ANNUAL REPORT 2016/17

i-sense
EPSRC IRC in Early Warning Sensing Systems for Infectious Diseases

EPSRC
Engineering and Physical Sciences Research Council

Contents

EPSRC Engineering and Physical Sciences Research Council · UCL · Imperial College London · London School of Hygiene & Tropical Medicine · Newcastle University · University of Surrey · Public Health England

Foreword

Professor Rachel McKendry, Director of i-sense EPSRC IRC

In 2017, the need for disruptive sensing systems to detect and limit infectious outbreaks has taken centre stage. Zika virus and Ebola add to the threats of pandemic influenza, HIV and antimicrobial resistance, for which the world remains unprepared.

Infections are a global problem and our response must therefore be global in nature. The House of Commons Ebola report* recognised the 'heroic' work of scientists, researchers and agencies, but highlighted that the UK response, like the international response, was 'undermined by systemic delay,' and 'we must take the opportunity now to ensure that the UK is not caught unprepared when the next disease emergency strikes. Lives can be lost for every day of delay.'

i-sense EPSRC Interdisciplinary Research Collaboration aims to build new digital sensing systems to track, test and treat infectious disease much earlier than ever before, and has the potential to bring major human and economic benefits to millions of people worldwide. Since i-sense began in 2013, we have grown to a network of over 100 researchers across five UK universities, NHS, Public Health England, industry and international partnerships in South Africa, Uganda, US, Switzerland, Holland, Australia, Japan and Korea.

This report shares highlights from our past year. We have seen some wonderful achievements, including: ultra-sensitive advanced nanomaterials, ultra-rapid diagnostic device prototypes, high impact publications, two new patent applications, strategic clinical and industry partnerships including those with Africa Health Research Institute, Uganda Virus Research Institute, and Foundation for Innovative New Diagnostics, and evaluation of our deep learning algorithms of Google searches for national influenza surveillance by Public Health England. Our communications highlights include the Llama Outbreak at Greenman Festival and our work being featured on a *BBC One* documentary. We have leveraged over £20M in funding from a portfolio of sources, including two new awards this year; the £600K m-Africa MRC GCRF Foundation Award and the £3.8M EPSRC IRC Next Steps Award to secure our transition to a sustainable National Centre of Excellence.

I am immensely proud of our young researchers, and we are committed to investing in their careers to become future leaders through our Education Alliance training events, including the strategy retreat in York and the all IRC meeting in Bath, and Mobility Fellowships, which have included policy placements at the World Health Organization, and leading academic and industry teams worldwide. Our collective success is evident from their 35 prizes and awards, and indeed many have gone on to secure positions in academia, industry and government.

We hope you enjoy reading about our progress and plans for the future. As we continue to make ground-breaking discoveries to address unmet health needs here in the UK, we also have the remarkable opportunity to help address health concerns in developing countries and build early warning sensing systems for the common good. We are always open to new collaborations so please do get in touch if you are interested in working together.

Professor Rachel McKendry
Director of i-sense EPSRC IRC (UCL)

*Science in emergencies: UK lessons from Ebola Contents (2015-16)

i-sense EPSRC IRC

Engineering new early warning sensing systems to track, test and treat infectious disease.

The i-sense mission is to engineer 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.

Outbreaks of infectious disease can spread rapidly and unpredictably, causing enormous losses to health and livelihood. Without adequate diagnostic tools, there is the threat of ongoing transmission of serious infections and delay in the identification of emerging outbreaks.

Our mobile phone-connected diagnostic devices aim to widen access to testing in the home, including self-tests and devices to support front-line health workers in care homes and remote African villages. The aim is to build tools that are simple to use, cheap to manufacture, and provide rapid and accurate results.

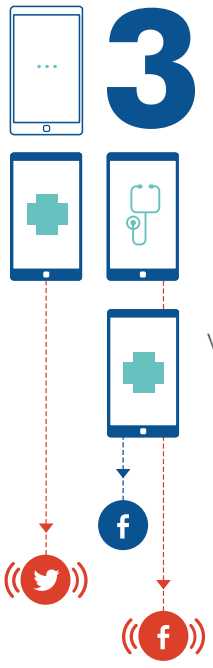
The capability to detect infections and then wirelessly connect test results to healthcare systems will help patients gain faster access to treatment and support public health efforts to map indicators of emerging infections in real-time.

We are also using the vast amount of web-based information on Google and Twitter to identify indicators of disease outbreaks before people attend clinics, or from geographical regions that are not covered by traditional public health systems.

With thanks to...
The work of i-sense is made possible through funding from the EPSRC. i-sense is one of three EPSRC Interdisciplinary Research Collaborations funded to build critical mass in disruptive sensing systems for healthcare.

Worldwide, many infections remain undiagnosed and untreated due to poor diagnostic tools. i-sense is engineering new technologies to help track, test and treat infectious diseases.

