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# Orbital Diagnostics: Rapid antibiotic sensitivity determination

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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

# The problem & opportunity

- There is a disconnect between microbiologists and clinicians
- Time is a factor
  
- SLIC addresses this issue
  - Allows near-real time results

# 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**

# How long does it currently take?

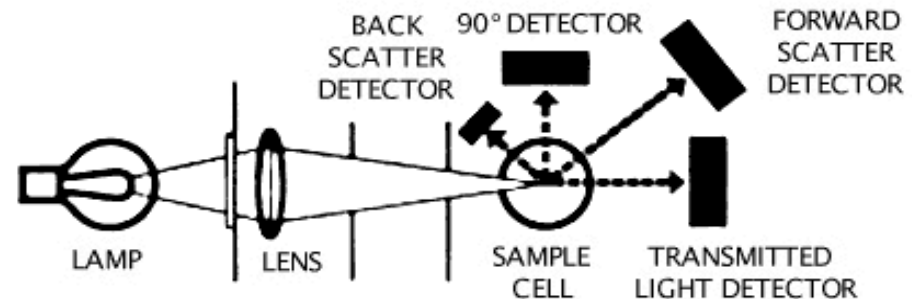
Name of Laboratory test	Target TAT	Actual (Average) TAT – July 2013
<b>Routine Microbiology</b>	<b>Time we aim to issue result by</b>	<b>From arrival in laboratory to first issued report</b>
Acid fast bacilli	Within 48 hours	22 hours
TB culture	7-12 weeks	6.5 weeks
Blood cultures (negatives)	48 hours	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!

# The Problem

- 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

- Spectrophotometry
- Flow cytometry
- Nephelometry



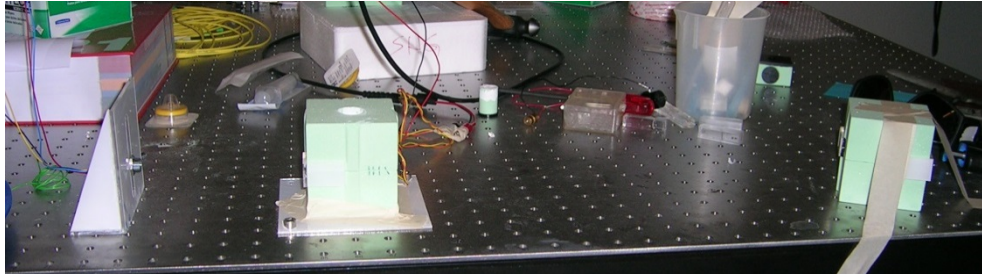
Courtesy of National Academies Press – [http://www.nap.edu/openbook.php?\\_record\\_id=12658&page=212](http://www.nap.edu/openbook.php?_record_id=12658&page=212)

# Our solution

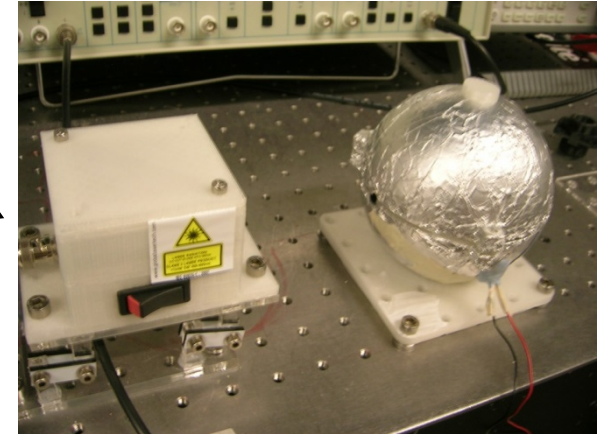
- Modify existing technologies – improve them
  - Coulter counter
  - Flow cytometry
  - Spectrophotometry + nephelometry!

