CHAIR

UNIVERSITY OF SURREY

CHAIR

Collaborative Hub for Advancing Interdisciplinary Research

AMR
Tackling Antimicrobial Resistance

EPSRC
Engineering and Physical Sciences Research Council

Two years of the exciting CHAIR project are coming to an end. We ran seminars, workshops and other networking events to bring people together and learn more about each others' disciplines.

It has been a fascinating and fun project, involving hearing about a lot of different research (both within and outside the University), looking at new funding opportunities, providing and eating cake and also learning a lot more about Antimicrobial Resistance (AMR) and what can be done to prevent it.

We hope that the cross-disciplinary networking continues after CHAIR, to help solve important global challenges like AMR.

All the best from

Angela Day and Dr Konstanze Hild
(CHAIR Administrator and Facilitator)

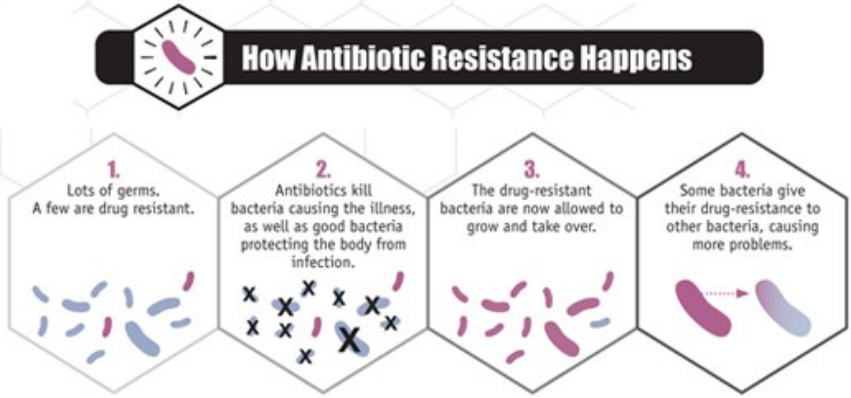
Project Investigators: Prof Rob Dorey, Mechanical Engineering Sciences, Prof Richard Curry, ATI, Electrical and Electronic Engineering (now University of Manchester), Prof Roberto La Ragione, Veterinary Medicine, Prof Johnjoe McFadden, Bioscience and Medicine, Dr Maxim Shkunov, ATI, Electrical and Electronic Engineering

The aim of the **EPSRC** funded Collaborative Hub for Advancing Interdisciplinary Research (**CHAIR**) is to **create** and **support** networks of researchers who together will develop a strong collaborative community. The focus is on developing novel strategies to detect and mitigate the emergence of antimicrobial resistance (AMR) in zoonotic pathogens. This has created some exciting funding opportunities for **engineering** and **physical scientists** to work with **biologists** and **veterinary scientists**.

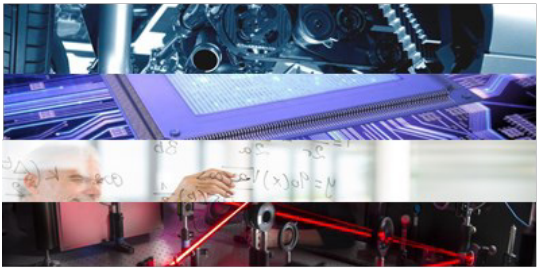
Part of a wider UK Bridging the Gaps (BtG) network.

Antimicrobial resistance (AMR) is the ability of a microorganism (like bacteria, viruses, and some parasites) to stop an antimicrobial (such as antibiotics, antivirals and antimalarials) from working against it. As a result, standard treatments become ineffective, infections persist and may spread to others. [WHO]

AMR
Tackling Antimicrobial Resistance



Engineering and Physical Sciences:



