i-sense Annual Report

2019

i-sense

UKRI Engineering and Physical Sciences Research Council

Working collaboratively to track, test, and treat infectious diseases

Welcome

Prof Rachel Mckendry

Prof of Biomedical Nanotechnology, UCL, and Director of i-sense EPSRC IRC

Welcome to the 2019 i-sense annual report. Our interdisciplinary research programme aims to engineer a new generation of agile and globally impactful early warning sensing systems for infectious diseases and antimicrobial resistance. We are harnessing the power of mobile phones, biomedical engineering, nanotechnology, genomics and big data to track, test and treat outbreaks much earlier than ever before. Highlights from the last year include landmark publications in *Nature* and *Nature Microbiology* on the challenges and opportunities for smartphone-connected REASSURED diagnostics, as well as an important breakthrough in in-vivo diagnostics published in *Nature Nanotechnology*. Our tools and technologies are being co-created with and increasingly being used by end users. Public Health England have adopted our machine learning algorithms for online searches as part of their weekly flu surveillance reports. The Africa Health Research Institute has adopted our data dashboards and mHealth tools for service delivery and to improve quality assurance of testing, at the epicentre of the HIV epidemic in South Africa. Moreover, our brilliant young researchers have worked with leading groups around the world including MIT and Population Services International through our Mobility Fellowship scheme. This year we held our first careers day and were delighted to welcome back our alumni who have gone onto careers in Microsoft, GSK, and academia in the UK, Switzerland and India. It was an incredibly inspiring day. Please do get in touch if you would like to find out more or work with us.

Prof David Heymann

Chair, i-sense Advisory Board, Prof of Infectious Disease Epidemiology at the London School of Hygiene & Tropical Medicine, and former Head of Centre of Global Health Security at Chatham House

As i-sense Advisory Board Chair, and along with the members of the Board, we would like to congratulate all those who have worked on the project since its inception. i-sense members continue to build extraordinary collaborations both nationally and internationally, bringing together world-class expertise to reach a common goal. We have had the immense pleasure of watching as the small team in 2013 developed into a truly interdisciplinary network of more than 150 working on rapid diagnostic testing, machine learning, big data, and app and dashboard development. We look forward to watching the project grow from strength to strength.

Katherine Freeman

Senior Portfolio Manager, Healthcare Technologies, EPSRC

i-sense is one of four Interdisciplinary Research Collaborations (IRCs) that the healthcare technologies theme at EPSRC supports. IRCs are centres of internationally-acknowledged scientific and technological excellence, with sufficient critical mass to make a real impact in areas of key future industrial relevance to the UK. The healthcare IRCs have huge potential for the UK scientific agenda in healthcare sensing and i-sense is revolutionising how we identify and respond to outbreaks of infectious diseases.

The i-sense IRC is helping to deliver our EPSRC priority of transforming healthcare, which is highlighted in our 2019 Delivery Plan. We are looking to invest in research that delivers the new materials, new sensors and imaging modalities, novel analytical techniques and innovation needed to improve prediction, diagnosis and treatment of disease that will deliver better quality of life and ensure higher standards of affordable healthcare.

About i-sense EPSRC IRC

The i-sense project supports world-class, interdisciplinary research and innovation aimed at engineering a new generation of early warning sensing systems to identify outbreaks of infectious disease much earlier than ever before, helping people gain faster access to care and protecting populations.

We want to help people benefit from faster diagnosis, and better access to treatment and care that could save their lives. We aim to help free up time for healthcare workers, allowing them to concentrate on improved service delivery and building more sustainable models of community care. We are working to help public health systems benefit from real-time information to improve outbreak response. We are developing collaborations with governments and policy makers to ensure science and legislation evolve together.

Our team is the most important part of our project and by investing in our people, research excellence will naturally flow. Our diverse team is made up of biochemists, chemists, physicists, engineers, computer scientists, microbiologists, statisticians, bioinformaticians, architects, philosophers, clinicians, and epidemiologists who are working collaboratively to achieve our vision. i-sense has grown from a small team in 2013 to a network of more than 150 people across the UK and 19 overseas partners across Europe, USA, South Africa, Asia and Australia.

Our key team work across University College London, Imperial College London, Newcastle University, London School of Hygiene and Tropical Medicine, University of Surrey, Africa Health Research Institute, Glasgow Caledonian University, Royal College of General Practitioners Research Surveillance Centre and Public Health England. Our ‘Plus Awards’ also include Strathclyde University, Columbia University, Cambridge Life Science Ltd, and iXscient Ltd.

The work of i-sense is made possible through funding from the Engineering and Physical Science Research Council (EP/K031953/1 and EP/R00529X/1). i-sense is one of four EPSRC Interdisciplinary Research Collaborations funded to build critical mass in disruptive sensing systems for healthcare.

Contents

Our research themes and impact

Upon receiving Next Steps funding for i-sense EPSRC IRC, we proposed a step change to engineer more 'agile' systems that are rapidly adaptable to different diseases, antimicrobial resistant strains and different countries. The aim is to track, test and treat infectious diseases.

Track

We use self-reported symptoms via social media and web searches to help track outbreaks of infectious disease, potentially before people visit their doctor and in resource-limited settings.

Our AI algorithms for influenza surveillance have been adopted by Public Health England to include in their weekly and annual influenza surveillance reports. This is one of the first examples of AI being adopted by Public Health England.

Our methods have also been applied to a variety of problems including detecting disease outbreaks at mass gatherings, estimating the effectiveness of an influenza vaccine for children, and estimating the virulence of influenza.

Test

Accurate diagnostic tests play a central role in early disease detection, informing treatment and public health strategies in the UK and resource-limited settings.

We are building smartphone-connected diagnostic tests to support front-line healthcare workers and self-testing, with real-time data linkage capabilities. Our low-cost device prototypes include a point-of-care test that uses ultra-sensitive nanomaterials to detect the early stages of HIV, antimicrobial resistance and a multiplexed test for Ebola serology.

Our portable mHealth tools and protocols have been adopted for quality assurance of HIV rapid tests by the Africa Health Research Institute, supporting healthcare workers and the local community by reducing the risk of false test results.

Treat

We are creating online care pathways and visualisation tools to link patients to treatment and map disease 'hot spots' to help inform health interventions.

Our mobile app, co-created with the Africa Health Research Institute, has been piloted with 30 participants in a local health clinic demonstrating the feasibility and acceptability of self-testing and linkage to care using mHealth technologies.

Our data dashboards, co-created with Africa Health Research Institute, were used in a HIV Treatment as Prevention trial and adopted for service delivery of the population health intervention platform.

Our data mapping tool looks at mobile network coverage against other publicly available data, such as population density and location of health facilities. This work was published in *Nature* and has led to ongoing collaborations with the head of the Africa Centre for Disease Control and Prevention and World Health Organization TDR to inform the rollout of mHealth technologies across the African continent.

01 Research highlights

Our international collaborations and partners in 2019

United Kingdom

- University of Surrey School of Veterinary Medicine
- University of Strathclyde
- Public Health England
- Google
- Positive East
- Connected Diagnostics
- Cambridge Life Sciences Ltd
- GSM Association
- Mologic
- Oxford Nanopore
- Microsoft
- Royal College of General Practitioners Research Surveillance Centre
- UCLH NIHR Biomedical Research Centre
- The Francis Crick World Influenza Centre
- NIHR London Diagnostic Evidence Cooperative
- iXscient ltd

USA

- Massachusetts Institute of Technology
- United States Army Medical Research Institute of Infectious Diseases
- Columbia University
- University of California, Los Angeles

Netherlands

- QVQ

Switzerland

- WHO TDR
- Foundation for Innovative New Diagnostics

Myanmar

- Population Services International

South Africa

- Africa Health Research Institute

Track

Aim: Develop accurate and agile online syndromic surveillance systems to track infectious disease outbreaks, potentially even before people visit their doctors and in remote locations.

Tracking flu in real-time

Since the beginning of the i-sense programme, our researchers have been focusing on alternative approaches for influenza surveillance that could complement traditional syndromic surveillance.

A key outcome of the research is the development of a software system that collects online search data and deploys the previously published machine learning models to compute and visualise influenza rate estimates. This tool, named 'i-sense flu' (fludetector.cs.ucl.ac.uk/), currently provides daily influenza-like-illness (ILI) rate estimates for England based on online search data. The model is trained on historical ILI rates obtained by the Royal College of General Practitioners and uses web search data from Google.

In an exciting new development for i-sense, these complementary ILI rate estimates have now been included, for the first time, in the weekly UK flu reports by Public Health England (PHE) for the 2019/20 flu season. The weekly flu report is a key flu surveillance tool and assists decision making throughout the flu season. PHE has also included 'i-sense flu' estimates in their annual flu surveillance report for 2017/18 and 2018/19.

Apart from the timeliness of predictions, including daily availability of outputs and the uninterrupted coverage (unaffected by weekend or holiday closures), online data can represent broader segments of the population who have not consulted the health care system. There are also potential applications of such systems in low- and middle-income countries that may be lacking an established surveillance infrastructure.