TRACK



3 IN 4

PEOPLE IN THE UK SEARCH FOR HEALTH INFORMATION ONLINE

We use self-reported symptoms via social media and web searches to help track outbreaks of infectious disease even before people visit their doctors.

Source: Department of Health and UK Trade and Investment (2016) 'The UK: your partner for digital health solutions'

TEST

95%

OF UK HOUSEHOLDS USE MOBILE PHONES

Our low-cost, user-friendly, mobile phone-connected diagnostics could widen access to testing and provide faster results, protecting patients and populations.

Source: Office of National Statistics: Percentage of households with durable goods, UK: Table A45

TREAT

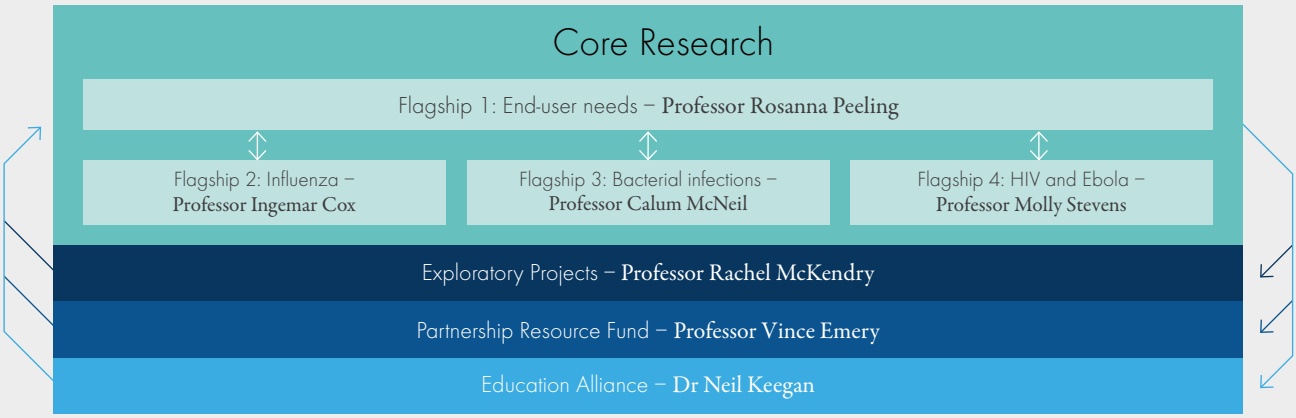
MORE THAN **245 BILLION**

APPS DOWNLOADED WORLDWIDE

Our diagnostic and digital technologies, including mobile apps, are being embedded into models of online patient pathways, to understand how they can impact online treatment and care for people in the UK and developing countries.

Source: The Statistics Portal
Google Play: number of Android app downloads 2010-2016
Apple App Store: number of downloads as of June 2017

Our Core Research and flexible funding



i-sense is made up of four interwoven Core Flagships, which are further supported by smaller projects under the Exploratory Projects programme and the Partnership Resource Fund. Our Education Alliance has also introduced new cross-disciplinary teaching and training opportunities to grow the skills of our young researchers. You can read more about the Education Alliance on page 32.

Exploratory Projects

In 2016, the third call for Exploratory Projects focused on growing our Core Research excellence and two projects were awarded funding:

1. Led by Professor Ingemar Cox in collaboration with partners from Public Health England and UCL, this project will review search query logs and social media to focus on three modelling approaches for infectious disease, expanding on recent research into influenza surveillance based on supervised learning, or machine learning.

2. Led by Professor Molly Stevens and Professor Rachel McKendry, this project aims to bring existing HIV and Ebola research from Flagship 4 to a stage of technology readiness where prototypes can be piloted in the UK, South Africa, and Uganda.

£1.75 MILLION has been awarded to 20 Exploratory Projects since the beginning of i-sense.

This programme supports new, short collaborative projects between two or more academic partner institutions, to ensure that i-sense benefits from the latest scientific developments. Importantly, Postdoctoral Research Associates have the opportunity to lead Exploratory Projects.

Partnership Resource Fund

The Partnership Resource Fund was created to grow i-sense into a self-sustained hub of innovation, by building networks of excellence with external academic, clinical and industry partners. By offering flexible funding opportunities to our members through Knowledge Transfer Grants and Mobility Fellowships, we're able to build national and international partnerships.

£430K
in funding for Knowledge Transfer Grants to date.

These projects aim to support the translation of i-sense technologies into products and practices.

£77K
in funding for Mobility Fellowships to date.

These projects offer our students the chance to expand their knowledge and experience in different dynamic scientific environments.