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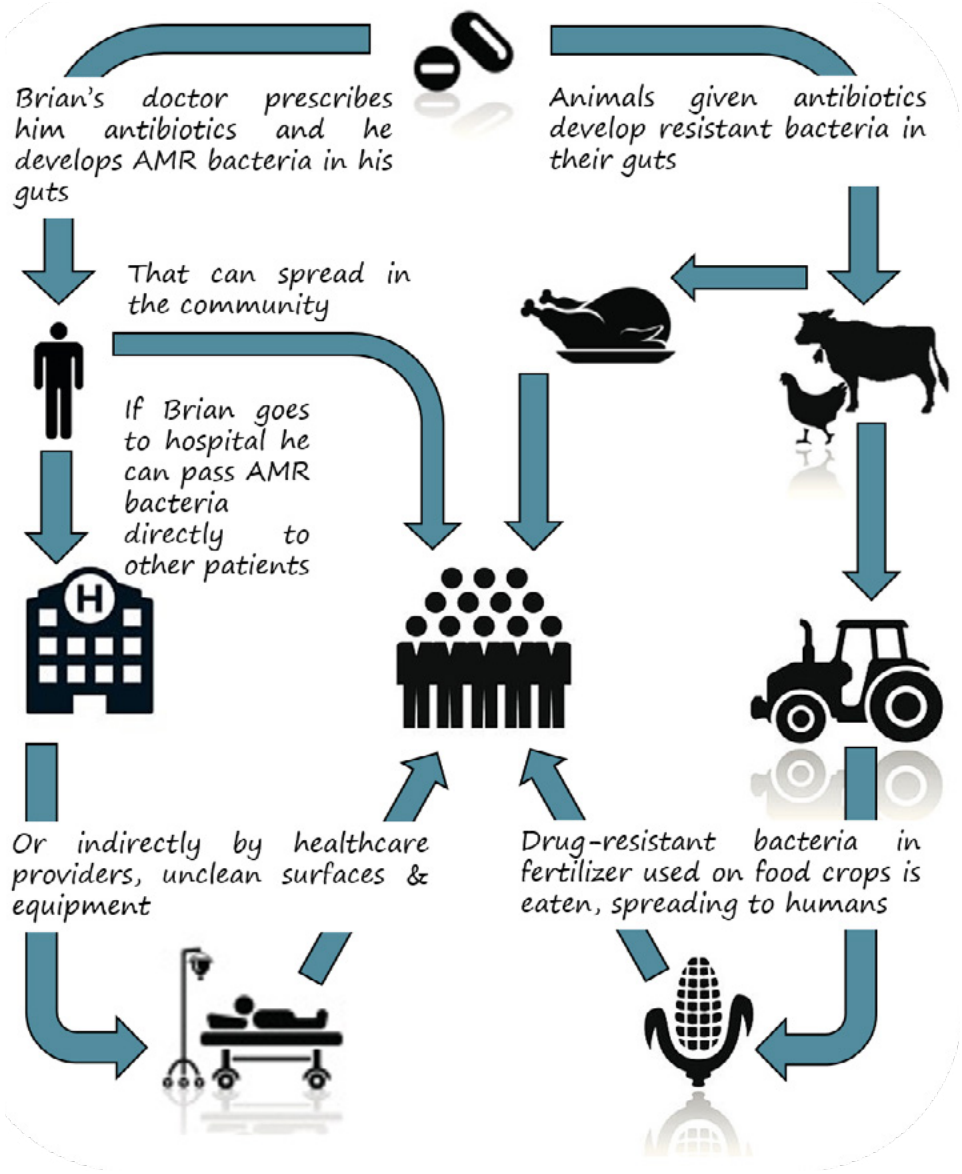
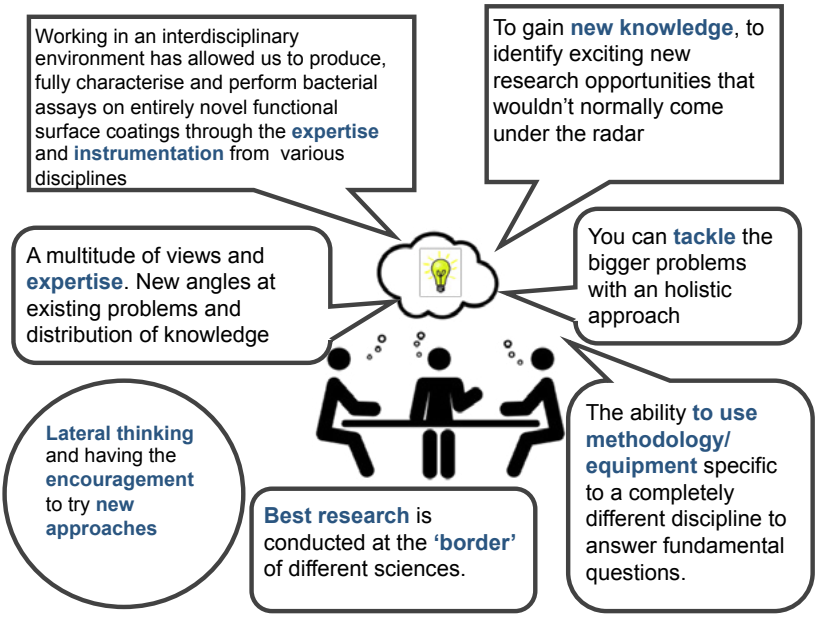
EPSRC
Engineering and Physical Sciences Research Council

The spread of antimicrobial resistance:



Collaboration: *'the action of working with someone to produce something'*

Benefits:



Challenges:

Language – same thing can be said differently in different disciplines, and different things can be said with the same name. Also mind set – engineers tend to focus on solving problems, whilst scientists tend to focus on understanding the mechanisms and new discoveries.

Understanding each other can sometimes be problematic.

Mostly – language, terminology, and sometimes, peoples' ability to convey specific technical details in a very comprehensive manner to non-experts in the field.

Communication across technical fields and working with biological agents outside of a conventional microbiology lab.

Language and terminology but also thorough enough understanding of the problems to gauge if new approaches are feasible.

It can be difficult to understand and appreciate the challenges and state-of-the art in fields outside of one's area of expertise. As a result, studies may take longer than anticipated or may not be possible at all.

Getting everyone to agree on the semantics and priorities of different subjects. Each area has its own particular way of working.

AMR challenges:

- improve the knowledge and **understanding of antimicrobial resistance**
- conserve and steward the **effectiveness of existing treatments**
- stimulate the **development** of **new** antibiotics, **diagnostics** and novel therapies

Review on Antimicrobial Resistance

Tackling drug-resistant infections globally

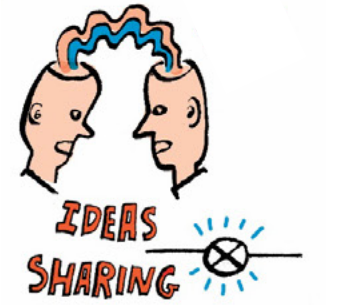
By 2050 ❝ without policies to stop the worrying spread of AMR, today's already large 700,000 deaths every year would become an extremely disturbing 10 million every year. ❞