# SLIC Prototype development

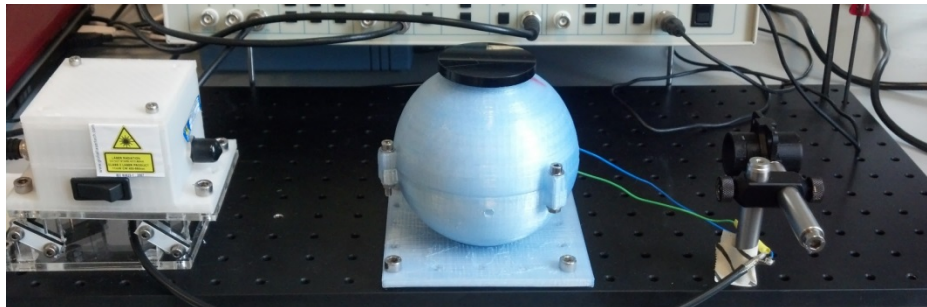
## 1. Modelling foam



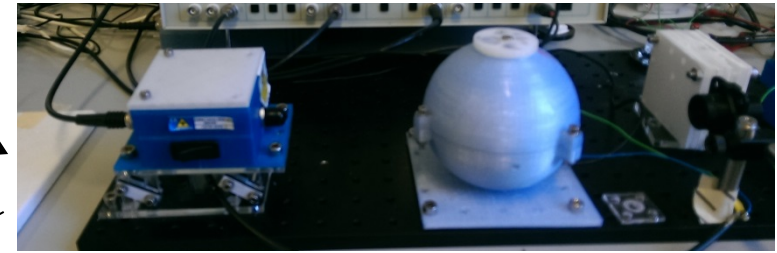
## 2. 3D print



## 3.1. 3D print, internals modified



3.2



4.0



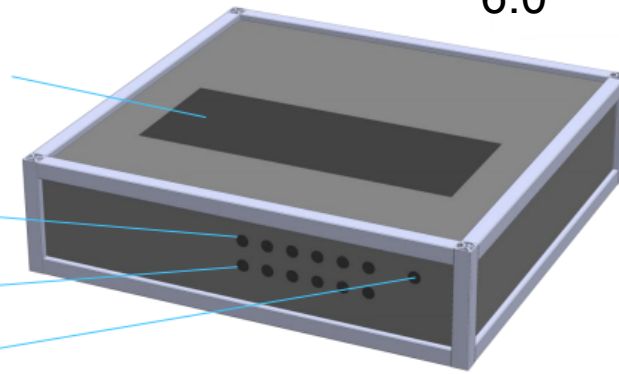
6.0

Opening for LIA access

6x signal inputs

6x outputs

1x Sig Gen input





# Laser scattering technology

## Scattered Light Integrating Collector

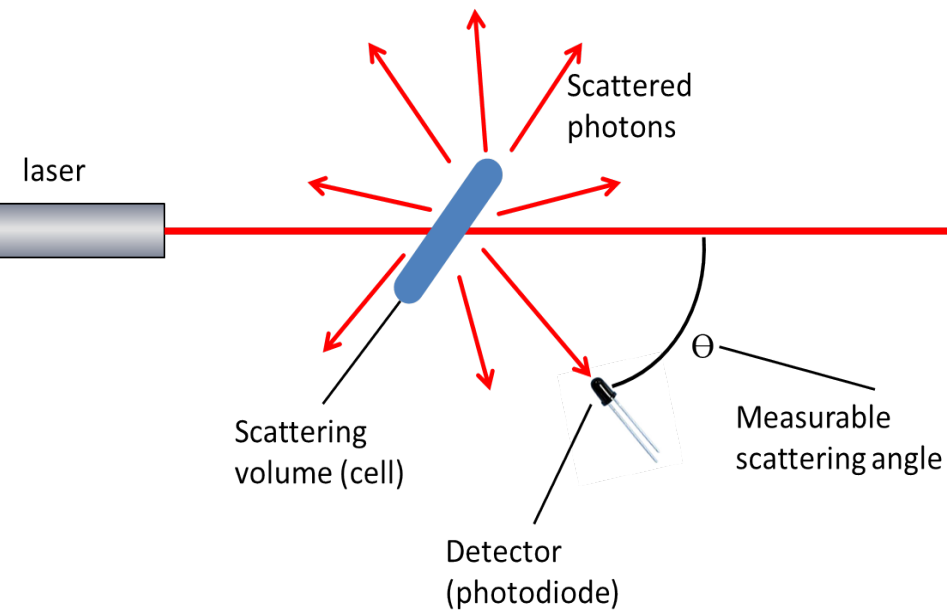
- What is it?
- The rapid and inexpensive ability to generate information about particles in a liquid non-invasively