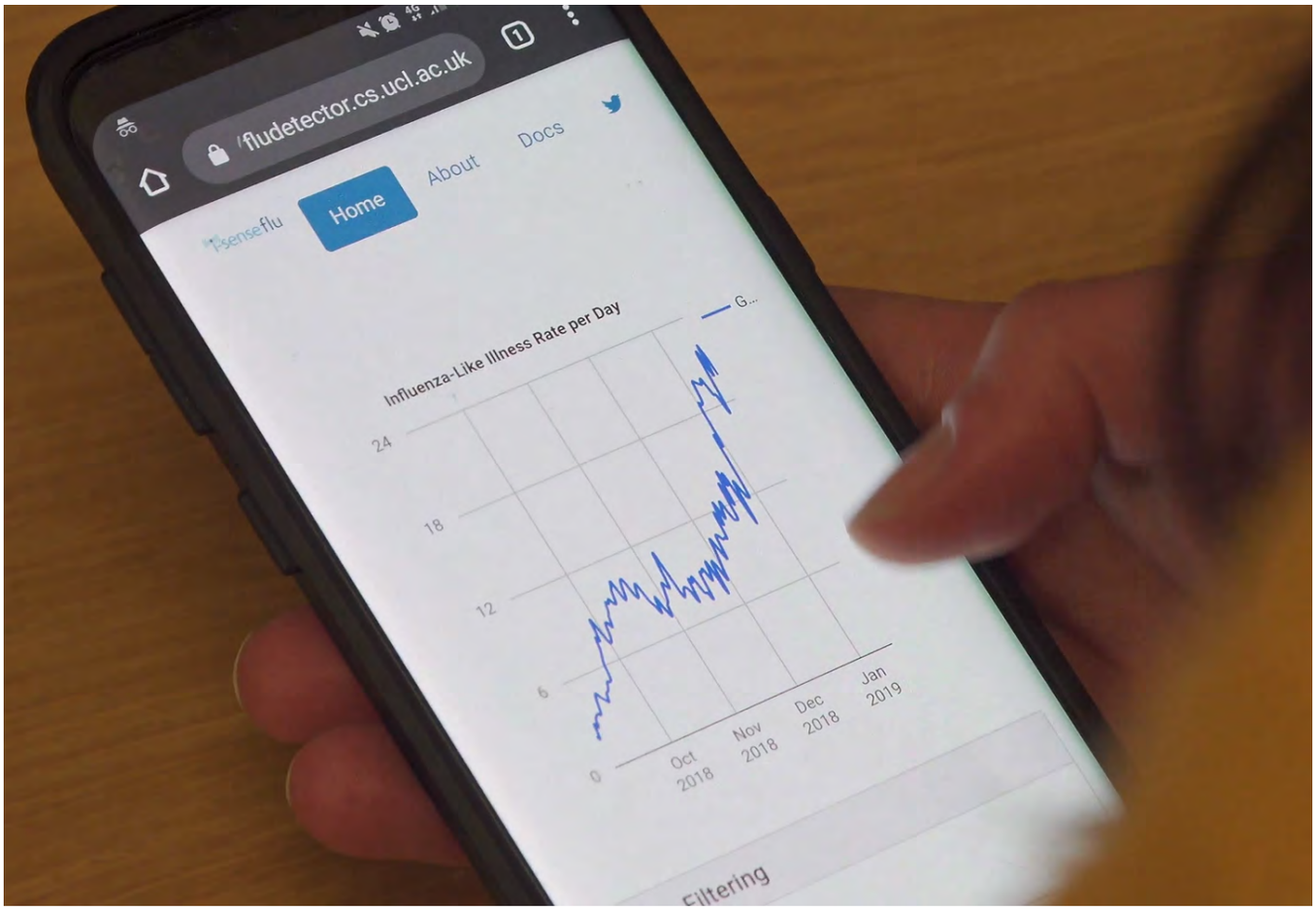
As a result of the ongoing evaluation process and given the various indicators of added value, PHE has adopted the current version of 'i-sense flu' so that they can further evaluate how this approach can support their current surveillance systems. This collaboration is an example of how i-sense research outcomes are translated to support active components of England's public health surveillance system.

Acknowledgements: This work is led by Dr Vasileios Lampos, Prof Ingemar Cox, and Dr David Guzman, UCL.

Wagner, M., Lampos, V., Cox., I. J., and Pebody, R. 'The added value of online user-generated content in traditional methods for influenza surveillance.' Scientific Reports (2018); DOI: 10.1038/s41598-018-32029-6

"i-sense daily machine learning models have been found to give an early indication of the circulation of influenza in the community when compared to the 'gold-standard' Royal College of General Practitioners data based on clinic attendance. i-sense flu, is one of the first examples of AI being adopted by Public Health England."

Dr Richard Pebody, Head of Influenza and Other Respiratory Virus Section, Public Health England



Transferring learnings to resource-limited settings

For many countries, information on historical disease rates are either sparse or not available due to poor health infrastructure. i-sense researchers have been developing ways to transfer their machine learning models that use online user search queries to gather population health statistics to these resource-limited regions.

To address this issue, a statistical framework first learns a supervised model for a region with adequate historical disease rates and is then transferred to a target region, where no syndromic surveillance data exists.

The proposed transfer learning method was evaluated on the task of estimating influenza-like illness (ILI) rates. i-sense researchers learned a source model for the United States, and subsequently transferred it to three other countries, namely France, Spain and Australia. Although there is significant data available for the identified target countries, it was only used for evaluating the accuracy of the transfer. Overall, the transferred models performed well (publications in progress).

Future work will look at performing a qualitative study that demonstrated ILI estimates for low- and middle-income countries that followed an expected seasonal pattern.

Zou, B., Lampos, V., and Cox, I. J. 'Transfer Learning for Unsupervised Influenza-like Illness Models from Online Search Data' WWW '19 The World Wide Web Conference (2019); DOI: 10.1145/3308558.3313477

"i-sense, in part, led to the Google Flu Trends team moving from the US to London, the creation of new jobs in London, and influencing Google policy to open access to search data for academics and Public Health England."

Andrew Eland, Engineering Director, Google

Test

Aim: Build smartphone-connected diagnostic tests to widen access to testing, support front-line health workers, and enable self-testing with linkage to online care. We are growing capabilities in ultra-sensitive nanomaterials (antibody and antigen detection), molecular sensing (DNA and RNA detection), and exploring handheld sequencing technologies.

REASSURED diagnostics to strengthen health systems and improve patient outcomes

It has been more than a decade since Prof Rosanna Peeling coined the acronym 'ASSURED' to guide the development of diagnostic tests to meet user needs, particularly in the developing world.

The new suggested update to 'REASSURED' sets new benchmarks for diagnostics to inform disease control strategies in real-time by leveraging developments in digital technologies and mobile health. With the addition of two new measures, those involved in developing tests are encouraged to incorporate the best of the existing diagnostic world with new and existing technologies.

Ideally, all new point-of-care diagnostics should meet the REASSURED criteria:

- Real-time connectivity
- Ease of specimen collection
- Affordable by those at risk of infection
- Sensitive with very few false-negatives
- Specific with very few false-positives
- User-friendly tests that are simple to perform and require minimal training
- Rapid, to enable treatment at first visit, and Robust, for example not requiring refrigerated storage
- Equipment-free and environmentally friendly
- Delivered to those who need

Land, K. J., Boeras, D. I., Chen, X., Ramsay, A. R., and Peeling, R. W. 'REASSURED diagnostics to inform disease control strategies, strengthen health systems and improve patient outcomes.' Nature Microbiology (2019); DOI: doi.org/10.1038/s41564-018-0295-3

Developing a point-of-care test for the detection of Ebola virus

Ebola virus disease is a serious viral infection that is most commonly found in Sub-Saharan Africa. Early diagnosis of Ebola virus is critical to control transmission, however there is still a great need for a portable, cheap and rapid diagnostic test for the detection of early stage viral infection.

i-sense researchers are developing a multiplexed point-of-care lateral flow test for the detection of specific viral antigens that can be performed in just 15 minutes. This test is comprised of unique monoclonal antibodies (mAb), originally designed for therapeutics by the United States Army Medical Research Institute of Infectious Diseases

The device is being designed to test and differentiate between two viral species; Zaire ebolavirus and Sudan ebolavirus (as pictured), which have previously caused outbreaks in rural regions in Sub-Saharan Africa. Next steps will evaluate the performance of the test in physiological conditions.

If successful, this test could be combined with the smartphone-connected Ebola serology test, designed by i-sense researchers in 2018, to form a highly useful system for epidemic control and population at risk surveillance.

Acknowledgements: This work is being led by Dr Polina Brangel, Dounia Cherkaoui and Prof Rachel McKendry, UCL

Brangel, P., Sobarzo, A., Parolo, C., Miller, B.S., Howes, P.D., Gelkop, S., Lutwama, J.J., Dye, J.M., McKendry, R.A., Lobel, L., Stevens, M.M. 'A Serological Point-of-Care Test for the Detection of IgG Antibodies against Ebola Virus in Human Survivors' ACS Nano (2018); DOI: 10.1021/acsnano.7b07021

"i-sense was at the vanguard of collaboration with developing nations in Engineering and the Physical Science prior to the introduction to the Global Challenges Research Fund, having strong collaborations with South Africa and also by responding to the Ebola crisis in West Africa."

Dr Annette Bramley, Director, N8 Research Partnership, former Head of Healthcare Technologies, EPSRC

Quantum materials for single molecule disease diagnostics

i-sense researchers have made an important breakthrough in the use of novel quantum materials as an ultra-sensitive label for paper-based point-of-care diagnostics. The limit of detection of this approach represents a significant five orders of magnitude improvement over conventional gold nanoparticles, the current standard for lateral flow. Applying this approach to a real assay for HIV diagnosis allowed for single-molecule detection of HIV RNA on paper, with a short amplification step. This novel platform is widely applicable to other molecular and protein targets. A patent application has been filed and a publication submitted.

Acknowledgements: This work is led by Dr Benjamin Miller and Prof Rachel McKendry, UCL.

Exploring quantum dots for use in point-of-care diagnostics

Quantum dots have long been used as fluorescent tags within basic biomedical research due to their intense brightness, high efficiency, and resistance to photobleaching. Use in point-of-care diagnostics, however, has been limited due to practical concerns such as stability and ease of functionalisation with disease targets.

i-sense researchers have been looking at new methods to facilitate the application of these promising materials in infectious disease diagnostics. By developing new methods of encapsulating differently coloured quantum dots inside fluorescent polymer nanoparticles the team have been able to lessen issues of stability, whilst simultaneously providing a simple method of attaching disease-targeting ligands through the chemical functionality of the encapsulating polymer.

Additionally, the interaction between the fluorescent polymer and the quantum dots provides a new means of tweaking the fluorescence profile of the particles, enabling the generation of different coloured particle blends. It is anticipated that this will facilitate efficient detection of different diseases within a single test by enabling differentiation based on colour.

Acknowledgements: This work is led by Dr Leah Frenette, Dr Adam Creamer and Prof Molly Stevens, Imperial College London.

Fluorescent polymer nanoparticles as multiplexable biosensors

A class of fluorescent polymers, 2,1,3-Benzothiadiazole, is being explored for use as biosensors in point-of-care diagnostics because of ideal characteristics including high fluorescence, easily tuneable colours, high photo and thermally stability, non-fouling, and can be readily functionalised with a variety of targeting ligands.

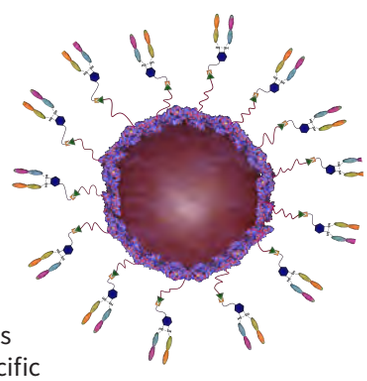
Latest results have shown that these particles can be successfully targeted towards disease biomarkers by incorporating disease-specific antibodies and antibody fragments. i-sense researchers are now exploring how best to take advantage of the unique properties of these materials for multiplexed point-of-care testing.

A recent collaboration has been set up with i-sense affiliate Prof Aydogan Ozcan from UCLA to develop a smartphone-connected device to aid with the automated readout of lateral flow tests that utilise these fluorescent polymers.

Acknowledgements: This work is led by Dr Adam Creamer, Dr Chris Wood, Dr Dan Richards, and Prof Molly Stevens, Imperial College London.