Lord O'Neill
The Review on Antimicrobial Resistance, May 2016

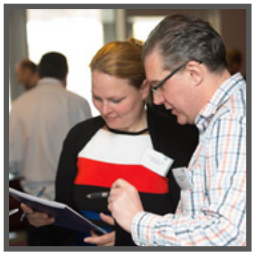
❝ Antimicrobial resistance poses a catastrophic threat. If we don't act now, any one of us could go into hospital in 20 years for minor surgery and die because of an ordinary infection that can't be treated by antibiotics. And routine operations like hip replacements or organ transplants could be deadly because of the risk of infection. ❞

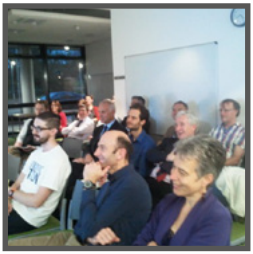
Dame Sally Davies
Chief Medical Officer UK

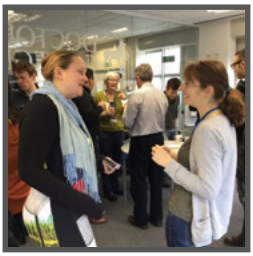
Through **seminars**, workshops and small project funds **CHAIR** has been **bridging the gap** between **engineering** and **physical sciences** on one side and **antimicrobial resistance** on the other side to come up with **innovative solutions** to the **global problem**.



Seminars, sand-pits, cafes, work-shops, networking events.







CHAIR events:

2015:

4th November: **Launch** of Chair – Current issues in **AMR**

13th November: **Rapid Diagnostics** workshop

10th December: **Sensing:** 3D metabolic imaging – the challenge going from tissue scale to single bacteria (*Dr Ian Gilmore, NPL*) + an engineering view on sensing (various short talks)

2016:

22nd January: **EHealth:** from sensing, the IoT to big data – digital innovation in animal health (Veterinary Science, Business School)

23rd February: **Big data** and modelling in healthcare (Computer Science, Health Care Management and Policy)

11th March: **Antibiotic resistance** in bacteria: the problem with TB (Bioscience)

12th April: **Sandpit:** Collaborative research funding event

6th June: Tackling antimicrobial resistance: human and animal **behaviour** (Veterinary Science, Psychology)

30th June: Collaborative AMR session at the Young persons' University Summer School

11th July: A systems based **one health** approach (*Dr Sid Thakur, North Carolina State University, Visiting Scholar*) + updates from two CHAIR projects concerning diagnostics

18th July: Repurposing **glucose monitoring** technology for detecting DNA of infectious organisms (*Prof Kirill Alexandrov, Molecular Warehouse*) + update from CHAIR biofilm project

28th September: **Sandpit II**

10th November: Participation in: Discoveries on your doorstep: 'Science Delivering **Global Wellbeing**' (community event at the University)

16th November: Researcher Café

18th November: CHAIR stand on European Antibiotic Awareness Day

24th November: (External presentation by CHAIR) The benefits and challenges of interdisciplinary research, talk at IFSTAL PhD Symposium, University of Reading

1st December: The **global challenge** of antimicrobial resistance (Victoria Wells, **Antibiotic Action**)

13th December: Pathogenic Bacteria in the **Environment** (*Prof Liz Wellington, University of Warwick*)

2017:

1st February: Researcher Café

22nd February: Stand at the opening of the 'Innovation for Health Learning Laboratory'

29th March: **Biofilms**, DNA and microbial pathogens: a market place for exchange of antimicrobial resistance? + CHAIR Projects: **Antifouling Coatings to Prevent Biofilm Formation, SPIDERS: Surface Printing to Investigate Drug Effects on Real Surfaces**

25th April: Bridging the Communications Gap between FEPS and FHMS researchers: Easter School

11th May: **Modelling and Big Data: AMR data in time and space, Animal- Human-Environment ESBL transfers, Modelling mycobacterial persistence**

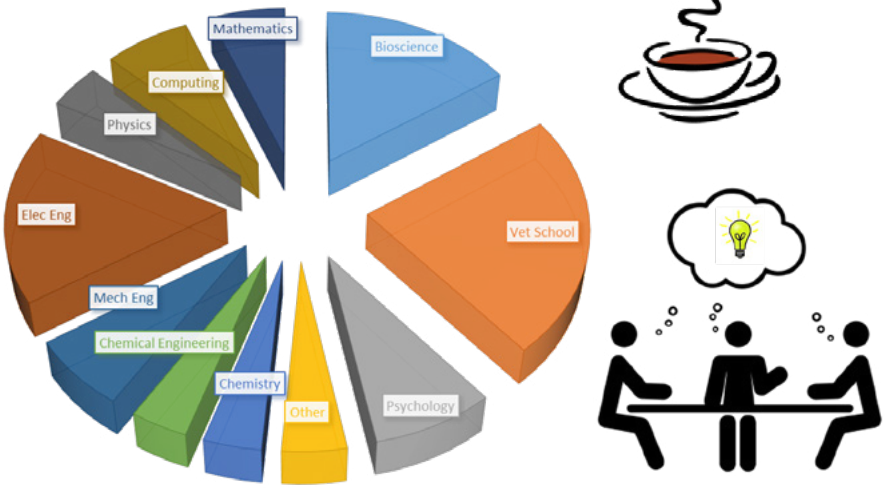
8th June: **Sensing and Pharmacokinetics: Towards selective detection of AMR bacteria with a disposable electrical sensor, Understanding the Pharmacokinetics of antibiotic implants for veterinary applications**