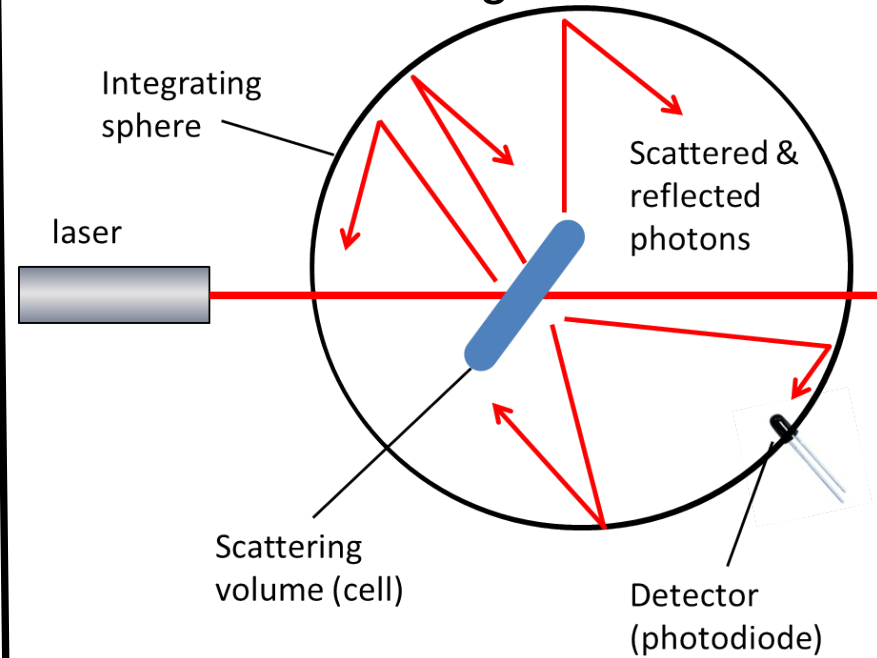
SLIC v4.0

# Laser scattering technology

## Classic Scattering

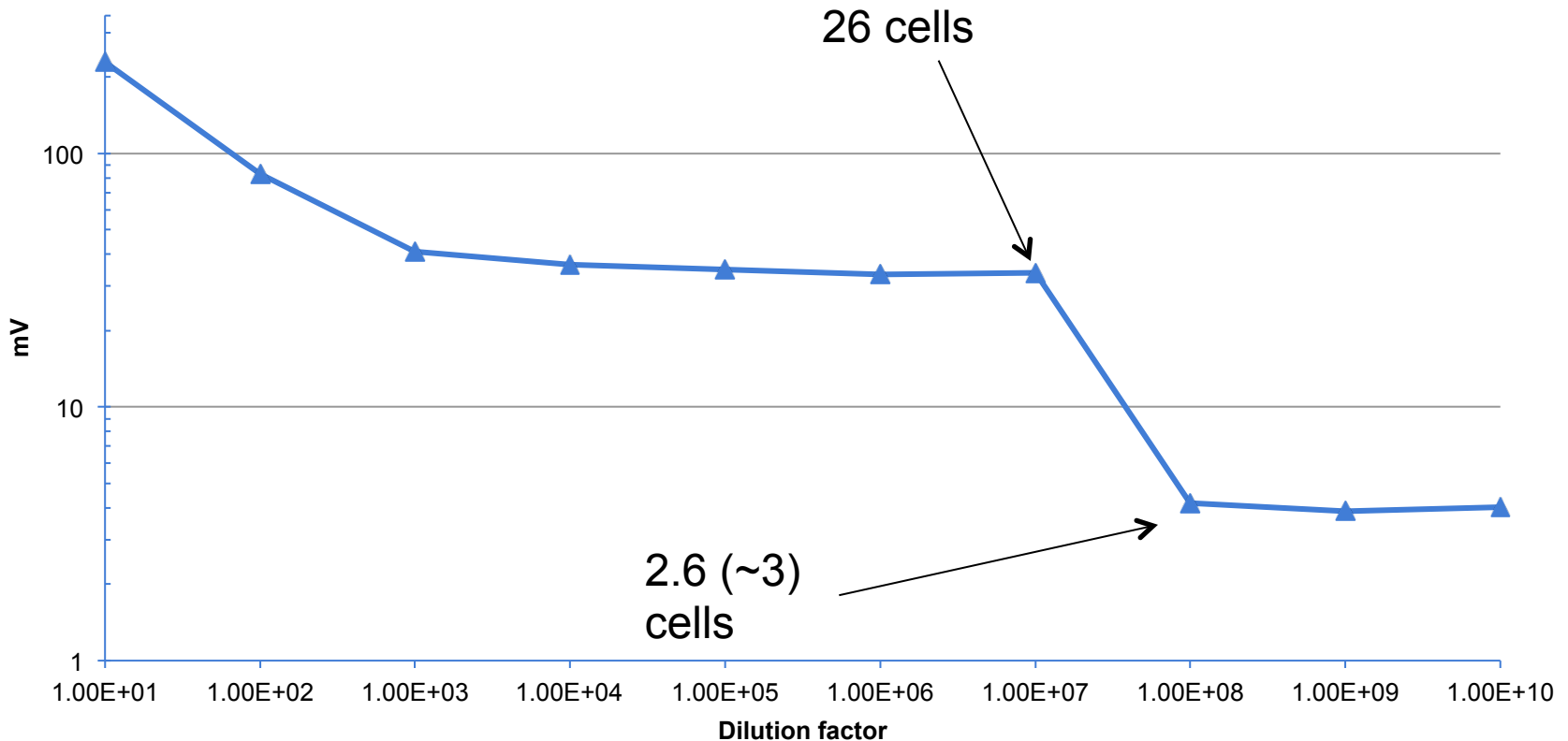


## SLIC Scattering



# SLIC - sensitivity

CFU =  $2.6 \times 10^8$

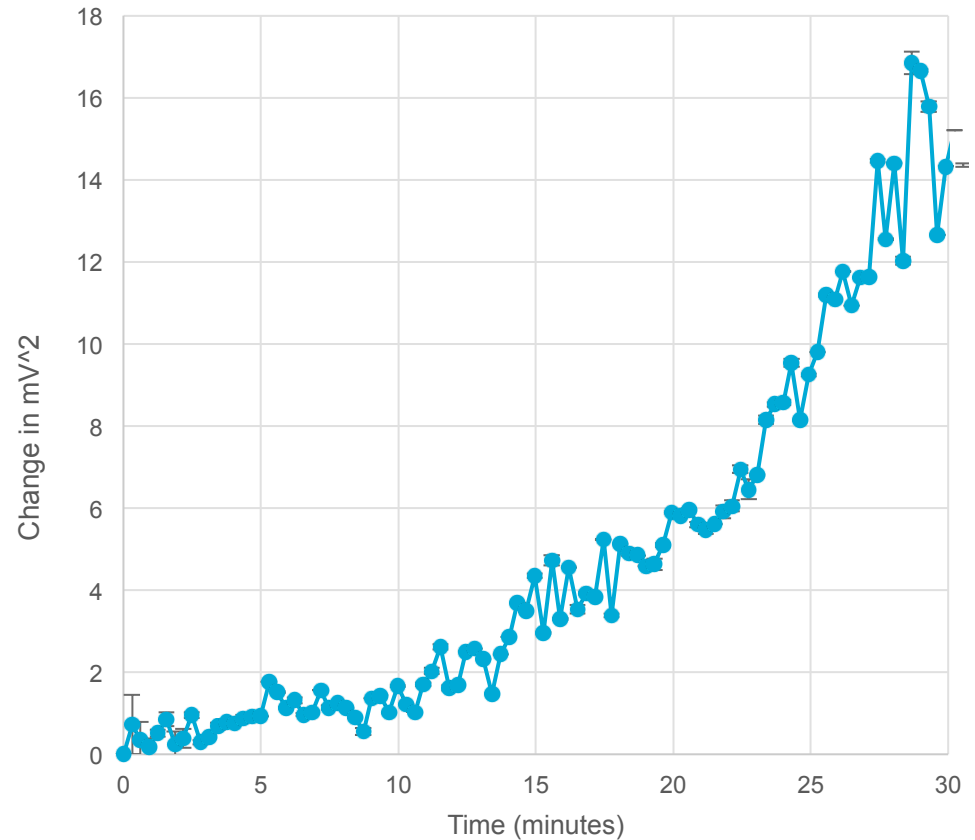
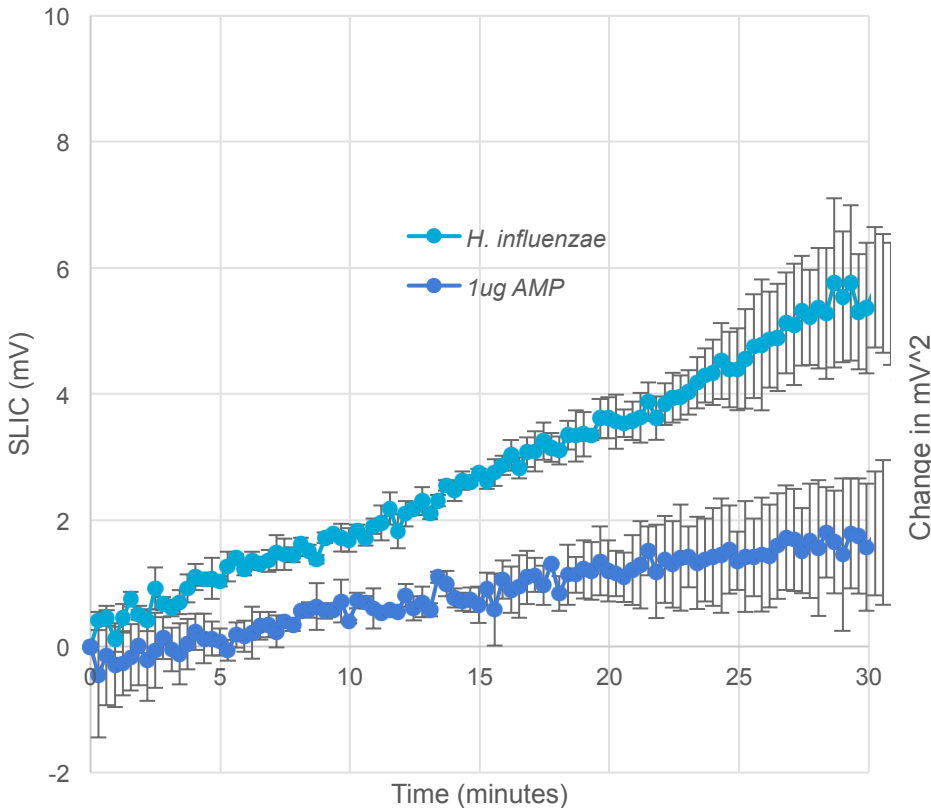


SLIC can 'see' concentrations of cells down to ~10 cells/ml, the abrupt drop in signal is indication that the limit of detection has been reached. The 'blank' reading that is taken at the beginning and end of every experiment must equal the lowest recording in order for the experiment to be declared valid