Creamer, A., Wood, C. S., Howes, P. D., Casey, A., Cong, S., Marsh, A. V., Godin, R., Panidi, J., Anthopoulos, T. A., Burgess, C. H., Wu, T., Fei, Z., Hamilton, I., McLachlan, M. A., Stevens, M. M., and Heeney, M. 'Post-polymerisation functionalisation of conjugated polymer backbones and its application in multi-functional emissive nanoparticles' Nature Chemistry (2018); DOI: doi.org/10.1038/s41467-018-05381-4

Exploring novel methods for attaching antibodies to disease-sensing nanoparticles



The vast majority of current tests for protein-based disease biomarkers rely on the use of whole antibodies for disease targeting. This requires antibody targeting ligands to be attached to the nanoparticle on the diagnostic to show an accurate test result. This approach, however, uses uncontrolled and unreliable chemistries, which can lead to sub-optimal test accuracy.

i-sense researchers have been working on transferring previous work developing novel methods for the covalent attachment of antibody and antibody-derived ligands to paper-based diagnostics and point-of-care applications. Coupling efficient click chemistries with high-affinity disease-specific antibody mimics are being explored to see how this can bring about significant improvements in test performance when compared to more traditional approaches.

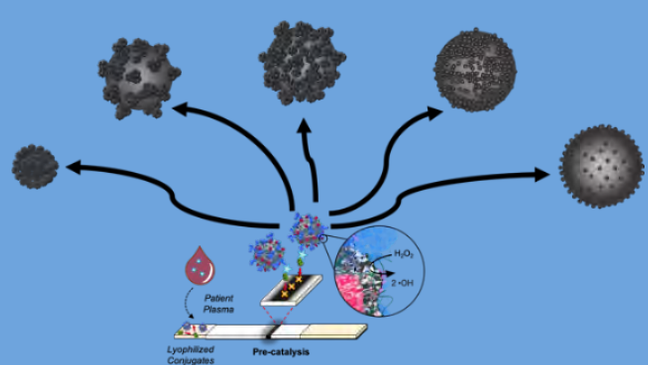
By carefully considering the way that various targeting ligands are attached to the surface of disease biosensors, significant improvements in test sensitivity can be achieved, opening up the possibility of detecting infectious disease at a much earlier stage.

Acknowledgements: This work is led by Dr Dan Richards and Prof Molly Stevens, Imperial College London.

Next-generation platinum nanocrystals for amplified lateral flow

i-sense researchers have been working on developing the next-generation of platinum-based nanoparticles for catalytic amplification in lateral flow point-of-care testing. They have been exploring how platinum interacts with different core nanoparticles, and the effects of morphology and size on the catalytic profile of these promising materials.

This work builds on previous i-sense research around the development of a paper-based point-of-care test for HIV that surpasses the sensitivity of the current industrial gold standard for detection of p24, an early biomarker for HIV. This research demonstrated significant advancements in absorbance-based lateral flow immunoassay technology.



Acknowledgements: This work is led by Brian Chen in collaboration with Dr Mike Thomas, Dr Colleen Loynachan, and Prof Molly Stevens, Imperial College London.

Loynachan, C.N., Thomas, M.R., Gray, E.R., Richards, D.A., Kim, J., Miller, B.S., Brookes, J.C., Agarwal, S., Chudasama, V., McKendry, R.A., Stevens, M.M. 'Platinum Nanocatalyst Amplification: Redefining the Gold Standard for Lateral Flow Immunoassays with Ultrabroad Dynamic Range' ACS Nano (2017); DOI: 10.1021/acsnano.7b06229

A smartphone-powered mRNA sequence detector

This project aims to create innovative, rapid, sensitive, specific, and affordable point-of-care tests designed to be implemented in South Africa for diagnosis of tuberculosis (TB). TB is the leading cause of death in South Africa and diagnosis is notoriously challenging, requiring long testing times and costly equipment. Complicating matters, about 60% of TB patients in South Africa are also infected with HIV, which renders the disease even harder to diagnose with current techniques.

Classical diagnostic tests generally can take about 10 days to result. More rapid and powerful techniques are expensive, hard to transport, or require specialist trained staff, which makes them difficult to perform in rural healthcare clinics.

i-sense researchers are designing diagnostic point-of-care tests for TB that incorporate nanomaterial-based approaches, microfluidic engineering, and smartphone readout to automate all aspects of testing. Self-testing has the potential to empower patients to manage their health and provide global healthcare organisations with improved methods to monitor TB.

Validation studies are planned for a small pilot study with AHRI, located in KwaZulu-Natal, a region of South Africa that has high rates of TB and HIV. The technology developed under this award will also be adaptable to other infectious diseases and non-communicable diseases alike, providing smartphone-based diagnostic technologies within resource-limited settings.

Acknowledgements: This work is part of the i-sense Next Steps Plus Award, titled ‘A smartphone-powered mRNA sequence detector’, which is led by Prof Molly Stevens, Imperial College London, in collaborations with Prof Ingemar Cox and Prof Rachel McKendry, UCL, Prof Michael Levin, Imperial College London, and project partners at Africa Health Research Institute and Columbia University.

Growing antimicrobial resistance (AMR) is a serious global threat to human health, with the report from the United Nations Interagency Coordinating Group on Antimicrobial Resistance estimating that AMR could lead to 10 million deaths per year by 2050 and damage to the economy comparable to the 2008 - 2009 global financial crisis. *

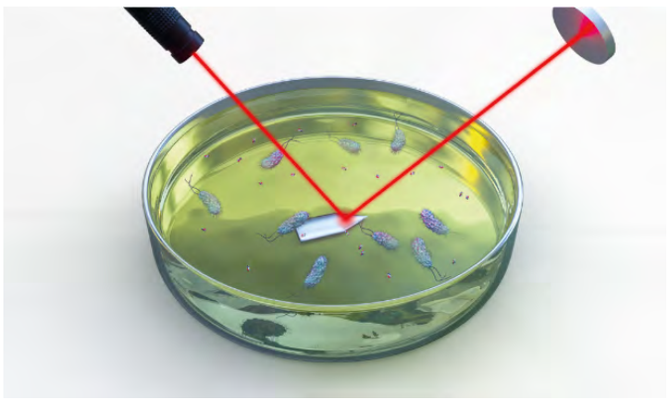
Using lasers to rapidly detect antimicrobial resistance

Current methods to detect resistance include phenotypic antibiotic sensitivity testing, which measures bacterial growth and is therefore hampered by slow time to result (between 12-24 hours). New rapid phenotypic methods for antibiotic sensitivity testing are urgently needed.

i-sense researchers are looking at a novel method for detecting phenotypic antibiotic resistance in less than 45 minutes, capable of detecting single bacteria. The method uses a sensitive laser and detector system to measure nanoscale optical changes caused by single bacterial cells present in media, with simple sample preparation.

This approach provides a read out of bacterial antibiotic resistance by detecting growth (resistant) or death (non-resistant) much faster than current methods. The optical interference method has been successfully tested to detect resistance to multiple antibiotics in both lab and clinical strains of *E. coli.*

This approach can be exploited as a new rapid phenotypic method for antibiotic sensitivity testing, to provide these time-critical results to inform patient care and antibiotic stewardship.



Bennett, I., Pyne, A., and McKendry, R. A. 'Rapid antimicrobial sensitivity testing by single cell nanoscale optical interference.' bioRxiv (2019); DOI: doi.org/10.1101/679399

Developing a bioinformatics tool to identify antimicrobial resistance

i-sense researchers have been developing a bioinformatics workflow, called Invisiogen, for identifying antimicrobial resistant (AMR) genes within sequence databases. The overall aim of the system is to detect the occurrence of new AMR genes in multiple data sources as they appear, and to predict the evolution of likely problematic variants before they arise.

The initial objective is to provide the bioinformatics knowledge needed to support rapid development of reagents for sequence-level AMR gene detection. The workflow compares specific gene searches against public genome and metagenome databases. It then builds models of global and site-specific patterns of evolution, and predictions of potential mutations.

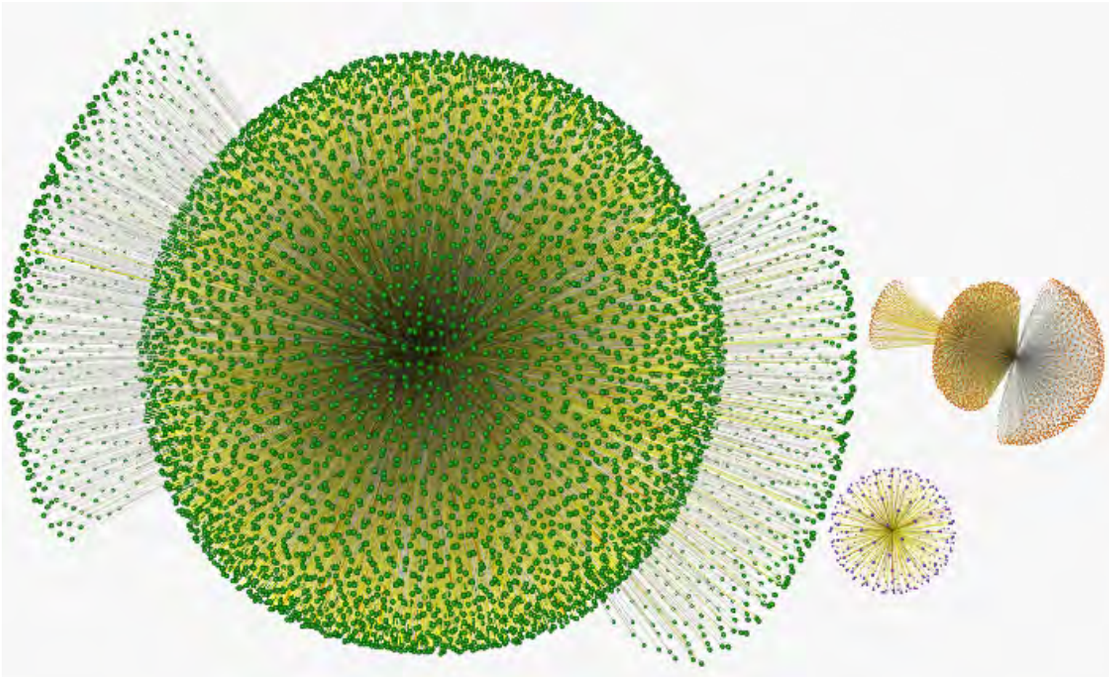
Currently, the Invisogen workflow is under active development. i-sense researchers are looking at which data sources should be searched by default, as well as how to distinguish between closely related proteins.

Acknowledgements: This research is led by Dr Matthew Pocock and Prof Anil Wipat, Newcastle University.

“i-sense was the EPSRC’s first major investment in research into antimicrobial resistance (AMR). i-sense raised the profile of AMR-related research in Engineering and the Physical Sciences. It influenced, to some extent, EPSRC’s engagement with the UKAMR Cross-Council Initiative and also to the EPSRC Call: Bridging the Gaps between EPS and AMR.”