14th/15th June: National Research Symposium (BtG), University of Warwick

18th July: New and emerging threats of AMR from a global perspective. *Dr Sid Thakur, North Carolina State University*

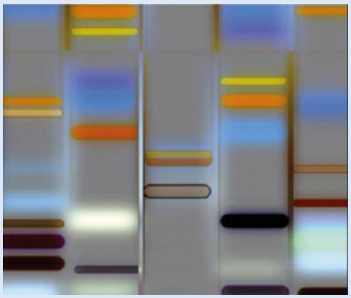
13th September: **CHAIR Celebration Event**, CHAIR projects + The Economics of Antimicrobial Resistance, and Solving the Threat, *Lord O'Neill*

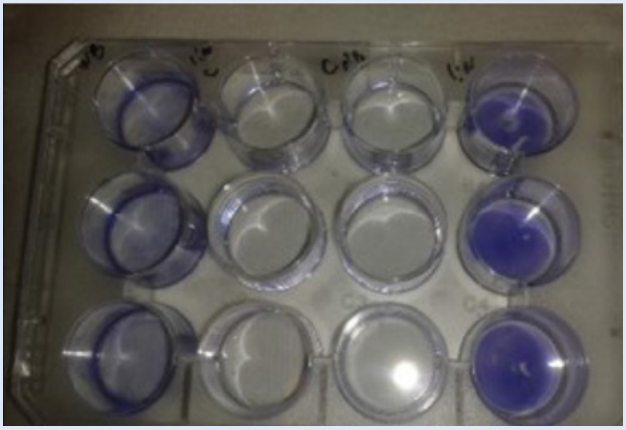
Participation:

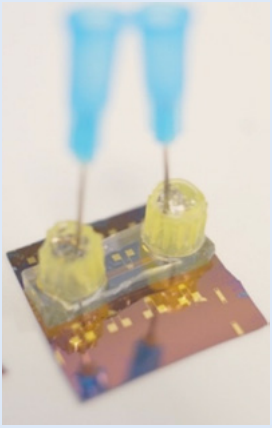


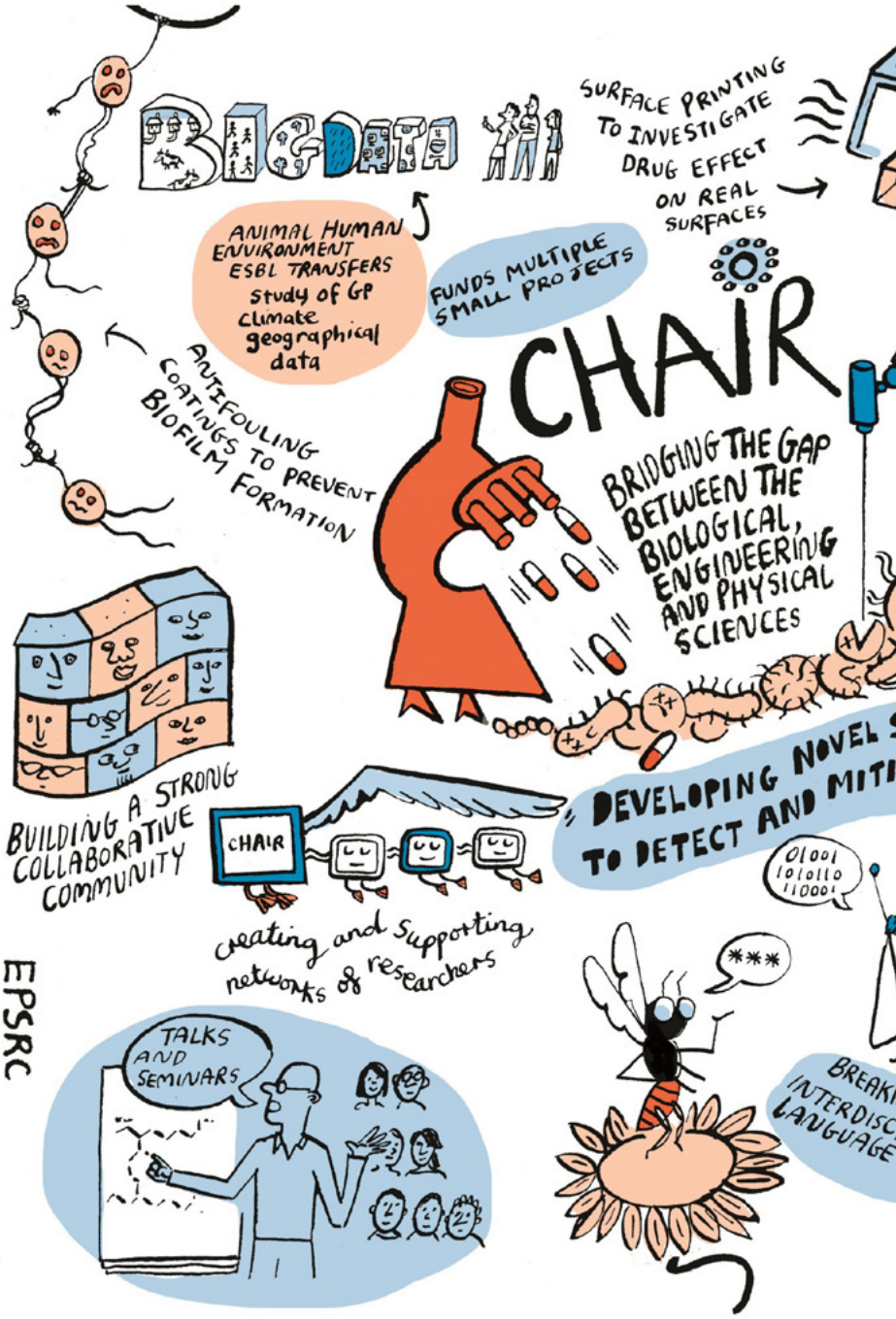
More than 600 attendees at our internal events, additional participation in outreach events and external AMR related events, the CHAIR network has over 100 members with a multitude of expertise.