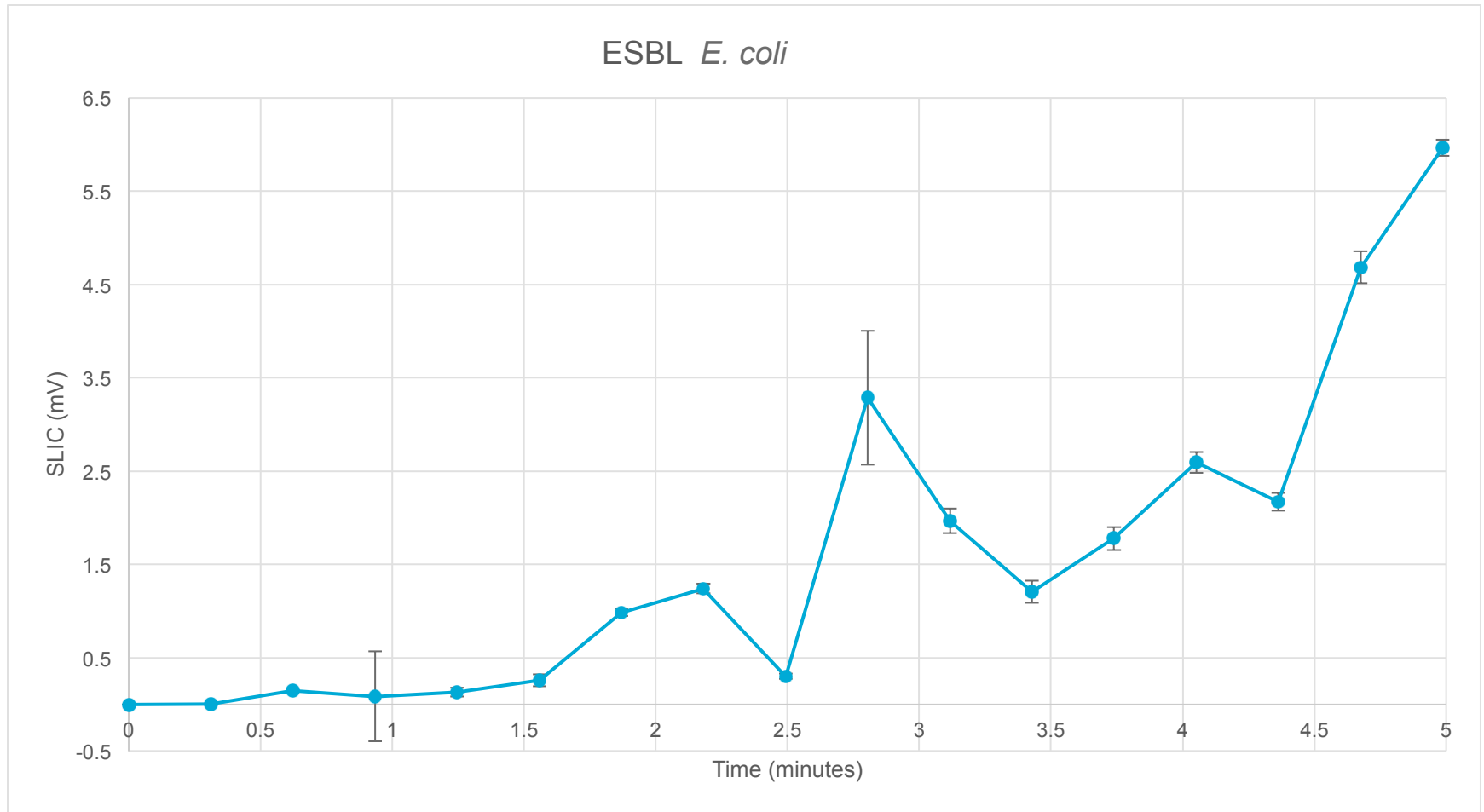
# SLIC- real-time monitoring



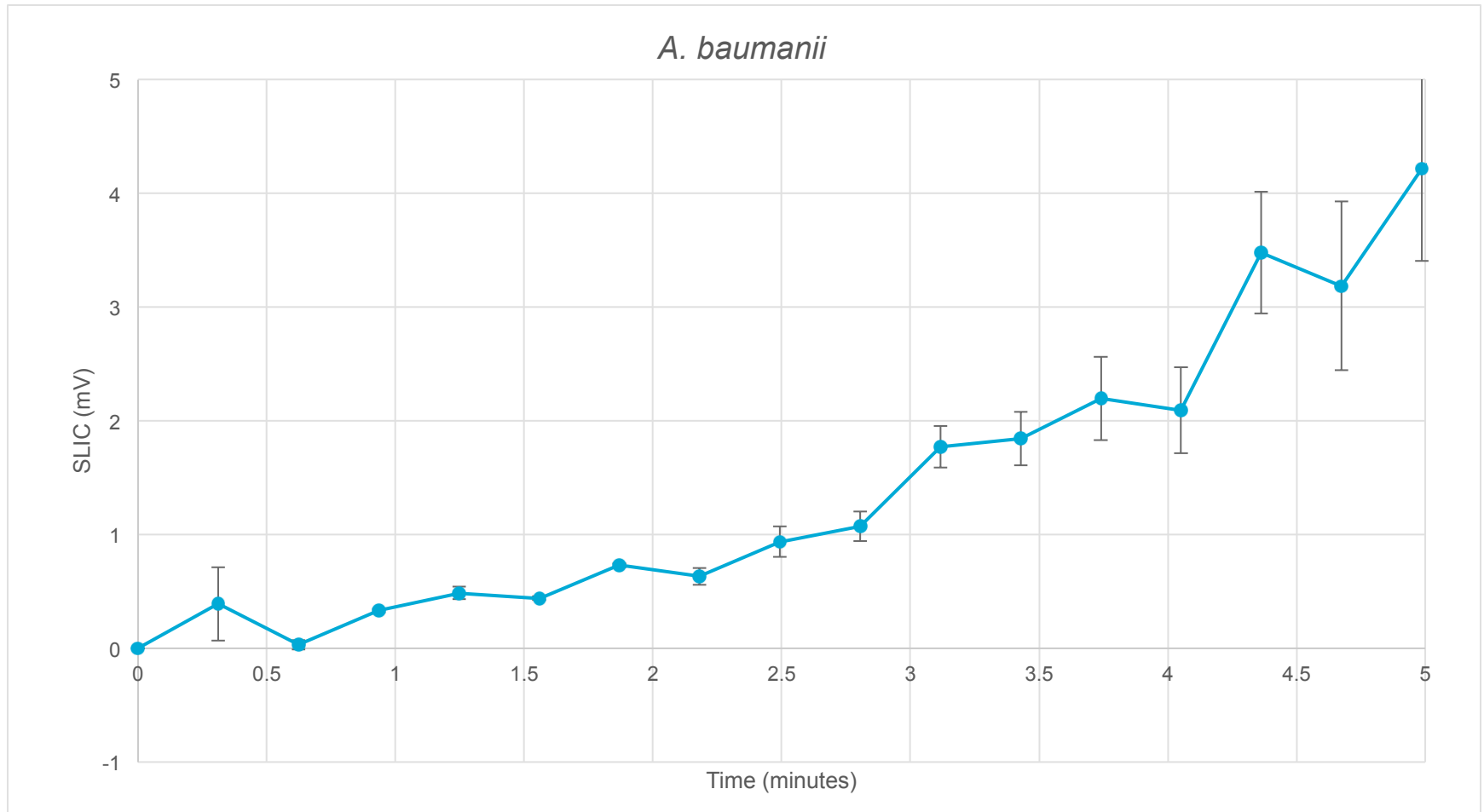
## Monitoring *H. influenzae* growth and susceptibility on SLIC