Dr Annette Bramley, Director, N8 Research Partnership, former Head of Healthcare Technologies, EPSRC

* United Nations interagency Coordinating Group on Antimicrobial Resistance report titled ‘No time to wait: Securing the future from drug-resistant infections’. Report to the Secretary General of the United Nations, April 2019



Invisiogen workflow results illustrated as a network of related genes and proteins

Detecting the 'big five' antibiotic resistant strains

Carbapenems are ß-lactams and were viewed as the last line of defence against bacteria with antimicrobial resistance (AMR) , but bacteria have evolved resistance mechanisms against carbapenems such as the synthesis of carbapenemases, enzymes capable of hydrolysing carbapenems. To date five carbapenemases, known as 'the big five' have been identified as the greatest threat to widespread dissemination of AMR. The 'big five' include, Klebsiella pneumoniae carbapenemase (KPC), Oxacillinase (OXA-48), New Delhi Metallo-ß-lactamase (NDM), Verona Integron-encoded metallo-ß-lactamase (VIM) and Imipenemase (IMP). There is currently a clinically unmet need for a point-of-care diagnostic targeting Carbapenem-resistant Enterobacteriaceae (CRE)/carbapenemase producers that can be implemented in both doctor's surgeries and hospital wards.

To address this need we are currently developing Recombinase Polymerase Amplification (RPA) assays against CRE. RPA primer sets have been designed against each of the 'big five' carbapenemase genes. Primer sets have been screened against their cognate genes and the best primer pairs for each gene have been chosen based on the amount of gene specific amplicon generated under different amplification regimes. Modified tail sequences have been designed for capture and detection of the gene specific amplicons using a bioinformatics driven approach. The sequences of the tails will be critical for the success of the project as minimal sequence homology between the tails and/or primers will be needed for a successful multiplex assay able to detect the 'big five' carbapenemases - in order to minimise primer dimers and non-target amplification.

Additionally we are exploring the possibility of solid phase RPA using modified versions of the primers specifically designed for the detection of the 'big five' carbapenemase genes. This involves tethering a forward primer, specific for one of the carbapenemase genes to a solid support via a streptavidin-biotin interaction. The RPA reaction mix, including reverse-tailed primer, is then added to the forward primer at the solid phase. In the presence of cognate target DNA, RPA is instigated at the surface, generating a double stranded amplicon with a single stranded oligonucleotide tail introduced by the reverse primer. Labelling of the RPA product is currently achieved using a HRP modified oligo - complementary to the reverse primer tail. This assay has been demonstrated to work successfully against both the VIM and KPC genes.

Going forward, we aim to adapt these solid phase assays to paper based detections systems coupled with high sensitivity SERS detection – swapping out the HRP for a SERS reporter molecule.

Acknowledgements: This work is part of the i-sense Next Steps Core award, as well as the Plus Award, titled 'Ultra-sensitive enhanced nanosensing of antimicrobial resistance (u-Sense)'. The Plus Award is led by Dr Neil Keegan, Dr Chris Johnson, Matthew Setterfield, Dr Matthew Pocock, and Prof Anil Wipat, Newcastle University, in collaboration with Prof Duncan Graham and Prof Karen Faulds, University of Strathclyde, and project partners at Cambridge Life Science Ltd, iXscient Ltd, and Public Health England.

Machine learning for diagnostic read-out

Machine learning approaches have showed promising results for use in disease diagnostics, however they have traditionally been trained using standardised medical datasets. i-sense researchers have been working in collaboration with the Africa Health Research Institute (AHRI) to develop a mobile app that uses machine learning to interpret test results in field conditions.

More than 60 field workers at AHRI collected more than 40,000 images of HIV diagnostic tests conducted as part of their routine surveillance for communities in rural KwaZulu-Natal, South Africa. These images formed the library used to train the model to classify the images into one of two categories; positive or negative. Training the model using 'real-world' images is important due to variations in photo quality, zoom, focus, tilt, lighting, shadows, and test formats.

The findings showed very high accuracy, sensitivity and specificity compared with interpretation of the test from an expert. This research paves the way for machine learning-enable REASSURED diagnostics that could increase quality control and inform disease control strategies.

Acknowledgements: This work was carried out by the field workers at the Africa Health Research Institute, as well as Dr Valérian Turbé, Dr Maryam Shahmanesh, and Prof Rachel McKendry, UCL.

"The mHealth tools and protocols [test 'tray' and protocols for acquiring photos of RDTs] have been adopted for quality assurance of HIV rapid tests and are now in routine use as part of their Population Implementation Platform, involving testing of over 170,000 people in the region. This innovative development of mHealth technologies for use in decentralised population settings is already contributing, at least in part, to reducing the number of false positive and negative test results, and supporting field worker training.

Dr Kobus Herbst, Chief Information Officer, Africa Health Research Institute

User testing HIV apps in rural settings

A smartphone app has been developed by i-sense researchers and a prototype has been piloted in clinic as part of the collaborating GCRF MRC-funded m-Africa project. As pilot test was conducted with young men and women in the rural setting of KwaZulu-Natal, South Africa. It aimed to investigate participant feelings about self-testing using an app, as well as participant reactions to being told their test results by a device (rather than by a healthcare professional), and the phone counselling and support that follows.

The app is designed to allow a person to self-test, get their results and link into medical care through, minimising the need for clinic visits. The system brings together artificial intelligence techniques for rapid diagnostic decision support, quality control, and the diagnostic tests use novel, ultra-sensitive nanomaterials to detect the early stages of HIV.

The outcome of the pilot study showed the acceptability and feasibility of introducing smartphone-assisted self-testing and linkage to care for HIV.

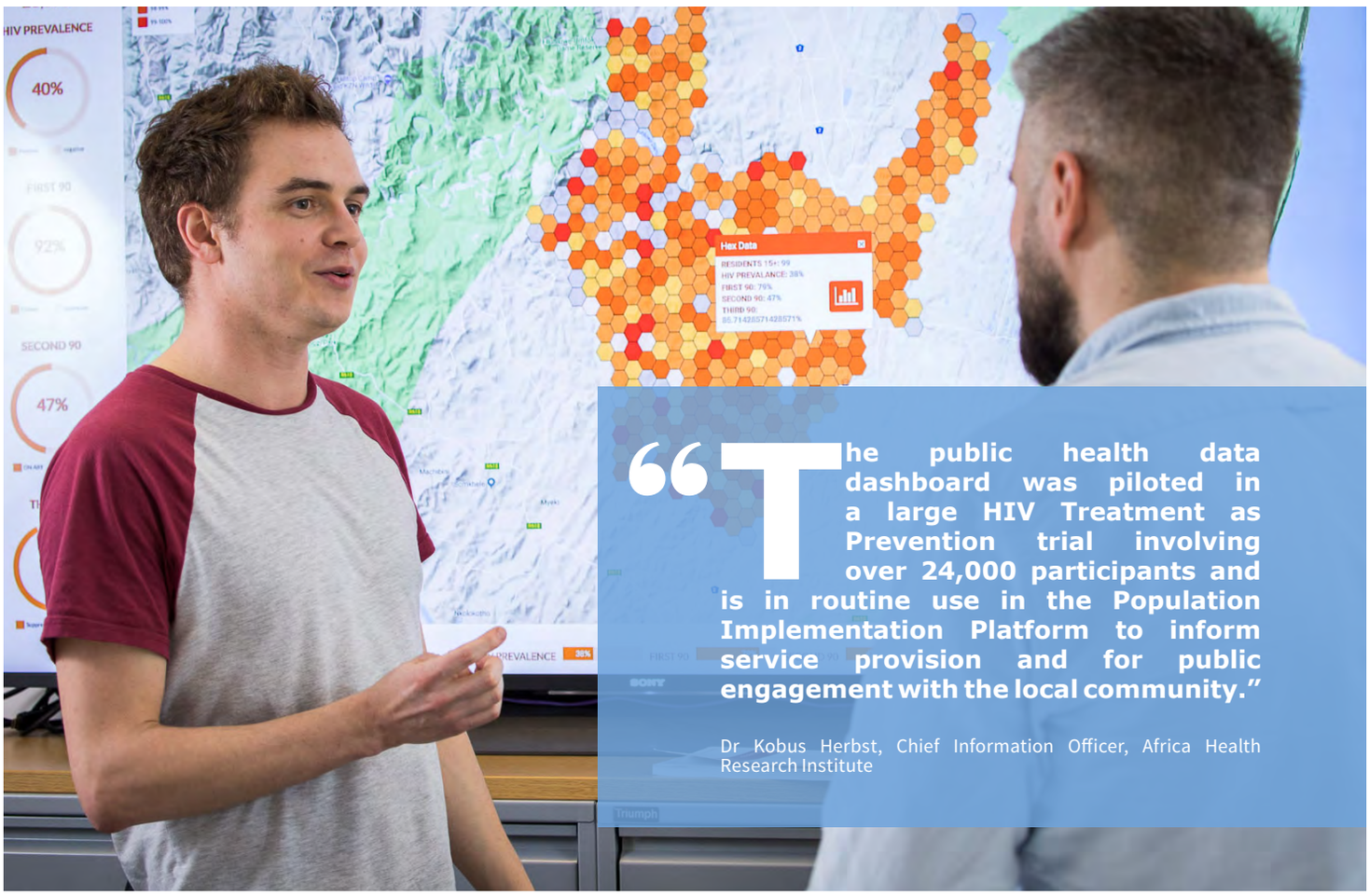
Acknowledgements: The work is led by Dr Maryam Shahmanesh, Dr Valérian Turbé, and Prof Rachel McKendry, UCL, in collaboration with other colleagues from across UCL, Imperial College London and at the Africa Health Research Institute. The project is funded by the Medical Research Council GCRF Global Infections Foundation Award (MR/P024378/1) and is part of the EDCTP2 programme supported by the European Union.

"We successfully piloted the Zenzele mobile application and online care pathway for HIV self-testing with 30 participants in a local health clinic in KwaZulu-Natal. We were able to investigate participant feelings about self-testing using an app, as well as participant reactions to being told their test results by a device, and the phone counselling and support that follows."

Dr Maryam Shahmanesh, Associate Prof UCL Institute for Global Health and Population Health, UCL.

Treat

Aim: To create real-time data visualisation tools to map disease ‘hotspots’ and support faster linkage to treatment by marrying mHealth, genomic, clinical, epidemiological and socio-economic data.



> “The public health data dashboard was piloted in a large HIV Treatment as Prevention trial involving over 24,000 participants and is in routine use in the Population Implementation Platform to inform service provision and for public engagement with the local community.”
>
> Dr Kobus Herbst, Chief Information Officer, Africa Health Research Institute

Can data visualisation help inform health interventions?

The i-sense data dashboards project, led by researchers at UCL, in collaboration with the Africa Health Research Institute (AHRI), has been looking at ways data visualisation can help population surveillance sites better utilise and understand the large data set they collect.

