40
P. mirabilis	100	<5	28
E. faecalis	1000	<5	26
S. maltophillia	1000	<5	63
S. pyogenes	1000	<1	25
H. influenzae	100	<5	23
C. albicans	1000	<5	77
MRSA	100	<5	28-40
S. aureus	1000	<5	27
M. smegmatis	100	<1	240
M. komossense	100	<10	360
M. bovis (BCG)	100	<60	1020-1440

SLIC- universal screening

SLIC Antimicrobial Susceptibility Testing

Classification	< 1 minute	< 2 minutes	< 5 minutes
Gram-Negative Bacteria			
Acinetobacter Baumannii	✓		
Citrobacter koseri			✓
Enterobacter aerogenes	✓		✓
Enterobacter cloacae			✓
Escherichia coli	✓		
Haemophilus influenzae			✓
Klebsiella pneumoniae		✓	
Proteus mirabilus			✓
Serratia marcescens	✓		
Stenotrophomonas maltophilia			✓

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SLIC- universal screening

SLIC Antimicrobial Susceptibility Testing

Classification	< 1 minute	< 2 minutes	< 5 minutes
Gram-Positive Bacteria			
Enterococcus faecalis			✓
Enterococcus faecium			✓
Methicillin-resistant	✓		
Staphylococcus aureus			
Staphylococcus aureus			✓
Staphylococcus epidermidis		✓	
Streptococcus agalactiae			✓
Streptococcus pyogenes	✓		
Mycobacteria			
Mycobacterium smegmatis	✓		
Yeast			
Candida albicans			✓

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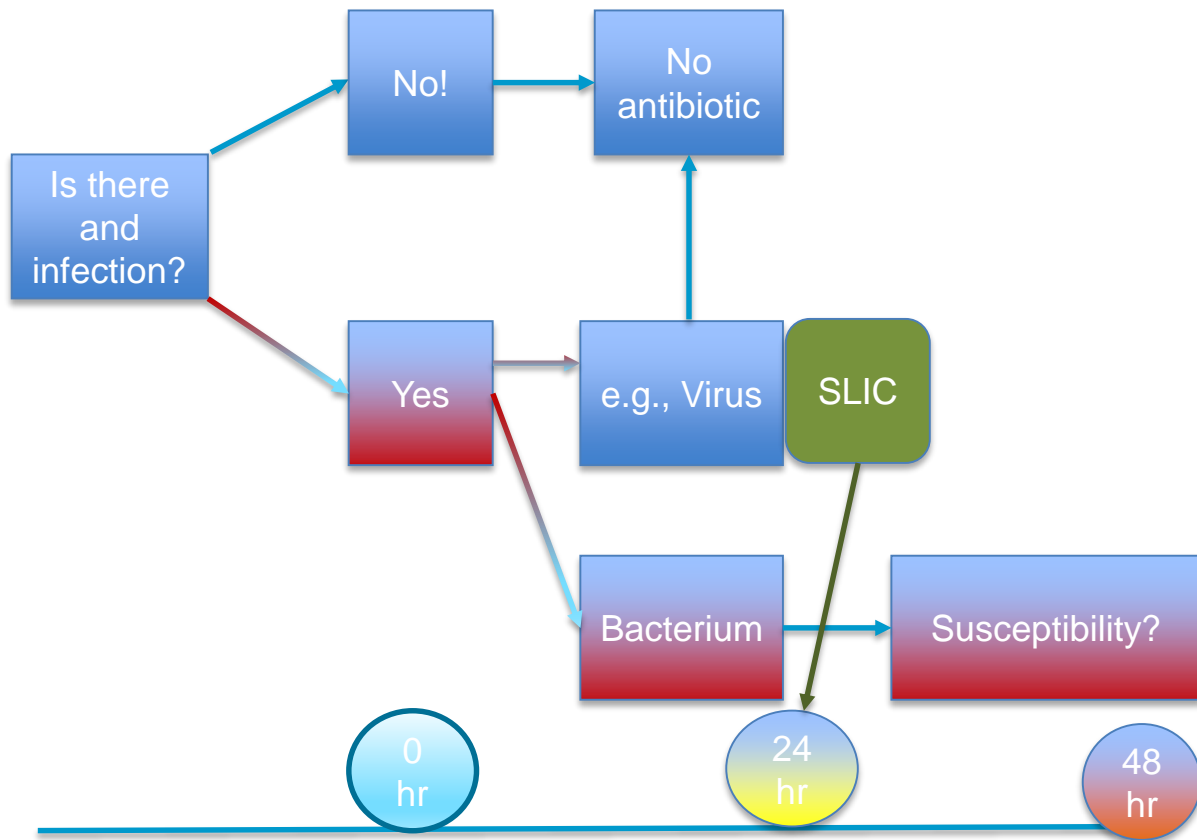
SLIC Development pathway