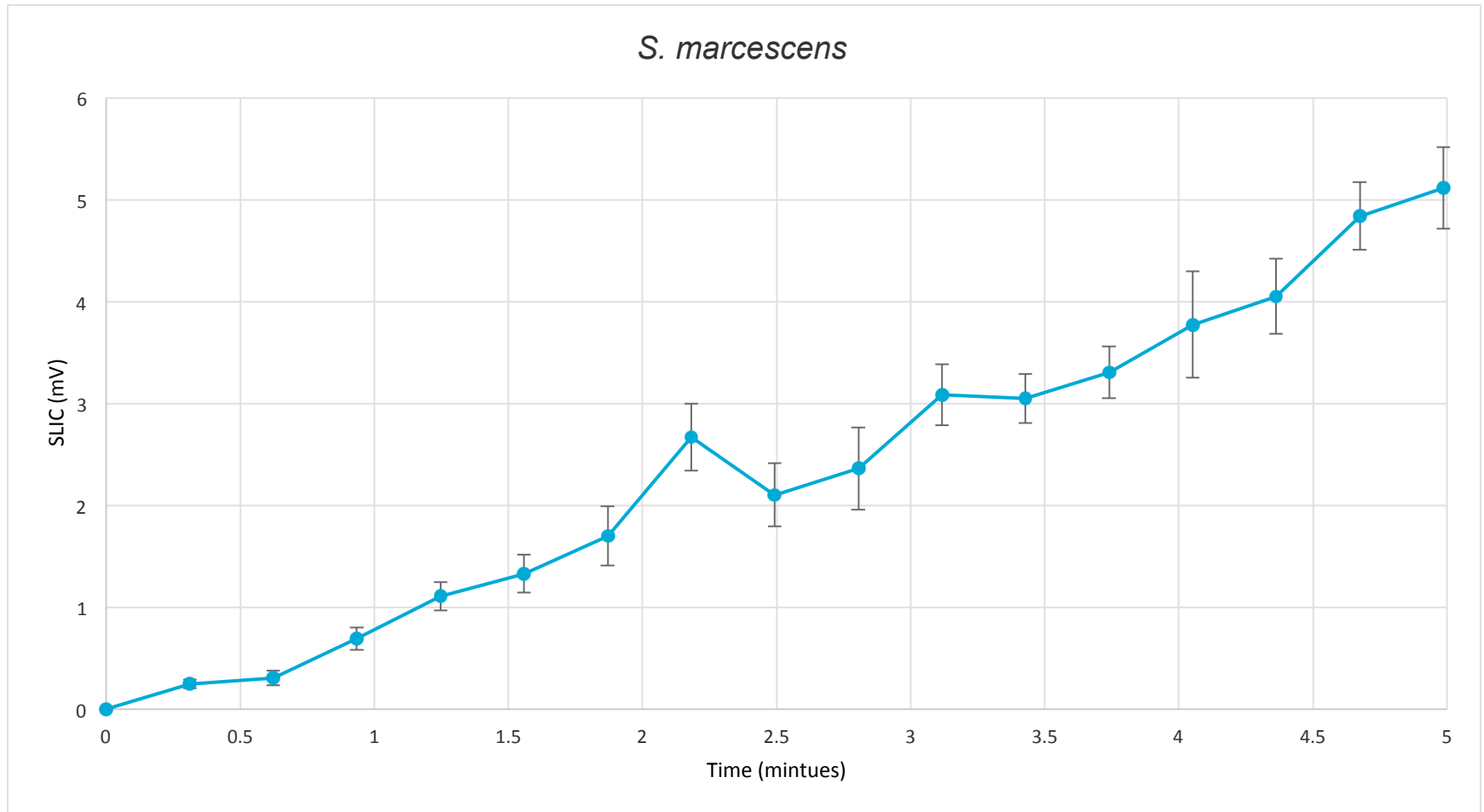
# SLIC- susceptibility



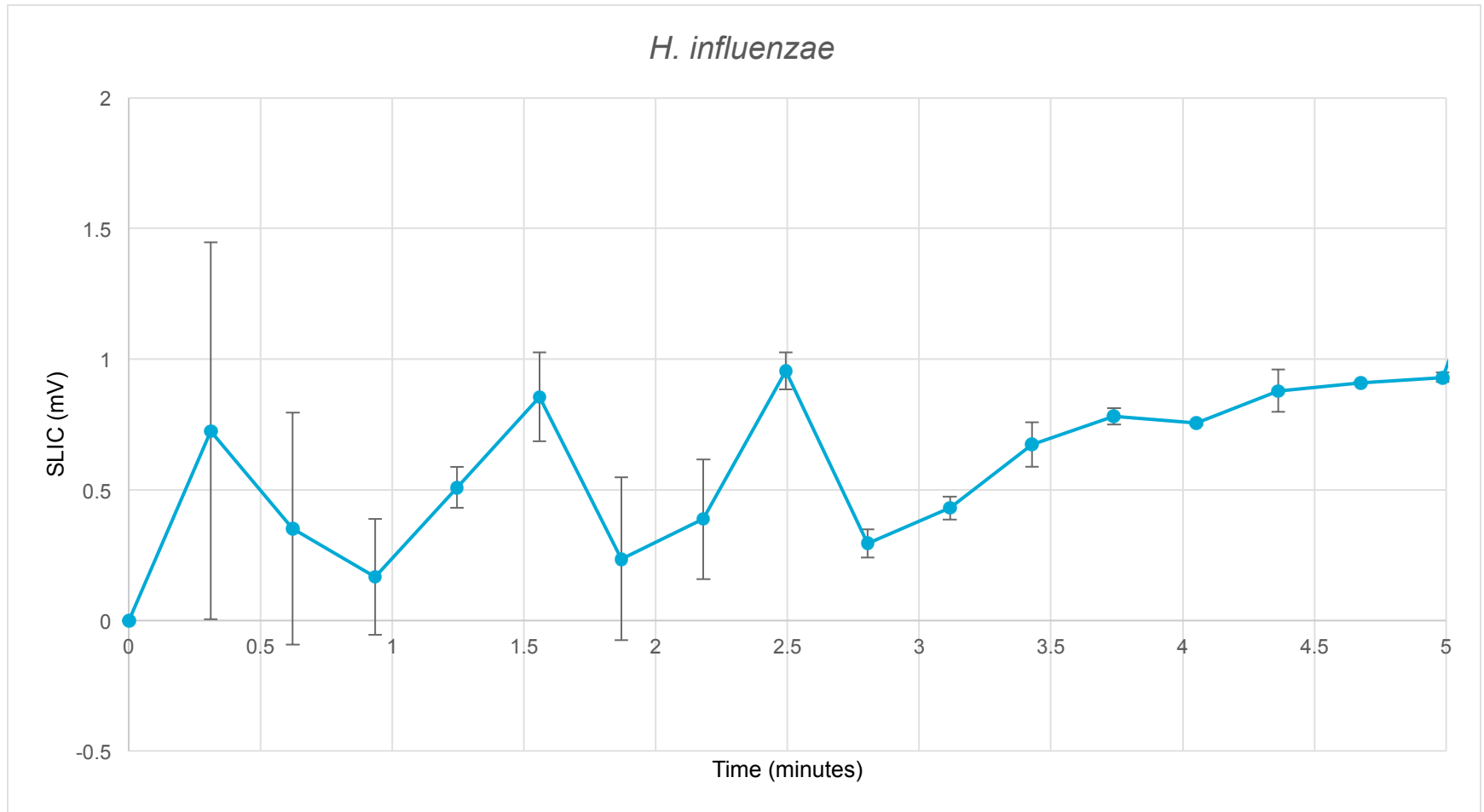