Advanced Technology Institute








BIG DATA
ANIMAL HUMAN ENVIRONMENT ESBL TRANSFERS study of GP climate geographical data
SURFACE PRINTING TO INVESTIGATE DRUG EFFECT ON REAL SURFACES
FUNDS MULTIPLE SMALL PROJECTS
CHAIR
BRIDGING THE GAP BETWEEN THE BIOLOGICAL, ENGINEERING AND PHYSICAL SCIENCES
ANTIFOULING COATINGS TO PREVENT BIOFILM FORMATION
BUILDING A STRONG COLLABORATIVE COMMUNITY
CHAIR
creating and supporting networks of researchers
EPSRC
TALKS AND SEMINARS
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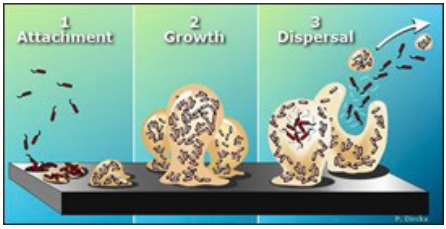
SPIDERS
SELECTIVE DETECTION OF AMR BACTERIA USING DISPOSABLE NANOWIRE ELECTRICAL SENSOR
UNDERSTANDING THE PHARMACOKINETICS OF ANTIBIOTIC IMPLANTS FOR VETERINARY APPLICATIONS
ANTIBIOTIC RESISTANCE
Happens when bacteria change and become resistant to the antibiotics used to treat infections they cause
STRATEGIES
GATE AMR
IDEAS SHARING
SANDPIT EVENTS
NH
FUTURE FUNDING AVAILABLE
NG DOWN
IPLINARY
BARRIERS
veronicawoodillustrations.co.uk

Projects: The funded projects looked into research on biofilms, better detection methods, modelling and further understanding of tuberculosis.

Biofilms: Biofilms are surface attached populations of microbes, consisting of either single or multiple species, which are surrounded by a self-produced extracellular matrix. The composition of the extracellular matrix differs depending on the species within the biofilm but typically comprises of DNA, proteins and polysaccharides, and usually accounts for more than 90% of the dry mass of a biofilm. It allows cells to remain hydrated and metabolically active by trapping nutrients and liquid near the bacterial cells. It also reduces access of larger molecules including antimicrobials and disinfectants, leading to increased bacterial persistence and reduced efficacy of antibiotic treatment,



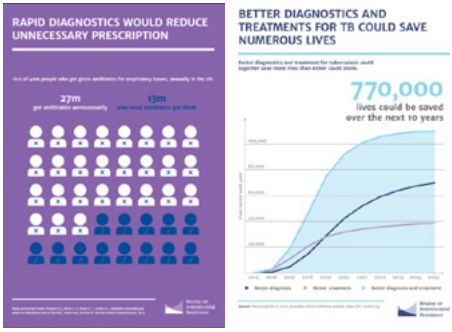
http://biofilmbook.hypertextbookshop.com/public_version/contents/chapters/chapter001/section001/blue/page001.html

and is structurally important, maintaining the shape of the biofilm and ensuring the biofilms cohesion. Next to a protective environment, biofilms may also facilitate the transfer of antibiotic resistance genes between populations within the biofilm community.

Antibiotic stewardship:

Diagnostics-Detection-Drug Delivery

Antibiotics are often prescribed when they aren't necessary. Faster and more selective detection methods of pathogens and better monitoring of drug delivery and drug taking will be a huge step towards better antibiotic stewardship and thus helping to prevent the antimicrobial apocalypse



From: Review on Antimicrobial Resistance (Lord O'Neill) https://amr-review.org/Publications.html

Modelling:

Mathematical **Modelling** helps to understand more about bacteria, drug delivery and health data. What role does the environment play in passing on antimicrobial resistance and which traits bacteria have that are more or less susceptible to antibiotics?

$$\dot{L}(t) = g(t)L(t)$$

$$\dot{g}(t) = \theta(\mu_g - g(t)) + \sigma\dot{W}_t(t)$$

$$T = t_0 + \frac{1}{\mu_g}\log\left(1 + \frac{\Delta}{L_0}\right)$$

Antifouling Coatings to Prevent Biofilm Formation (Chemistry, Physics, NPL, Bioscience, Veterinary Medicine)

Project Summary: Biofilms form when bacteria attach to surfaces and provide excellent environments for bacteria to develop resistance against antibiotics. Many health risks are associated with biofilms. This project investigates the modification of surfaces (glass and metals that are often plagued by biofilms) by using a combination of reactive polymers and chemical functional groups in an approach that offers high versatility. Modified surfaces are exposed to bacteria (a fluorescent strain of E. coli) and the extent of fouling (biofilm formation) is determined by measuring the amount of (i) bacteria, (ii) live bacteria, and (iii) all biological material (including adhesion-promoting secretions) on the surfaces. Results show that the modification protocol provides well-defined coatings with tuneable thickness and chemical and physical properties. The project has further identified suitable chemical functional groups to reduce fouling on glass and intends to show that optimised antibiofilm properties can easily be bestowed on metal surfaces.