From July 2016 to June 2017, six new Knowledge Transfer Grants, totalling more than £353K, were awarded. These projects are outlined throughout this report. During round two of the i-sense Mobility Fellowships, a total of £53K was awarded to six applicants. These projects include collaborations with the University of New South Wales in Sydney, Africa Health Research Institute in South Africa, Tufts University in Medford, USA and a placement at the World Health Organization in Geneva.

We're not your ordinary research team

As an EPSRC Interdisciplinary Research Collaboration, i-sense is uniquely placed to offer training and collaboration opportunities beyond the ordinary research environment.

Our team

Biochemists, chemists, physicists, engineers, computer scientists, microbiologists, statisticians, bioinformaticians, architects, philosophers, clinicians, epidemiologists, and social scientists.

Our opportunities

Understanding end-user needs

Our members have the chance to carry out landscape reviews to understand the pathway to adoption for our generation of new technologies. They also have the chance to work in the field at the Africa Health Research Institute, or with industry partners and healthcare providers to improve their understanding of end-user needs.

Networking and collaboration

We provide opportunities to meet science and industry leaders to build the knowledge and networks needed to foster good collaboration and maximise impact.

Engagement

Our members have the chance to gain experience in other labs, at relevant organisations, and in industry. Active public engagement also helps members discuss their research to a broader audience.

Teaching and training

Our Education Alliance helps researchers and students build on a range of skills from novel research skills to soft and business skills.

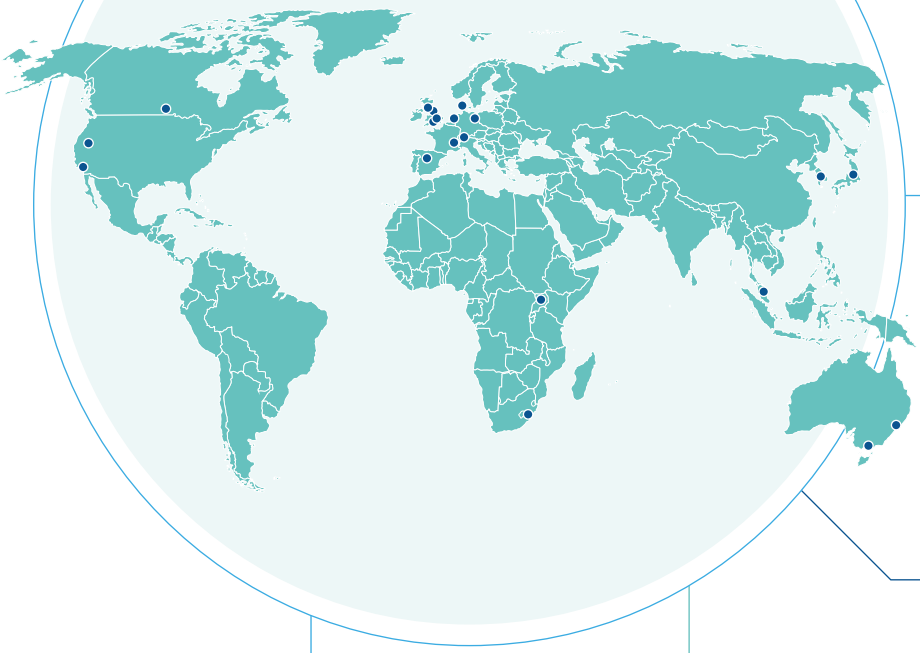
Tech transfer

Our staff and network share advice on working with companies, patenting, technology development, applying for follow-on-funding and start up funds, placements with industry, and CASE studentships.

An i-sense snapshot

United Kingdom | America | Japan | Uganda | South Africa | Canada | Australia | Netherlands
France | Switzerland | Denmark | South Korea | Spain | Germany | Malaysia

Where we've worked



28 workshops and events

From bug hunters to llama outbreaks, our members have been sharing their research with stakeholders to maximise the impact of our work and share ideas.

40 published papers

Appearing in publications such as *ACS Nano, Scientific Reports, Science,* and *Nature Nanotechnology*, our members are supported to produce quality research papers.

39 funded projects

By supporting smaller projects, we're able to share knowledge and expertise, and test our technologies. The projects we've funded include 11 Mobility Fellowships, eight Knowledge Transfer Grants, and 20 Exploratory Projects.

£20M in leveraged funding

To date, i-sense has received £3.8M in funding from the EPSRC for the Interdisciplinary Research Collaboration Next Steps Award, plus £10M in-kind leveraged funding to build a National Centre of Excellence, and a further £1.2M from the EPSRC for other projects. We have also received £1.3M from the Medical Research Council, including £600k for the m-Africa Global Challenges Research Fund Foundation Award, as well as £1M from the EU, £1M from industry including CASE studentships, in-kind access to data, reagents and sponsorship, and £2M from partner and institutional contribution to i-sense, including studentships and investigator time.

116 i-sense members

Since we started in 2013, i-sense has grown year-on-year from just 31 members to a cohort of professionals with various backgrounds and expertise.