# SLIC- susceptibility



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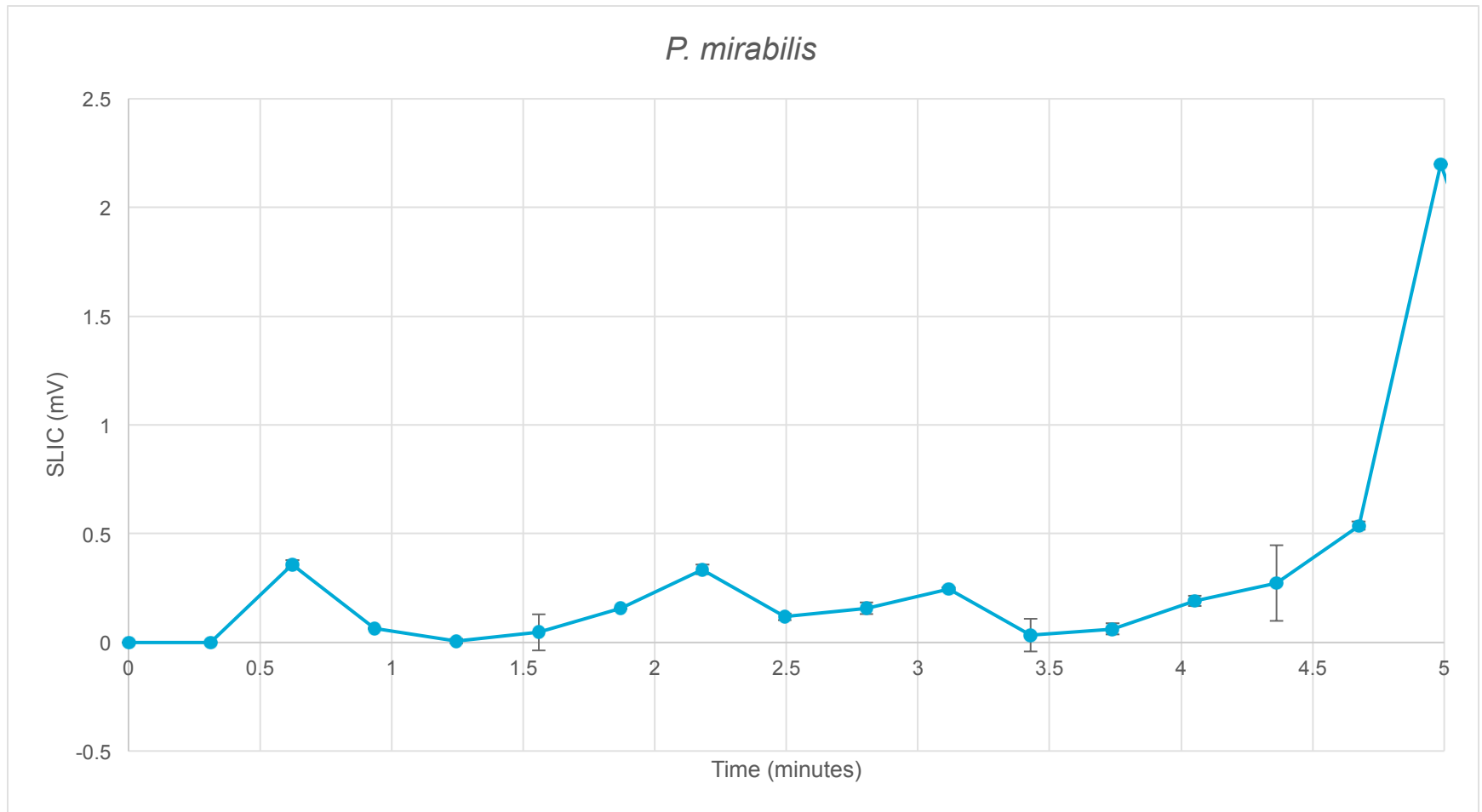