Value: £9000, 9 RA months and 2 summer students
Main achievement: Developed and tested large number of functional surfaces with respect to biofilm formation.

The team: Dr Peter Roth, Chemistry, Prof Joe Keddie, Physics, Dr Jane Newcombe and Dr Suzie Hingley-Wilson, Bioscience and Medicine, David Truman, Physics

Other collaborators: (past and present): Prof Roberto La Ragione, Veterinary Medicine, Dr Paulina Rakowska, NPL Niki Bardi, Physics, Dr Jenny Ritchie, Bioscience and Medicine, Dr Izabela Jurewicz, Physics

NPL National Physical Laboratory

PI: Dr Peter Roth, Chemistry

Peter's main research interests are the synthesis of multi-functional polymers and polymer nanoparticles and gaining a better understanding of structure–property relationships. A focus lies on biologically compatible polymers and "smart" materials that respond reversibly to changes in environmental conditions.

SPIDERS: Surface Printing to Investigate Drug Effects on Real Surfaces

(Bioscience, Mech Engineering, NPL)

Project Summary: Bacterial **resistance** to **antimicrobials** is exacerbated by their propensity to **form biofilms** on inorganic and organic surfaces. Bacterial resistance or tolerance of antimicrobials has been studied in 'flow-cells': compartmentalised devices in which bacteria are suspended and grown and to which antimicrobials can be introduced in a controlled manner. Introducing the **real world into flow-cells** and recreating natural bacterial biofilms in them is difficult.

We have demonstrated that we can grow biofilms within our bespoke chambers 3D printed onto surfaces of interest and that we can see biofilm dispersion through connecting bridges (using rezasurin which measures metabolism colourmetrically).

These bespoke chambers provide the scientific community with an adaptable platform with which to dynamically observe biofilm dispersal and formation.

Value: £3500, 3 RA months
Main achievement: Developed and printed flow-cells to study real world biofilms.

The team: Prof Rob Dorey, Mechanical Engineering Sciences, Dr Jane Newcombe and Suzie Hingley-Wilson Bioscience,

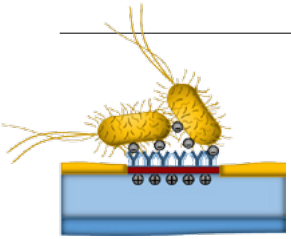
Other collaborators: Prof Mark Chambers Veterinary Science, Dr Paulina Rakowska, NPL, Neophytos Hadjichristou , Mechanical Engineering Science

NPL National Physical Laboratory

P I: Dr Suzie Hingley-Wilson, Bioscience and Medicine

Suzie's main research interests are the host-pathogen interaction in tuberculosis (TB) and antimicrobial resistance (AMR). She and her colleagues conduct multidisciplinary research, much at the single cell level, looking at antimicrobial resistance and persistence often in the context of the host cell. They aim to identify novel mechanisms and immunotherapeutic targets by taking a global approach utilising microfluidics, mycobacterial mutagenesis, patient and environmental samples.

TB and AMR remain major global health problems and her research aims to understand why, and what effect the host-pathogen interaction has on these issues.



Towards selective detection of AMR bacteria with a disposable electrical sensor

(**Electrical and Electronic Engineering**, Veterinary Medicine, Chemistry, **Bioscience**)

Project Summary: The goal of the project is to address challenges in rapid, direct diagnostics in the field of AMR research. The aim is to demonstrate the feasibility of selective detection of AMR bacteria with a low-cost nanomaterials based sensor with electrical readout. Nanowire field effect transistors will serve as transducer elements functionalised with antibodies to selectively bind resistant bacteria and promote changes in the electrical output. It is envisioned that in the future, arrays of nanowire-biosensors equipped with biological and chemical probes will be capable of almost instantaneous mapping of biological species, thus advancing the AMR detection capabilities.

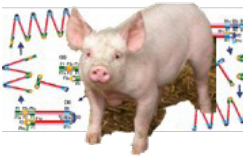
Value: £9500, 10RA months
Main achievement: Fabricated Sensors that can distinguish between different types of bacteria.

The team: Dr Ruth Rawcliffe and Dr Maxim Shkunov, ATI, Electrical and Electronic Engineering Other Collaborators (past and present): Prof Roberto La Ragione, Veterinary Medicine, Dr Daniel Whelligan, Chemistry, Dr Claudio Avignone Rossa, Biosciences and Medicine, Dr Charles Opoku, Electrical and Electronic Engineering

PI :Dr Maxim Shkunov, Electrical and Electronic Engineering

Maxim's focus research area can be described as "Printed electronics with solution processable nanomaterials and organic semiconductors".

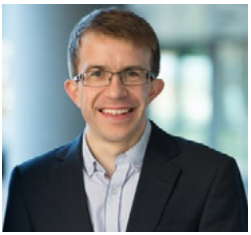
This serves as a platform for the development of novel devices for large area electronic applications with strategic overlap with EPSRC directions in Energy, Environment and Health.