The collaboration allowed for the dashboards to be developed alongside the Treatment as Prevention trial to explore some of the challenges faced by public health communities to extract information from large data set.

Overall, the results of the study demonstrated a positive attitude towards the future use of such platforms across AHRI studies. These systems have huge potential as they allow for real-time analysis, require fewer resources than manual data analysis and have the ability to be adaptable for changes in need.

Current work is looking at visualisation literacy with end users, as well as working on developing a user adaptive visualisation framework, by analysing user interaction with the dashboard. The results aim to guide the development of a system useful for effective decision support.

Concannon, D., Herbst, K., and Manley, E. ‘Developing a Data Dashboard Framework for Population Health Surveillance: Widening Access to Clinical Trial Findings’ JMIR Formative Research (2019); DOI: doi:10.2196/11342

Can digital resources for HIV provide appropriate emotional support?

Although self-testing and online resources can empower people to make decisions about their health care, little has been done to understand the emotional impact of receiving a HIV diagnosis outside of traditional healthcare settings.

i-sense researchers surveyed more than 200 participants over three stages to understand how and why people access information related to HIV, and their experiences of using these resources. Our findings suggested that current resources are not designed to address the emotional needs of people seeking information on HIV testing, treatment, or care, and may reinforce stigma or neglect.

Study results found four key recommendations for designing online or remote resources:

1. Aligning with people's mental models and reasons for accessing the resources: consider the pathway end users will take when accessing your resource.

2. Acknowledging and supporting emotional needs of people: testing is individual and implications of a positive result will depend on someone's interpersonal, societal and cultural contexts.

3. Personalising to different levels of knowledge and experience of HIV and testing for HIV: how often are people testing? What is their prior knowledge?

4. Ensuring messages are supportive and do not reinforce stigma: communication should be reassuring and supportive, promoting self-testing as a matter of user choice.

Participants also felt that they favoured information from trusted resources, such as the NHS, information that was up-to-date, and that they would prefer to use an NHS app (or similar) rather than a separate app for their HIV testing, treatment and care.

The findings of this study have been used to inform the development of an online clinical care pathway for people who are testing for HIV using HIV self-tests or HIV self-sampling kits. The aim of the pathways is to link users to treatment and care, while offering support through the next steps. User testing of these pathways has recently been completed and the findings from this research will support their optimisation.

Singh, A., Gibbs, J., and Blandford, A. 'Emotion and Experience in Negotiating HIV-Related Digital Resources: "It's not just a runny nose!"' CHI '19 Proceedings of the 2019 CHI Conference on Human Factors in Computing Systems, Paper No. 599 (2019); DOI: 10.1145/3290605.3300829

Singh, A., Gibbs, J., Estcourt, C., Sonnenberg, Pam., Blandford, A. 'Are HIV Smartphone Apps and Online Interventions Fit for Purpose?' Proceedings of the 2017 International Conference on Digital Health (2017); DOI: 10.1145/3079452.3079469

02 Engagement

Industry and policy engagement

i-sense Digital Health Conference

In July 2019, the i-sense Digital Health Conference took place to celebrate five years of the project and aimed to share the latest innovations in digital health research around infectious diseases. The conference attracted around 200 delegates over two days.

The inspiring two-day programme covered topics including the need for digital health, infectious disease surveillance, harnessing genomics, sensors and nanomaterials for connected diagnostics, delivering mobile health in developing country settings, and developing integrated ecosystems for treatment and care.

Speakers included i-sense members from UCL, Imperial College London, London School of Hygiene and Tropical Medicine, and Newcastle University, and invited talks from the Department for International Trade, NHSX, ISI Foundation and ISI Global Science Foundation, Scripps Research Institute, University of Oxford, GSM Association, Alan Turing Institute and University of Cambridge.

The four panel discussions and two networking receptions gave delegates the invaluable opportunity to explore topics further, engage in fruitful discussions, build new collaborations, and strengthen existing partnerships.

“A fantastic couple of days learning about how cutting edge biological and computational research is being applied to address existing and future needs in healthcare worldwide,” and “It was amazing to see the progression of the i-sense projects and how they have all flourished from seeds of ideas to tangible products and platforms,” was just some of the positive feedback from attendees.

Acknowledgements: This workshop was led by Prof Rachel McKendry and Erin Manning, UCL.

28

Poster presentations

23

Speakers

3

Research demonstrations

Matthew Setterfield

Best poster presentation

m-Africa workshop

m-Africa is a two-year GCRF Global Infections Foundation Award that received funding from the Medical Research Council in April 2017. i-sense researchers worked collaboratively with the m-Africa project, helping develop and adapt diagnostic tools and technologies for a rural South African setting.

To present the outcomes from the grant, a workshop was held at the Africa Health Research Institute (AHRI) in Durban. It was an opportunity for researchers working across the project to present the results of their work to academics, industry leaders, and members of the South African Department of Health.

m-Africa has allowed researchers from University College London, Imperial College London, and AHRI to work together to evaluate the feasibility of introducing mobile phone-connected tools to improve access to HIV testing, as well as linkage to care, in KwaZulu-Natal.

The two-day event, which was attended by around 40 people, included talks and open discussions to help understand where m-Africa may fit into the longer term plans for industry and healthcare providers, and the benefits that the tools and technologies being developed can bring to help address the issues these groups may face.

Acknowledgements: This workshop was organised by Dr Kobus Herbst and Carina Herbst, Africa Health Research Institute, and Erin Manning, UCL. The m-Africa project is led by Prof Rachel McKendry and Prof Deenan Pillay, UCL.

Exploring technical and cultural barriers for veterinary diagnostics

An i-sense funded workshop, run by the School of Veterinary Medicine at the University of Surrey, brought together experts in diagnostic test development and digital technology to examine state-of-the-art tools available, as well as explore technical and cultural barriers to implementation.

Attendees included biologists, veterinarians, data mangers and engineers, and ranged from research scientists at The Pirbright institute, University of Brunel, University of Plymouth, University of Liverpool, Imperial College London, and University of Surrey, as well as industry leaders from Zoetis, Optigene, World Reference Laboratory for Foot and Mouth Disease Virus, and Veterinary Health Innovation Engine.

The workshop is a catalyst for multiple collaborations between academia, industry and government reference laboratories. Concrete steps have already been made in the form of joint PhD studentships between Surrey and Pirbright and further opportunities are in the pipeline.

Workshop themes are also now being directly incorporated into a literature review. The manuscript will demonstrate clear priorities for research in this area, and highlight opportunities and barriers with potential to influence policy for implementation of new technology.

Acknowledgements: This workshop was organised by Dr Jonathan Betts, School of Veterinary Medicine, Mirela Dumic, Institute of Advanced Studies, and the staff of Wates House for organisation.

Environmental scan of current early warning systems

The team at London School of Hygiene and Tropical Medicine, Prof Rosanna Peeling and Dr Noah Fongwen, have been conducting an environmental scan of the current early warning system for infectious diseases in the UK and evolving technology landscape worldwide. The environmental scan has been supplemented by a series of one hour informal interviews with key opinion leaders to understand the current UK surveillance system. Prof Rosanna Peeling is a member of the Academic Steering Group of the UK Public Health Rapid Support Team that provides outbreak support to the WHO Emergency Response Team.

Implementing HIV tests at-scale

i-sense researchers have been working with Populations Services International (PSI) in Myanmar looking at the introduction of HIV self-testing to the country. The i-sense Mobility Fellowship project also aimed at forging links between i-sense and an NGO with experience in fieldwork and large scale implementation past the research stage.

Acknowledgements: This work is led by Dr Valérian Turbé and Prof Rachel McKendry, UCL, in collaborations with Kiira Gustafson, Than Naing Oo, Kaung Htet Han, Sai Woon Serth, Hein Ko Ko, and Daniel Crapper, PSI.

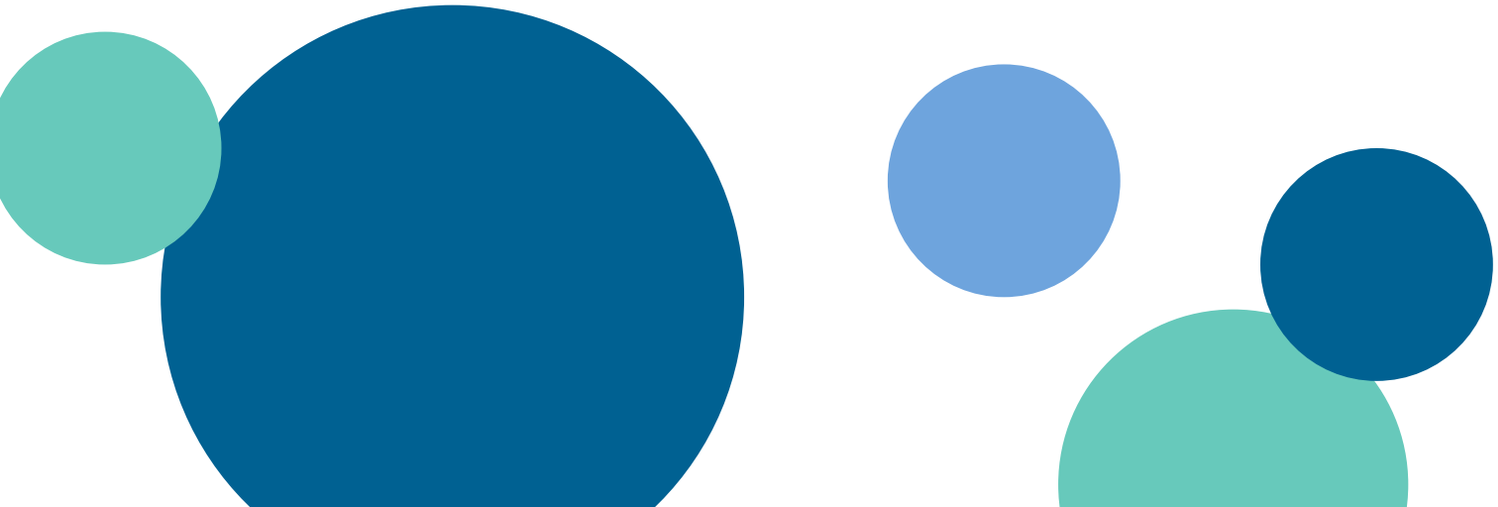
Translating mobile apps to market

i-sense has collaborated with Chris Isaacs at Connected Diagnostics on a translational strategy for our mobile phone app for HIV testing and quality assurance. To date, the i-sense app has focused on proof-of-concept early stage research. This project builds on the existing research and associated data sets, and will develop a commercialisation strategy to translate this early stage research into products and practices.

Acknowledgements: This work is led by Chris Isaacs, Connected Diagnostics, in collaboration with Prof Rachel McKendry and Dr Valérian Turbé, UCL.