# SLIC- susceptibility

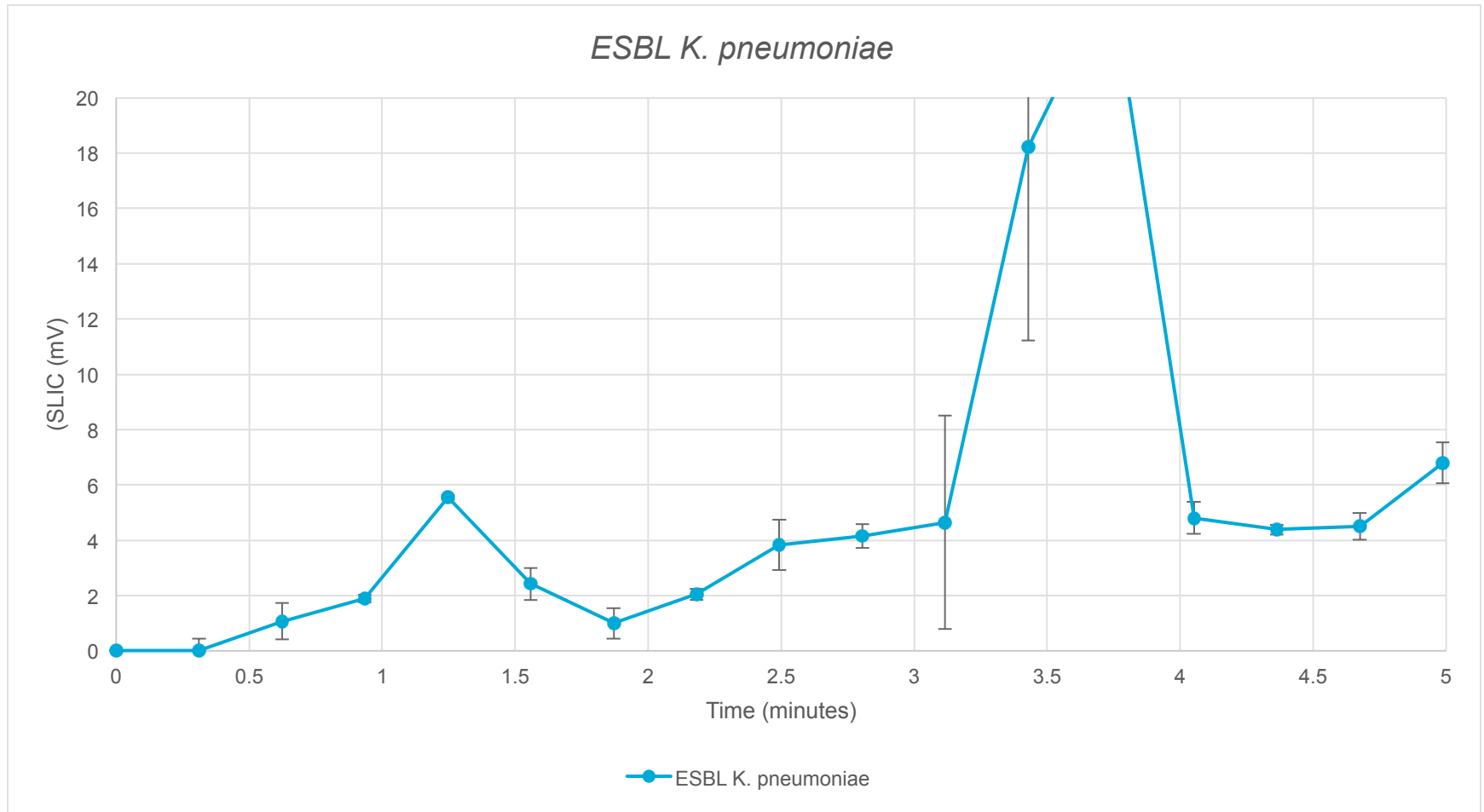




# SLIC- susceptibility

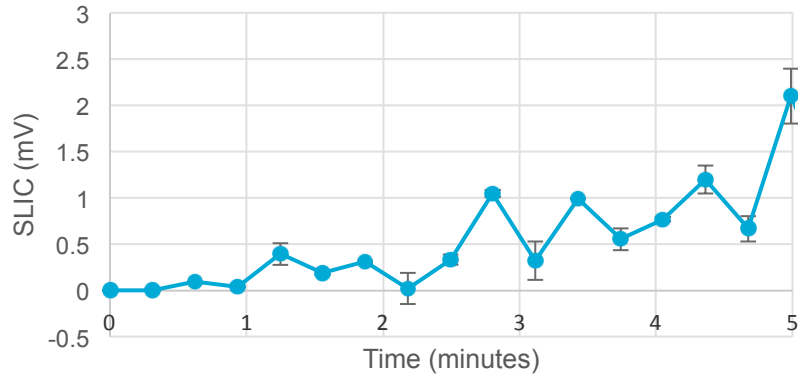


# SLIC- susceptibility

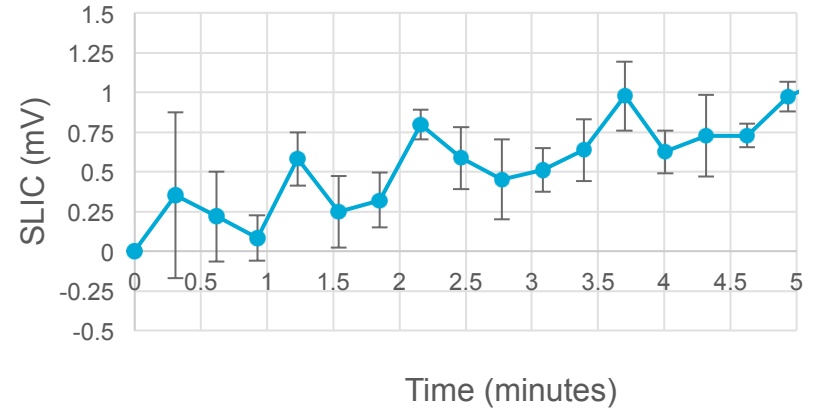


# SLIC- susceptibility

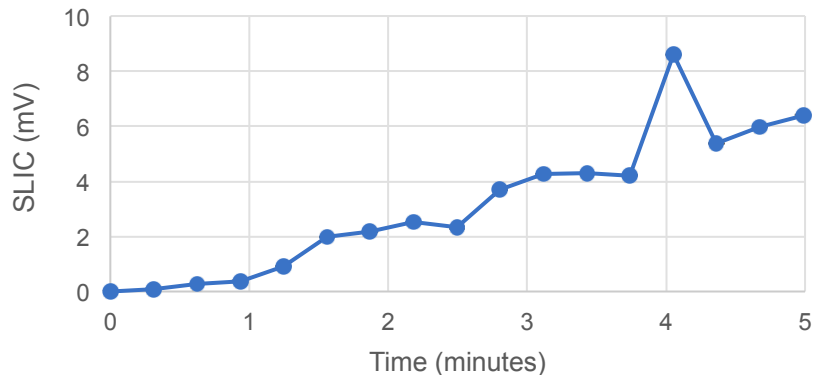
*C. albicans*



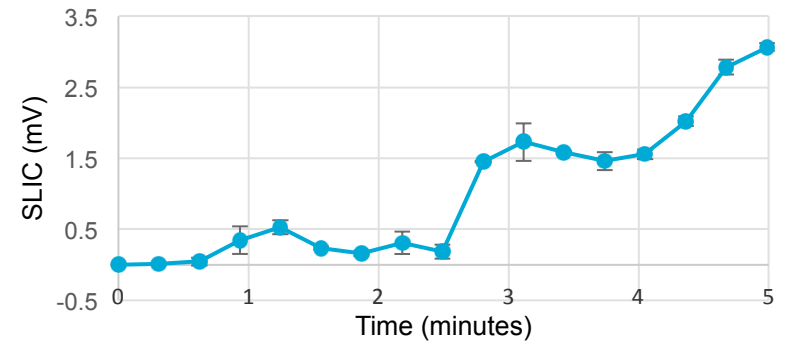
*M. smegmatis*



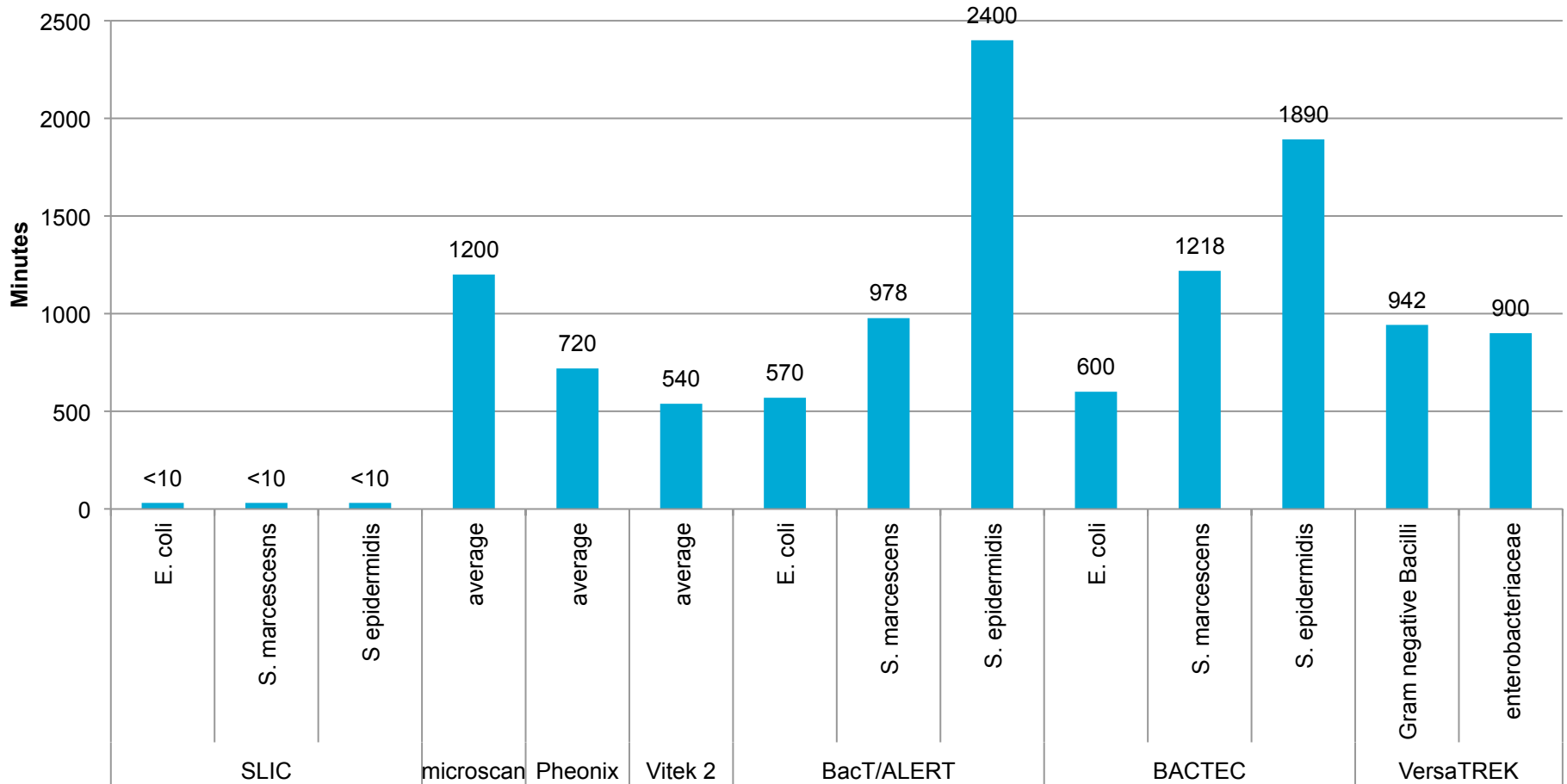
*S. aureus (MRSA)*



*S. pyogenes*





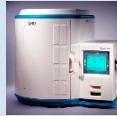

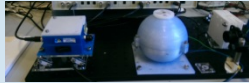


# SLIC Vs. The Market (time to positive result)



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.

# 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
<b>Orbital Diagnostics</b>	<b>SLIC</b>		<b>5000 upwards (currently- in production much less)</b>	<b>&lt;5</b>

Gram-VE Bacteria. spp	VITEK 2 Analysis Time (hours)	Single cell SLIC (CTRL-SUS)^2 (minutes)	SLIC Time (SUS-RES)^2 (minutes)
ATCC 25922 Escherichia coli	10.25	37s	
ATCC 35218 Escherichia coli	7.75	3m 44s	
ESBL Escherichia coli (Patient isolate 619)	N/A	1m 33s	2m 48s
ATCC 700603 Klebsiella pneumonia	9.00	8m 43s	2m 29s
ATCC BAA 1705 Klebsiella pneumonia	9.25	2m 10s	2m 48s
ESBL Klebsiella pneumonia (Patient isolate 603)	N/A	18.6s	1m 52s
Citrobacter Koseri	8.25	2m 10s	2m 10s
Enterobacter cloacae	9.5	5m 55s	
Enterobacter aerogenes	11.00	1m 52s	2m 48s
Stenotrophomonas maltophilia	11.75	4m 03s	3m 06s
Haemophilus influenzae	N/A	2m 10s	
ATCC 27853 Pseudomonas aeruginosa	12.00	Limited growth	
Acinetobacter Baumannii	7.75	5m 55s	
Proteus mirabilis	N/A	4m 21s	