Towards low cost very rapid diagnostics

(Veterinary Medicine, **Electrical and Electronic Engineering**)

Project Summary: Rapid and sensitive pathogen detection is a key component of disease control. Combining state-of-the-art biological and engineering techniques provides great potential to improve this detection. A precedent has been set combining the natural ability of certain enzymes (polymerases) to amplify the genetic material of pathogens to detectable levels at isothermal temperatures (Loop-mediated isothermal amplification, LAMP). Current limitations with these techniques include cost effectiveness and reliability of test readouts. In this pump-priming project we will optimise the production and detection of LAMP products using simple, low cost fluorescence detection.



P I: Dr Dan Horton, Veterinary Medicine

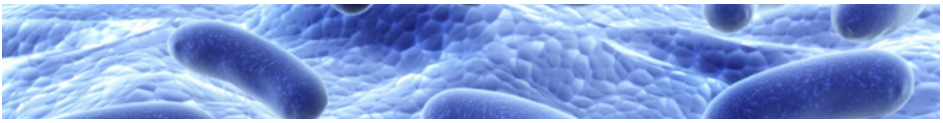
Dan's research interests are focussed on reducing the animal and human health burden caused by diseases that cross species barriers.

Researcher: Dr Mike Hornsey, Veterinary Medicine

Other collaborators (past and present): Prof Richard Curry, Electrical and Electronic Engineering, Prof Roberto La Ragione and Dr Elizabeth Royall, Veterinary Medicine, Dr Ruth Rawcliffe, Electrical and Electronic Engineering, Dr Martha Betson, Veterinary Medicine, Dr Konstanze Hild and Dr Andy Prins, Physics

Value: 11 RA months, £500

Main achievement: Developed an assay that can specifically detect a certain zoonotic pathogen and developed ideas for the miniaturisation of the testing platform.



Non-invasive testing for antibiotic drugs

(Chemistry, Veterinary Medicine, NPL, NHS)

Project Summary: Treatment of **tuberculosis** requires taking multiple antibiotics for several months. Failure to stick to the full course of treatment is a risk factor in the emergence of antibiotic resistance, which in the case of TB is difficult and expensive to treat. Clinicians need a rapid and cheap method of measuring antibiotics and their metabolites in patients where they suspect they are not adhering to treatment.

The project successfully detected the antibiotic Isoniazid in TB patients non-invasively and is now exploring other TB drugs and making further improvements to the detection.

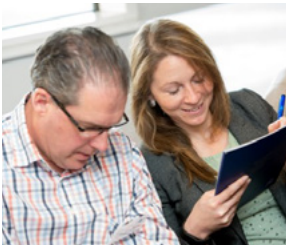
The team: Dr Catia Costa, Ion Beam Centre, Mahado Ismail and Dr Melanie Bailey, Chemistry,

Other collaborators: Prof Mark Chambers, Veterinary Medicine, Dr Josephine Bunch, NPL, Dr Vladimir Palitsin, IBC, Electrical and Electronic Engineering, Dr Mark Atkins and Dr Sarah Menzies, NHS

NPL National Physical Laboratory

PI: Dr Melanie Bailey, Chemistry

Melanie's research focusses on developing and applying new methods in mass spectroscopy and in ion beam analysis



Value: £6000, 2 RA months

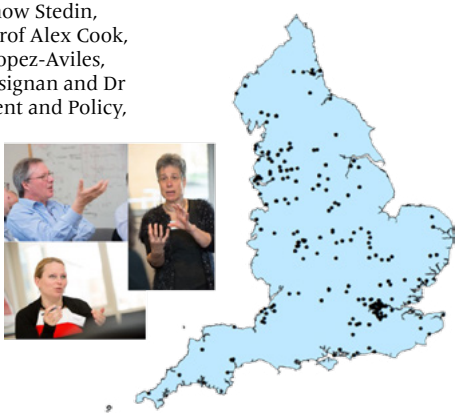
Main achievement: Being able to non-invasively detect the TB antibiotic Isoniazid in patients..

AMR data in time and space, Animal-Human- Environment ESBL transfers

(Veterinary Medicine, Mathematics, Engineering)

Project Summary: ESBLs [Extended spectrum beta-lactamase (enzymes)] can be found in humans, animals and the environment and have been extensively researched in each field. This proof of concept study aims to use readily available data from various fields, e.g. GP data, vet practice data, climate data, geographical data, and combine this to answer the main question: How do **ESBLs transfer between animals-human and environment.** We have started by combining geographical data, GP data and environmental data. Despite different formats, we have found a geographical grid that seems to be able to combine all types of data and allows for spatial-temporal analysis. Subsequent to the acquisition of veterinary data, specific drivers for transfer of ESBLs will be modelled in more detail.

The team: Dr Ingrid den Ujil, Veterinary Medicine, (now Stedin, The Netherlands), Prof Gianne Derks, Mathematics, Prof Alex Cook, Veterinary Medicine. Other Collaborators, Dr Alma Lopez-Aviles, Centre for Environmental Strategy, Prof Simon de Lusignan and Dr Stacey Shinneman Centre for Health Care Management and Policy, Vivek Bokinala, Computer Science



Value: £3000, 2RA months
Main achievement: Combined geographical data, GP data and environmental data to allow for spatial-temporal analysis.