- Test in labs of clinical partners against a range of samples (field trial, NHS Fife/Nottingham)
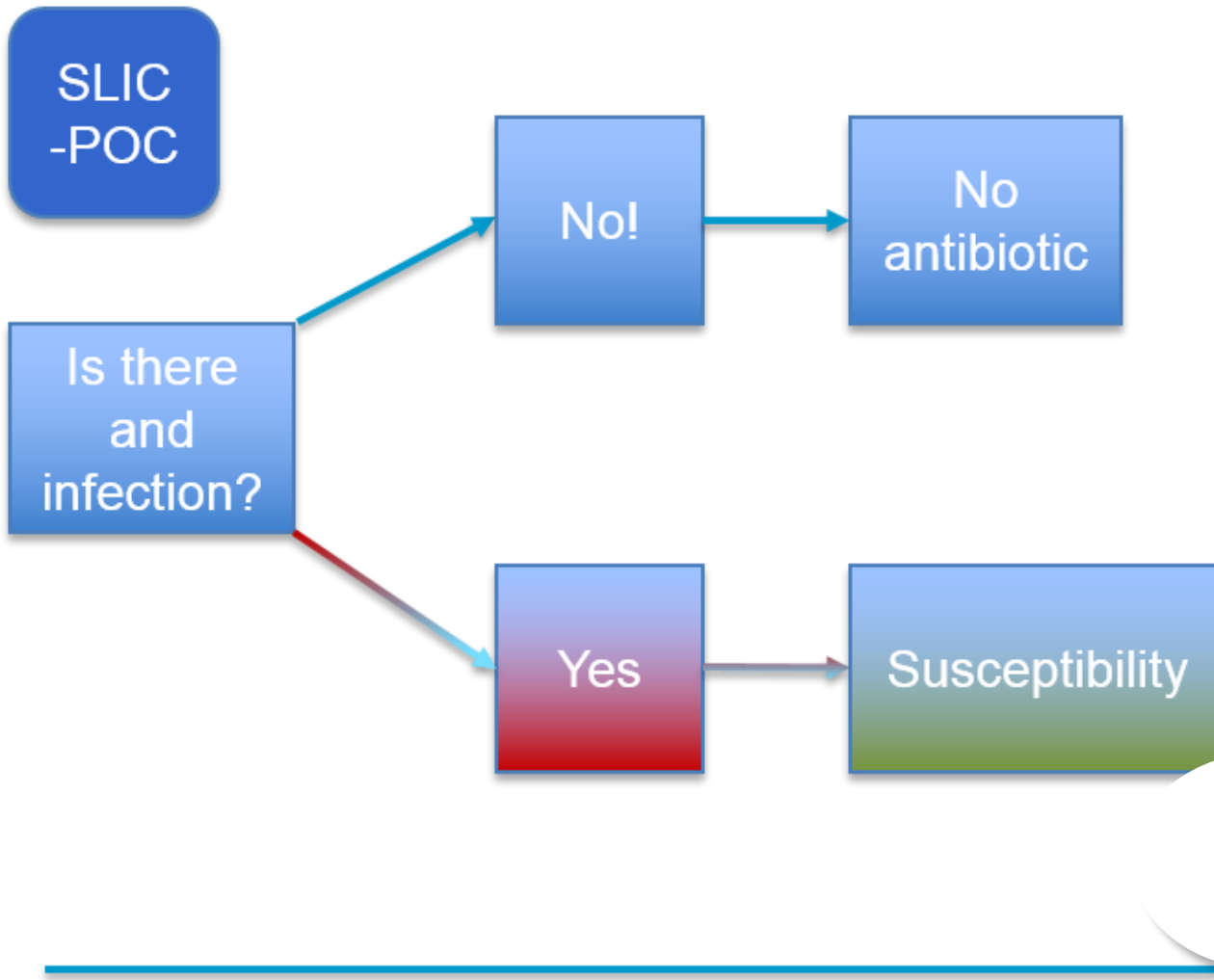
- Develop x3 forms of instrument
  - High throughput multi-sample device for Hospitals
  - **POC instrument**
  - Low cost variant for developing nations

- Add capacity to identify organism

Developing SLIC for clinical practice -
High throughput

SLIC POC

SLIC-POC

Is there and infection?