Serratia marcescens	7.75	6m 19s	8m 06s

Yeast	VITEK 2 Analysis Time (hours)	Single cell SLIC (CTRL-SUS)^2 (minutes)	SLIC Time (SUS-RES)^2 (minutes)
Candida albicans (2.5ug Amphotericin B)	15.50	2m 29s	

Fast-growing Mycobacterium	VITEK 2 Analysis Time (hours)	Single cell SLIC (CTRL-SUS)^2 (minutes)	SLIC Time (SUS-RES)^2 (minutes)
Mycobacterium smegmatis	N/A	1m 51s	

# SLIC- universal screening

## SLIC Antimicrobial Susceptibility Testing

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

# SLIC- universal screening

## SLIC Antimicrobial Susceptibility Testing

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



# SLIC Development pathway

- Confirm specification of prototype instrument, make several and test these in our own laboratory and in the labs of clinical partners against a range of samples (field trial)
- Collate data, revise instrumentation as needed
- Develop x3 forms of instrument
  - high throughput multi-sample device for developed economies
  - POC instrument
  - Low cost variant for less developed countries
- Add capacity to identify organism

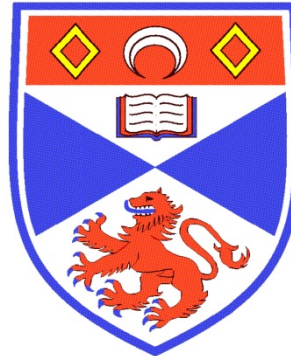


Innovative Medicines Initiative



## SLIC Team

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



University  
of  
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- 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](http://www.imi.europa.eu)



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Scottish Enterprise

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