GSMA Mobile World Congress 2019

i-sense members from UCL, Jobie Budd, Erin Manning and Prof Rachel McKendry, worked together to create a one minute video about i-sense tools and technologies that was shown at the GSMA Mobile World Congress in Barcelona.



Patient and public engagement

i-sense at Great Exhibition Road Festival

The i-sense team within the Prof Molly Stevens Group at Imperial College London put on an interactive display at the Great Exhibition Road Festival. The event attracted over 50,000 visitors. The group set up three zones with activities for children of all ages to engage in research concepts underway in the group.

Part of this exhibit included a large scale model of a lateral flow test constructed by the team. The test was a game used to demonstrate the principle of the lateral-flow diagnostics being developed through i-sense. In this game, visitors to the stand rolled magnets up a slanted board, trying to get as many to stick on the magnetic 'test line' as possible. Visitors also learned how our devices use nanoparticles and antibodies in a similar way to see whether or not someone is infected with a virus.

Acknowledgements: This activity was led by Dr Jonathan Wojciechowski and Dr Leah Frenette, in collaborations with Dr John Goertz, Ms Ilona Sunyovszki, Dr Hyejeong Seong, Dr Jonathan Yeow, Mr Mike Potter, Dr Axel Moore, Ms Katya Pchelintseva, and Ms Charlotte Lee-Reeves, Imperial College London.

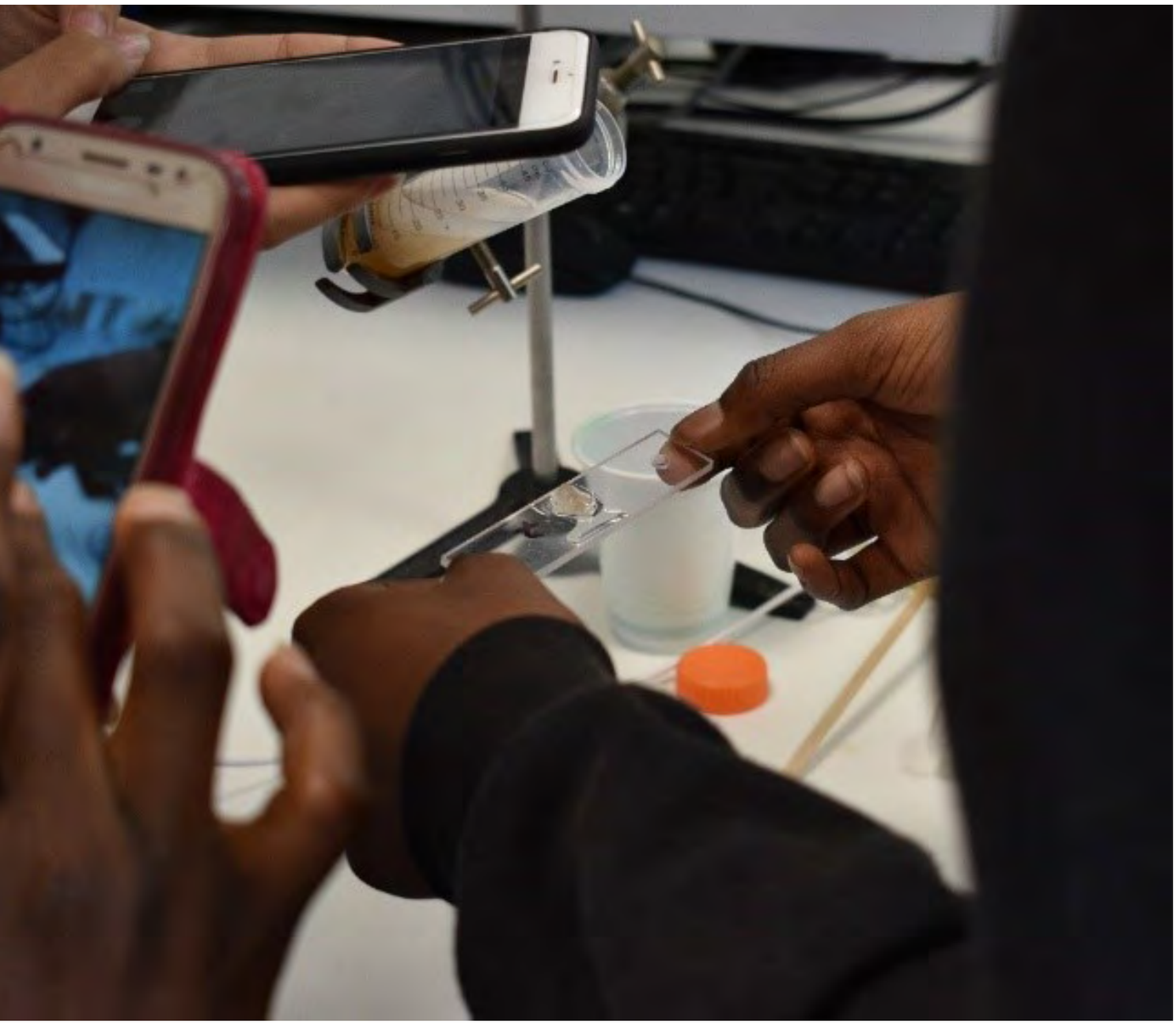
Summer work experience with the McKendry group

Over the summer, the i-sense McKendry group hosted two London-based secondary school students in our lab at the London Centre for Nanotechnology. The students spent time shadowing experiments, learning about lateral flow tests and coding techniques, and developing their science communication and engagement skills.

Acknowledgements: This work was led by Dr Ben Miller with support from Dr Valérian Turbé, Erin Manning, Dr Polina Brangel, Nestor Arsenov, Dr Eleanor Gray, Dr Mike Thomas, Sepehr Meshkinfamfard, Georgina Benn, and Dounia Cherkaoui.

Chatbot user interface testing for HIV charity Positive East

In the first half on 2019, i-sense PhD Student in the McKendry group at UCL, Jobie Budd, volunteered for the London-based HIV charity Positive East. Jobie helped to research, design and test the user interface testing of a sexual-health advice chatbot, called 'Pat'. The chatbot was built to answer questions about sexual health and direct users to trusted information and testing or support services. 'Pat' is now live on Positive East's website.



i-sense joins the Science Summer School for young migrants

This summer a group of PhD students from the London Centre of Nanotechnology and the Institute of Education, including i-sense PhD student in the McKendry group at UCL, Dounia Cherkaoui, ran a two week summer school for refugees, young migrants, and asylum seeking students.

The team built on the success of the pilot event in 2018, which was made possible thanks to essential funding from the Ogden Trust and UCL Widening Participation. This year the programme was expanded to a two week, day time course for 40 students. The attendees joined English language classes, physics lessons, and learnt the basics of computing and robotics.

> **“It was great to participate in the summer school and spend some time with such curious and enthusiastic students who genuinely wanted to practice their English and learn about science. It was a unique opportunity to reach out to these young migrants who aspire to study science, but had to interrupt their studies.”**
>
> Dounia Cherkaoui, i-sense PhD student

Acknowledgements: This Summer School was led by Safe Khan, Maeve McLaughlin, Jonathon Fouchard, Ana Lisica, Massimiliano Ramsay, and Alex Pakpour-Tabrizi, UCL.

Institute of Healthcare Engineering Autumn Research Symposium

This year the Institute of Healthcare Engineering held their annual Autumn Research Symposium at the Wellcome Collection. They conveyed the diversity of UCL's healthcare engineering excellence through a mix of panel discussions, demonstrations and stories from people with lived experience. i-sense researchers held a public engagement stand at the Symposium, showcasing our research from dashboard development to the engineering behind lateral flow tests.

Acknowledgements: This symposium was organised by Alice Hardy and Georgina Cade, UCL.

i-sense patient and public involvement

With the help of a Patient Public Involvement Starter Grant from the NIHR University College London Hospitals Biomedical Research Centre, i-sense researchers held our first patient focused workshop. The workshop was a consultation with people who are living with HIV to understand feasibility and acceptability of using a mobile phone-connected self-test for HIV viral load at home.

The survey helped us to understand how the participants felt about how their viral load testing is currently performed, as well as their attitudes towards digital healthcare technology. The small group discussions revealed a number of insights, which will be used to guide the development of the technical aspects of the test. These include the importance of the test's specificity and ease of use.

Since the workshop, we have established a patient group for people living with HIV. These individuals have stayed involved in our research projects and will continue to help inform our research.

Acknowledgements: This workshop was led by Dr Harriet Gliddon in collaboration with Erin Manning, Prof Rachel McKendry, Dr Jo Gibbs, Dr Valérian Turbé, Dr Ben Miller, Jobie Budd UCL, and Chris Isaacs, Connected Diagnostics .

User testing of i-sense HIV online pathways

This year i-sense researchers engaged with potential end users of the i-sense HIV online pathways of the eSexual Health Clinic. The online platform aims to support people who are testing for HIV at home using HIV self-tests or self-sampling kits. Think aloud qualitative interviews were conducted with a sample of twenty-seven users, including some living with HIV who were recruited through a London-based HIV charity, Positive East. To generate the input of people living with HIV in the development of these pathways, one or more focus groups will be held in 2020 to engage in collaborative analysis of the data.

Acknowledgements: This research was led by Dr Karen Lloyd, Dr Jo Gibbs, Prof Pam Sonnenberg and Prof Ann Blandford, UCL, and Prof Claudia Estcourt, Glasgow Caledonian University

i-sense in numbers 2019

15
Publications

Including in *Nature, Nature Microbiology, Nature Nanotechnology* and *ACS Nano.*

73
Talks and presentations

Including at Scripps Research Future of Individualized Medicine in America (Prof Rachel McKendry), Bioel2019 in Austria (Dr Adam Creamer), Royal Pharmaceutical Society, Science and Research Summit in the UK (Prof Molly Stevens), BSAC Spring Conference 2019 in the UK (Dr Isabel Bennett), Spatial Data Science Conference 2019 in America (Dr Mengdie Zhuang), TED talk in Germany (Dr Polina Brangel), the Materials Research Society Fall 2019 Meeting in America (Dr Colleen Loynachan), International Conference on Re-emerging Diseases in Ethiopia (Dr Polina Brangel and Jobie Budd), and the 6th International Conference on Multifunctional, Hybrid and Nanomaterials in Spain (Yiyun Chen).