Understanding the Pharmacokinetics of antibiotic implants for veterinary applications

(Electrical and Electronic Engineering, Veterinary Medicine)

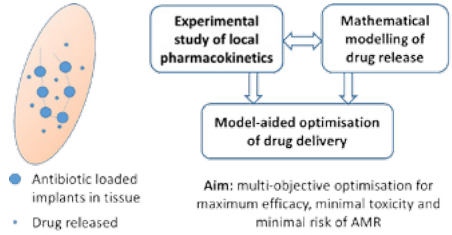
Project Summary: Antibiotic implants are widely used for treating surgical site infections in veterinary and human medicine. However, there is a paucity of information available regarding the **pharmacokinetics** at site of action and this poses a serious risk for the development of antimicrobial resistance. In this project, pharmacokinetic experiments have been conducted in biological tissues, and the data generated have been used to support the development of a prototype computational model. The preliminary results demonstrate the importance of understanding pharmacokinetics in local antibiotic delivery through implants, and the great potential of the integrated experimental-computational approach. The results also stimulated a plan for more comprehensive research in the future, hopefully leading to **optimised drug delivery** with minimal risk of antimicrobial resistance, while achieving maximal efficacy.

P I: Dr Tao Chen, Chemical Engineering

Tao's research focusses on process systems engineering, in particular model parameter estimation, model-based process optimisation, control and fault detection/diagnosis and Process chemometrics, including the mining of process data and the calibration of advanced process sensors.

Collaborators: Prof Roberto La Ragione and Dr Mike Hornsey, Veterinary Medicine, Dr Eirini Velliou, Chemical and Process Engineering

Value: £3000, 3RA months
Main achievement: Established a working framework of the combination of experimental study with mathematical modelling to further explore drug delivery.



Modelling mycobacterial persistence

(Computer Science , Bioscience and Medicine)

Project Summary: The nature of the factors controlling **mycobacterial growth** and their relationship with persistence is a fundamental question yet to be answered. McFadden's lab has discovered the evidence of the loss of phenotypic inheritance that causes high rates of persistence, through tracking the growth of bacterial cells over several generations in a microfluidic device using high throughput single-cell time-lapse microscopy and computer-aided image analysis. In this project we aim to establish a model, involving epigenetic inheritance of stochastically-fluctuating variables measured in the experiments, through multi-objectives optimization to replicate the mechanism of cell growth as well as the phenomena when **persisters** occur.

The approach is to use a numerical simulation that is easily adaptable to different mathematical models in order to find a good fit to the experimental data. Given constraints for the cell growth parameters in the model, machine learning and optimization techniques are used to find the parameters that best fit the experimental data, subject to the given constraints. Importantly, the parameter optimization is model-independent to as large a degree as possible, allowing for rapid development of new models with very little modification to the underlying system.

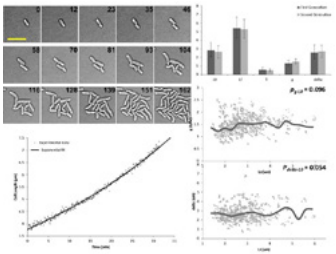
PI: Dr Lilian Tang, Computer Science

Lilian's focus research interests are Computer vision, Image processing, Machine learning, Natural language processing.

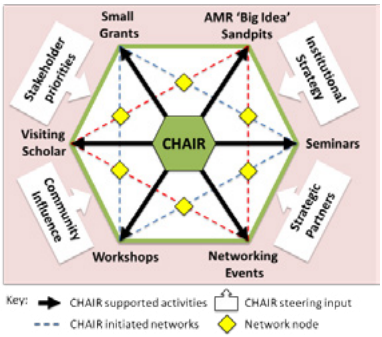
Collaborators: Prof Johnjoe McFadden, Suzie Hingley Wilson and Dr Andrea Rocco, Bioscience and Medicine, Daniel Mansfield, Mathematics

Value: Project student

Main achievement: A mathematic model was implemented. The model was able to replicate most of the correlations between mother vs. daughter and daughter vs. daughter which are consistent with the experimental data.



CHAIR



Towards the future:

Establishing further networks:

CHAIR established networks within the university but also at a national and international level, allowed researchers to undertake proof-of-concept studies and will thus enable them to further deepen their collaborations in this and other important global challenges.

Further Funding opportunities:

AMR
Tackling Antimicrobial Resistance

Outreach/ public awareness:

ANTIBIOTIC GUARDIAN

ANTIBIOTIC ACTION

Ongoing Challenges:

At Surrey:

Innovation for Health: 'The healthcare sector is increasingly driven by technology. By 2030, healthcare delivery will rely on rapidly assimilating and analysing large quantities of data.

We aim to lead in the use of data for identifying trends and emerging threats in infectious disease and for improving outcomes for people who are living with chronic conditions e.g. in mental health, diabetes and cancer. Through applications in veterinary medicine, our aims is to use transformational digital and data analytics tools to advance the wellbeing of animals in developing and developed countries.'

UNIVERSITY OF SURREY

EPSRC
Engineering and Physical Sciences Research Council

CHAIR

Supporting work across the university to tackle antimicrobial resistance

The Collaborative Hub for Advancing Interdisciplinary Research (CHAIR):

» *educates and **informs** on the antimicrobial resistance (AMR) issue*
» ***develops** novel strategies to detect and mitigate the emergence of AMR in zoonotic pathogens*

Our activities:

» *develop researcher **networks***
» ***fund** AMR research pilots*
» *engage international experts*
» *work with stakeholders*

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NPL National Physical Laboratory

Veterinary Medicines Directorate

Universidade de São Paulo

defra Department for Environment Food and Rural Affairs

NC STATE UNIVERSITY College of Veterinary Medicine

The Royal Surrey County Hospital NHS Trust