No! → No antibiotic

Yes → Susceptibility

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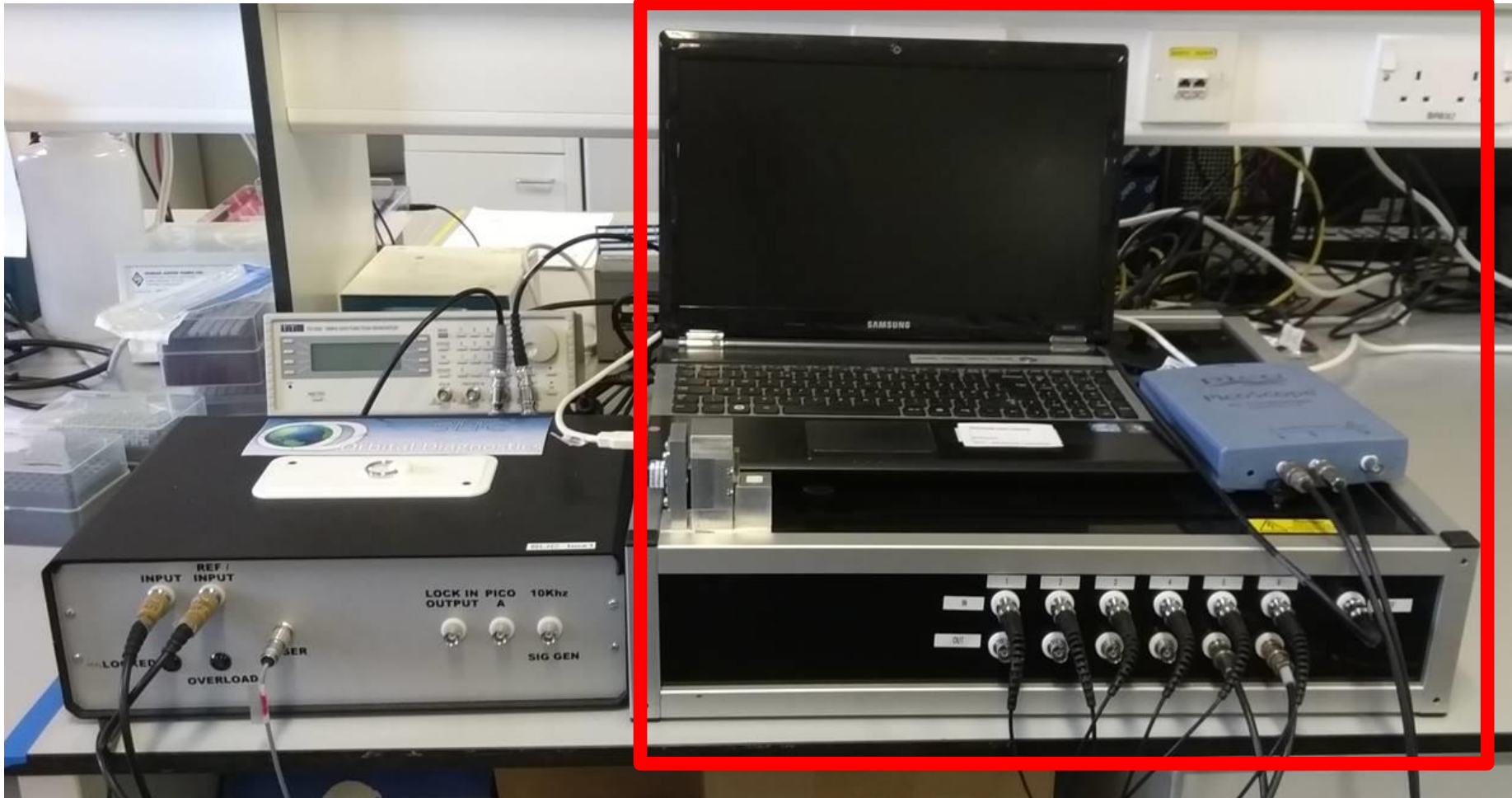
SLIC POC – Mock Urinalysis

Organism	Conditions	TTP [mins]
E. coli	Low pH; 3	<1
	pH 4	<1
	pH 5.25	<1
	pH 6	<1
	High pH; 8.25	<1
	pH 10	<2
	Starting inoculum; 10 CFU/mL	723 (12 hours)
	100 CFU/mL	119
	1,000 CFU/mL	**<5**
	10,000 CFU/mL	**<1**

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SLIC POC - Mock Urinalysis

Organism	Conditions	TTP [mins]
E. faecalis	Low pH; 3	<1
	pH 4	<1
	pH 5.38	<1
	pH 6	<1
	High pH; 8.18	<1
	pH 10	<1
	Starting inoculum; 100 CFU/mL	200
	1,000 CFU/mL	**6**
	10,000 CFU/mL	**<1**

Acknowledgements

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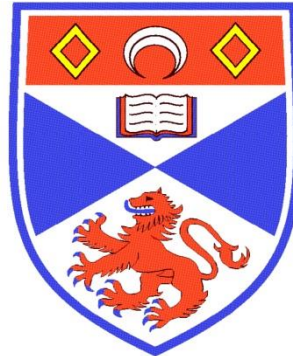
SLIC Team

- Stephen Gillespie
- Kerry Falconer
- Giles Hamilton
- Ewan Chirnside

- Innovative Medicines Initiative Joint Undertaking under grant agreement No. 115337
- European Union's Seventh Framework Programme (FP7/2007-2013)
- EFPIA
- IMI: www.imi.europa.eu

Any Questions?

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