Media appearances

Prof Vince Emery, University of Surrey
The Telegraph

Prof Molly Stevens, Imperial College London
Reuters , World Economic Forum,
and *Daily Mail*

Dr Jenny Brookes, UCL
BBC Four, The Secrets of Quantum Physics

Dr Vasileious Lampos, UCL and
Dr Richard Pebody, Public Health England
Nature Outlook

Social media

Twitter impressions (Dec 2018 – Dec 2019)
20% increase in tweet impressions

Twitter Followers (Dec 2018 – Dec 2019)
18% increase in Twitter Followers

28,600 + unique page views on i-sense.org.uk

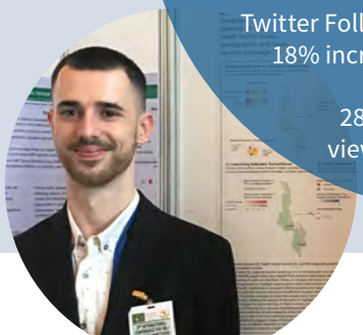


Figure 2. (a) Scheme showing synthesis of Au–Pt core–shell structure (PtNC), where 15 nm gold nan

03 Education and training

Education Alliance

The i-sense Education Alliance was created to introduce new teaching and training events to grow the interdisciplinary skills of our PhD students and researchers.

Led by Dr Neil Keegan and supported by a team of i-sense members the unique programme is designed to inspire and prepare our members for their future careers. With follow on funding for the i-sense project, the programme now supports i-sense staff members using a structured career development action plan, including allocated funding and regular mentorship. In addition, innovative career workshops are being developed for all affiliated members of the i-sense network.

i-sense Careers Day: Learning from i-sense alumni

The main aim of the day was to give i-sense early career researchers the opportunity to discuss their future careers and hear from others who have been in similar positions.

i-sense alumni were invited back to share their tips and experiences moving into new roles in academia, industry and policy.

3 Funder talks

7 Alumni talks

42 Attendees

We had the pleasure of welcoming back:

Dr Phil Howes
Postdoctoral Researcher, deMello group, ETH Zürich

Dr Natascha Kappeler
Lecturer at the Institute for Chemistry and Bioanalytics and Research Associate, FHNW

Dr Christopher Wood
Marie Sklodowska-Curie Individual Fellow, Department of Medical Biochemistry and Biophysics, Karolinska Institutet

Dr Kristina Schlegel
Programme and Alliance Specialist, Galvani

Dr Subinoy Rana
Assistant Prof, Indian Institute of Science

Dr Tania Saxl
Programme Manager, AI Residency (Europe), Microsoft Research Cambridge

Dr Isabel Bennett
Secondment to Government Office for Science

Our three talks from funders included Dr Annette Bramley, who has worked alongside i-sense in her role at EPSRC and now at N8 Research, Katherine Freeman from EPSRC and Anna Myat from the Wellcome Trust.

Finally, we trialled a small CV workshop during the lunch break, which saw academics, funders, alumni and strategic advisors volunteer 10 minutes per person to review and give feedback to our early career researchers on their CVs.

Acknowledgements: This workshop was organised by Erin Manning and Prof Rachel McKendry, UCL.

> **"The careers day was the perfect chance to talk to peers that we really identified with. They were able to give us a real perspective of our career opportunities and what we should take into account."**

Dr Marta Broto Aviles, Postdoctoral Research Associate in the Stevens group at Imperial

Secondments and Mobility Fellowships

Working with PSI on at-scale implementation of HIV self-tests

Dr Valérian Turbé's Mobility Fellowship was a seven week placement with Population Services International (PSI) in Myanmar. The project was focused on the introduction of HIV self-testing to the country. The project also aimed at forging links between i-sense and an NGO with experience in fieldwork and large scale implementation past the research stage.

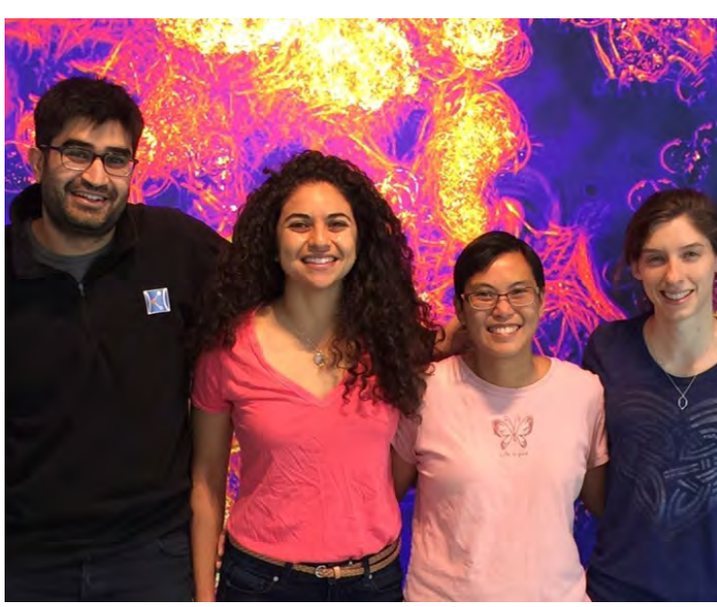
Val, who is from the McKendry group at UCL, helped design and write up the timeline, protocol and study design for the organisation's three stage approach to at-scale implementation of HIV self-tests for key populations. He planned the first pilot study at one of PSI's clinics and produced the required supporting materials, including instructions video, consent forms, and information sheets. Val also initiated contacts with HIV self-test providers to start the process of registering their products in the country, in collaboration with the government. While he was based in the largest city in Myanmar, Yangon, he was also allowed to meet and shadow PSI's health workers at a number of clinics in different regions of the country.

This opportunity gave Val great insight into everyday life at an NGO and the challenges involved in implementing the outputs of our research. The opportunity to work together with members of the key populations targeted by PSI's various programmes was truly enriching and made for a great overall experience.

Acknowledgements: This work was led by Dr Valérian Turbé, UCL, and Kiira Gustafson, Than Naing Oo, Kaung Htet Han, Sai Woon Serth, Hein Ko Ko, Daniel Crapper, PSI.

Trans-Atlantic nanosensor engineering

The Mobility Fellowship awarded to Dr Colleen Loynachan, allowed her to pursue a research programme that combined expertise from Prof Sangeeta Bhatia's group at Massachusetts Institute of Technology (MIT) and Prof Molly Stevens' group at Imperial College London. The group at MIT have been working on diagnostic technologies that introduce nanoparticle sensors into the body, which then release reporter probes into urine to detect the presence of disease (tumours or bacterial infections). To date, processing the urine sample still requires complex equipment that would be difficult to use outside a lab or hospital setting.



In parallel, the Stevens group have been developing sensitive paper-based diagnostic tests using nanomaterials that can catalyse a simple colour change reaction to improve test sensitivity. These tests are also designed to be cheap to manufacture, portable, and easy to use, making them suitable for resource limited settings.

Working with Ava Soleimany, a PhD student at MIT, Colleen explored how advanced nanomaterials used by the Stevens group could be

introduced to reduce the cost and complexity of processing the urine samples, specifically for early detection of cancer. The system they came up with works by injecting nanosensors, made of ultra-small catalytic gold nanoclusters, into the bloodstream. The nanosensors are then cut up by enzymes released by the tumour, known as proteases. Once cut by the enzymes, the gold nanoclusters were designed to be small enough to filter through the kidneys and accumulate in the urine where they can catalyse a colour change reaction that provides a simple visual readout, signalling the presence of disease-related enzymes.

The researchers injected nanosensors into 14 healthy mice and 14 mice with colon tumours, and collected urine one hour after injection. The urine was treated with a chemical substrate and within 30 minutes, urine from tumour-bearing mice became bright blue – a visual indication of tumour-associated enzymes in the body.

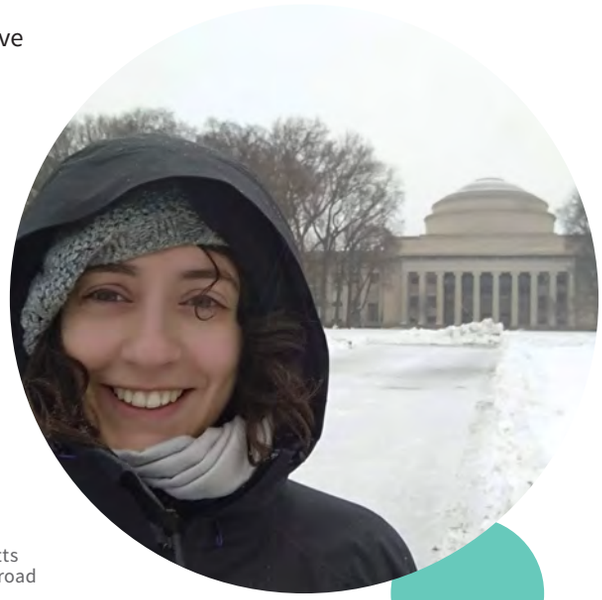
The simple readout could potentially be captured by a smartphone picture and transmitted to remote caregivers to connect patients to treatment. The two groups are now looking into how they can adapt this technology for detection of other diseases and how they can translate this technology beyond the lab.

Loynachan, C. N., Soleimany, A. P., Dudani, J. S., Lin, Y., Najer, A., Bekdemir, A., Chen, Q., Bhatia, S. N., and Stevens, M. M. 'Renal clearable catalytic gold nanoclusters for in vivo disease monitoring.' Nature Nanotechnology (2019); DOI: doi.org/10.1038/s41565-019-0527-6

Looking at new markers for disease diagnosis with MIT

Investigating short RNA sequences is becoming an increasingly popular way to gain a deeper understanding of the biology of a cell and assess changes that may indicate disease. This approach is an important source of information not only for diagnosis, but for ongoing treatment and care. Traditionally, these RNA sequences have been analysed by trained personnel and use expensive, lab-based equipment. Simple point-of-care approaches in this area are still scarce.

Recent developments of a tool known as the CRISPR-Cas toolkit have unleashed the possibility of detecting RNA at low concentrations with high accuracy. In light of this, Dr Marta Broto, a Postdoctoral Research Associate in Prof Molly Stevens group at Imperial, was granted an i-sense Mobility Fellowship to learn about this technology in Prof James Collins laboratory at Massachusetts Institute of Technology (MIT). Prof Collins has pioneered the development of CRISPR-Cas paper-based, inexpensive, fast and simple biomolecular tools for their use in global healthcare and self-diagnosis.



After acquiring the basic knowledge to work with this toolkit, Marta began designing a point-of-care diagnostic test that was tailored to target short RNA sequences and to provide a quantitative readout. Initial results of this collaboration have proved successful, the developments of the diagnostic in a paper-based format are underway.

Acknowledgements: This work is led by Dr Marta Broto, Christopher Adrianus, Dr Hyemin Kim, and Prof Molly Stevens, Imperial College London, Dr Eleanor Gray, UCL, Dr Michael Kaminski, Massachusetts Institute of Technology, and Prof James J. Collins, Massachusetts Institute of Technology, Broad Institute of MIT and Harvard, and Wyss Institute for Biologically Inspired Engineering.

Data Science for Social Good summer fellowship

Over the summer, i-sense PhD Student from the McKendry group at UCL, Jobie Budd, worked at the Alan Turing Institute and University of Warwick after being accepted for the Data Science for Social Good Fellowship programme. The programme aims to train aspiring data scientists to work with machine learning projects with social impact.

Internal workshops

Innovations in mapping and spatial epidemiology

The main aim of the workshop was to discuss how different i-sense Flagships could apply mapping and spatial epidemiology to help track, test, and treat infectious diseases.

Prof Rosanna Peeling opened the meeting by calling for combined digital health surveillance including mapping to target and tailored interventions. Attendees heard from speakers with experience ranging from health policy and geo-spatial modelling to those with industry perspectives.

The workshop also included two activities, the first of which was run by Dave Concannon who quizzed attendees on their interpretation of map designs. The second activity was run by Jobie Budd and asked participants to consider outbreak scenarios and work as teams to develop collaborative solution to halt the outbreak.

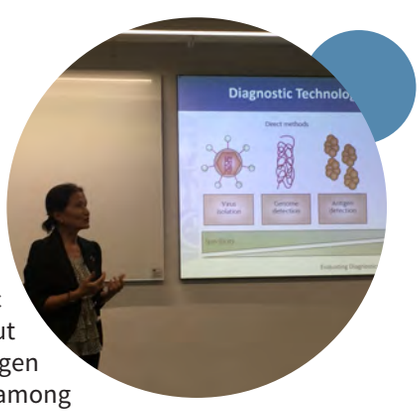
Outcomes following the workshop:

- i-sense was invited to present at the Mobile World Congress 2019
- The workshop's 'Outbreak!' group activity was shared with GSM Association with the intention to use in workshops with Ministries of Health
- i-sense members attended a PHE course on infectious disease modelling
- i-sense members contributed to the Humanitarian Open Street Map Team's 'Missing Maps' project

Thank you to our invited speakers Dr Sarah Wise, UCL Centre for Advances Spatial Analysis, Kim Viljoen, GSM Association, Dr Chantal Hendriks, the Oxford Big Data Institute, Dr Mike Short, UK Department for International Trade, and Andrew Eland, DeepMind Health.

Acknowledgments: This workshop was led by Jobie Budd, UCL, and Prof Rosanna Peeling and Dr Noah Fongwen, London School of Hygiene and Tropical Medicine.

Ultrasensitive antigen tests in infectious disease diagnostics



The main aim of the workshop was to discuss how different i-sense Flagships could apply the technologies within i-sense in the development of ultrasensitive antigen tests for priority diseases.

During this meeting attendees heard from speakers with experience ranging from diagnostic development to those with vast end user perspectives. Prof Rosanna Peeling talked about the Global Good project and how it ranked the case for investments into improved antigen detection needed for different infectious diseases. Trachoma and Schistosomiasis ranked among the top priorities.

This was followed by breakout group discussions for participants to draw from the technologies within i-sense to see how they could come up with a more sensitive antigen detection test for Schistosomiasis. They discussed the needs and limitations and were given five minutes to report back to the whole group.

The final item of the day was an open discussion in which Prof David Mabey and Dr Amaya Bustinduy, from the London School of Hygiene and Tropical Medicine, talked about how ultrasensitive antigen tests can be useful in the field. They shared their experiences from diseases such as Schistosomiasis, Trachoma, and Malaria.

Acknowledgements: This workshops was led by Prof Rosanna Peeling and Dr Noah Fongwen, London School of Hygiene and Tropical Medicine.

04
Our people and partners

2019 Awards and recognition

Dr Neil Keegan, Newcastle University

Outstanding Contribution to Teaching award in the Faculty of Medical Sciences at Newcastle University

Matthew Setterfield, Newcastle University

Best oral presentation at the ICM Directors Day

Prof Molly Stevens, Imperial College London

Elected Foreign Member of the National Academy of Engineering
Award in Colloid Chemistry, American Chemical Society
Honorary Doctorate, University of Bath
Acta Biomaterialia Silver Medal
Kabiller Young Investigator Award in Nanoscience and Nanomedicine
Royal Society 2019 Surfaces and Interfaces Award

Dr Michael Thomas, UCL

i-sense Lectureship at UCL

Dr Alice Pyne, The University of Sheffield

Lecturer in Soft Matter/Polymers & MRC/UKRI Innovation Fellow in the Department of Materials Science and Engineering, University of Sheffield

Erin Manning, UCL

LCN Annual Community Award

Jobie Budd, UCL

SLMS Graduate Conference Fund for travel and accommodation in Ethiopia

Alan Turing Institute and University of Warwick Summer Studentship

Dr Dan Richards, Imperial College London

Marie Sklodowska-Curie Fellowship to work at ETH Zürich

Dr Dan Richards and Marta Broto Aviles, Imperial College London

CRUK EdX primer award (joint lead applicants) for £100,000

Prof Ingemar Cox, UCL

2019 Tony Kent Strix Award for ‘outstanding contributions to information retrieval’

Dr Polina Brangel, UCL

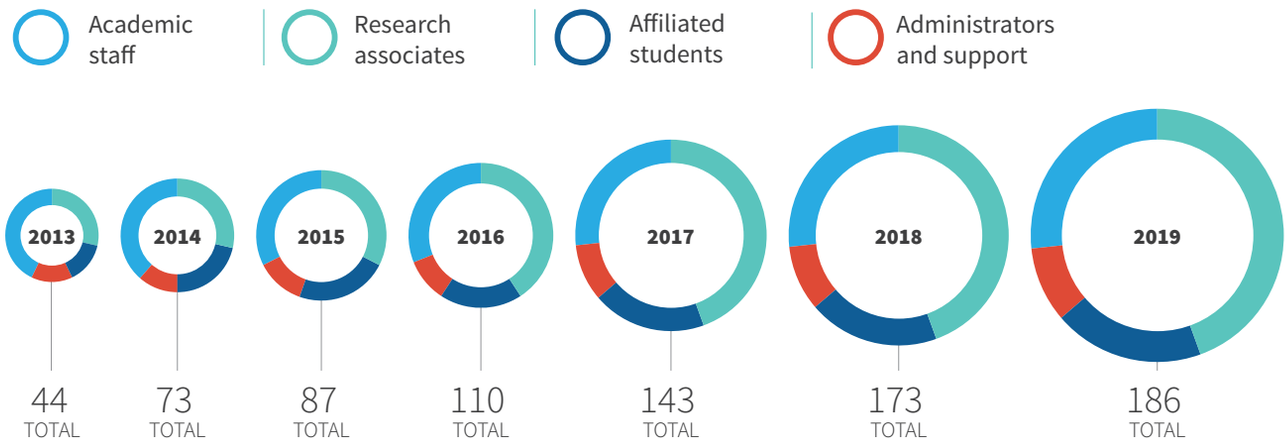
UCL EPSRC Impact Acceleration Account Grant

2019 completed PhDs

Isabel Bennett, McKendry group, UCL

Ben Miller, McKendry group, UCL

The i-sense network



Our organisational structure

External Advisory Board
Chaired by Prof David Heymann (LSHTM)

Director
Prof Rachel McKendry (UCL)

Management Committee

Strategic Operations Team
Erin Manning and Jo McHugh (UCL)

Core research

Track: Online syndromic surveillance to track outbreaks – Led by Prof Ingemar Cox (UCL) and Dr Richard Pebody (Public Health England)

Test: Smartphone-connected diagnostic tests - Led by Prof Molly Stevens (Imperial College London), Prof Rachel McKendry (UCL), and Prof Deenan Pillay, and Dr Neil Keegan and Prof Anil Wipat (Newcastle University)

Treat: Real-time data visualisation tools and linkage to care - Led by Dr Ed Manley and Prof Deenan Pillay (UCL)

Career development education alliance – Led by Dr Neil Keegan (Newcastle University) and Prof Ingemar Cox (UCL)

Partnerships, impact, sustainability –Led by Prof Rachel McKendry and Prof Deenan Pillay (UCL)

Plus Award: A smartphone-powered mRNA sequence detector – Led by Prof Molly Stevens (Imperial College London)

Plus Award: Ultra-sensitive enhanced nanosensing of antimicrobial resistance (u-Sense) – Led by Dr Neil Keegan (Newcastle University)

Management Committee

Prof Rachel Mckendry (Director)
Prof of Biomedical Nanotechnology, UCL, and i-sense Director

Prof Ingemar Cox
Prof of Computer Science, UCL, and i-sense Deputy Director and Flagship (Track) lead

Prof Deenan Pillay
Prof of Virology, UCL, and i-sense Deputy Director and Flagship (Treat) co-lead

Prof Molly Stevens
Prof of Biomedical materials and Regenerative Medicine, Imperial College London, and i-sense Deputy Director, and Flagship (Test) and Plus Award lead

Prof Vince Emery
Emeritus Prof of Translational Virology, University of Surrey

Prof Dame Anne Johnson DBE
Prof of Infectious Disease Epidemiology, UCL, Chair UCL Population and Lifelong Health Domain, and i-sense Deputy Director

Dr Neil Keegan
Senior Lecturer, Institute of Cellular Medicine, Newcastle University, and i-sense Plus Award and Education Alliance lead

Prof Ed Manley
Prof of Urban Analytics, University of Leeds, and i-sense Flagship (Treat) co-lead

Dr Richard Pebody
Health of Respiratory Disease Surveillance and Influenza Surveillance, Public Health England

Prof Rosanna Peeling
Prof and Chair of Diagnostics Research, London School of Hygiene and Tropical Medicine

Advisory Board

Prof David Heymann (Chair)
Prof of Infectious Disease Epidemiology, London School of Hygiene and Tropical Medicine, and Health of the Centre on Global Health Security, Chatham House

Dr Annette Bramley
Director, N8 Research Partnership

Prof John Brownstein
Associate Prof of Paediatrics, Harvard Medical School, and co-founder of HealthApp

Andrew Eland
Founder, Diagonal

Prof Christoph Gerber
Prof, Swiss Nanoscience Institute, University of Basel

Prof Patrick Maxwell
Regius Prof of Physics and Head of the School of Clinical Medicine, University of Cambridge

Dr Mike Short CBE
Chief Scientific Advisor, Department for International Trade

Dr Harpreet Sood
NHS Doctor, Co-Founder of the NHS Digital Academy, and Visiting Senior Fellow at the London School of Economics

Strategic Advisors

Prof Peter Dobson OBE
Former Director of Begbroke Science Park, University of Oxford

Prof Ciara O'Sullivan
Research Prof Nanobiotechnology and Bioanalysis, Universitat Rovira I Virgili

Prof Calum McNeil
Prof of Biological Sensor Systems, Newcastle University

Contact details

Address:
i-sense EPSRC IRC
London Centre for Nanotechnology
17-19 Gordon Street
London WC1H 0AH

Email:
isense@ucl.ac.uk

Website:
i-sense.org.uk

Twitter:
@isenseIRC

Facebook:
facebook.com/isenseIRC

Instagram:
instagram.com/isense_irc/