Flagship 1: Systems level perspective of end-user needs

“Our flagship works to carry out environmental scans and explore pathways to adoption for a new generation of diagnostic technologies. We need to understand the needs and priorities of our end-users, and be aware of the impact our work will have on clinical practices and on surveillance for antimicrobial resistance and epidemic preparedness in the UK, as part of the global health security agenda.”

Professor Rosanna Peeling, LSHTM

Preparing for large global epidemics

By Dr Adriana d'Souza-Goncalves, LSHTM

i-sense strategy retreat to York

In collaboration with the Education Alliance, Flagship 1 held an all i-sense retreat in the historic city of York on 10 and 11 November 2016.

The retreat was designed with two goals in mind; to create awareness of the rapidly changing landscape of diagnostic needs for emergency preparedness (ways of working and lessons learned); and to generate strategic ideas on how i-sense can embrace the new paradigm and add value.

The retreat began with i-sense Flagship 1 lead, Professor Rosanna Peeling, giving an introduction to the global landscape and priorities. This was followed by Dr Penny Wilson from Innovate UK and Dr Bill Rodriguez from Foundation for Innovative Diagnostics presenting on the changing landscape.

Case studies from previous global epidemics illustrated the need of a systems approach to guide test design and product adoption. Participants learned the importance of considering the technology, as well as the properties of the pathogen, the host response to infection, and the diagnostic setting when designing diagnostic tests for infectious diseases.

Participants were also shown how an evidence-based approach to estimate both the risks and the benefits of a new technological innovation is important to drive adoption.

Expert advice from industry

Dr Wilson discussed why a multi-level evidence-based approach is important, but also not sufficient to drive the adoption of technological innovation within healthcare institutions.

From a global perspective, Dr Rodriguez showed how new sample-in-result-out nucleic acid amplification technologies can offer improved performance as well as the potential to test for multiple pathogens using a single specimen. Regarding the management of fever and the rise of antimicrobial resistance, he stressed the importance of simple, rapid diagnostic tests to guide the use of antibiotics at a community level. Dr Rodriguez concluded his presentation by discussing the role of open platform technologies and connectivity solutions as possible ways to move forward.

Simulating a global epidemic

A variety of brainstorming and interactive activities were organised to get participants thinking about the relevance of the presented topics to i-sense research.

A simulation exercise developed in collaboration with the Global Health Sim, allowed participants to understand first-hand the major real-life challenges of diagnostic development in response to a global health emergency.

The retreat provided a unique opportunity for the i-sense community to grow their knowledge and develop strategies on how i-sense could add value to this changing landscape in a more informal setting while having a lot of fun!

Dare to dream: Scenarios for early warning systems

By Professor Rosanna Peeling, LSHTM

Assessing current systems

Infectious diseases continue to pose serious threats to human health and global health security. Enhancing the capacity of early warning systems to rapidly detect and respond to these infectious disease threats is crucial for the prevention and management of outbreaks.

Flagship 1 conducted consultations with key stakeholders at national and global level to assess how the current systems work and, in the wake of recent outbreaks, what changes have been made and what can be envisioned for the future.

The UK landscape

The results of this work show that the current UK surveillance system is considered 'fit-for-purpose.'

It consists of a combination of clinic or syndrome based surveillance and laboratory based reporting systems from 180 laboratories across the UK. The information is shared nationally and fed into various global reporting systems, including the Global Early Warning System, which combines and coordinates the alert and disease intelligence mechanisms of the Organisation for Animal Health, Food and Agriculture Organisation and the World Health Organization.

The need for a global approach

A global effort to predict, prevent and control animal disease threats is important, as infections transmitted from animals to humans have been frequent sources of recent outbreaks.

In the wake of the Ebola and Zika outbreaks, early warning surveillance systems in the UK have evolved and will continue to evolve at a rapid pace in response to future outbreaks.

i-sense dare to dream

With advances in novel diagnostic technology and data capture systems from social media, the dare to dream scenario for a future early warning system in the UK will consist of earlier warning through diversification of data sources, including automated reporting and alerts from laboratories as well as point-of-care testing sites across the country.

i-sense is uniquely positioned to link advances in diagnostic innovations, data capture from social media and communications technologies through the works of its four flagships to ensure the continued effectiveness of early warning systems against future epidemics.

i-sense has the potential to bring major human and economic benefits to millions of people worldwide.

Flagship 2: Influenza

“Identifying the source of an outbreak early is key to controlling the spread of disease and protecting populations. Flagship 2 is focused on developing an early warning sensing system for flu by using symptoms reported on the web and combining this with mobile phone-connected diagnostic tests.”

Professor Ingemar Cox, UCL

Using the web to track flu outbreaks

By Dr Vasileios Lampos and Professor Ingemar Cox, UCL, and Dr Richard Pebody, PHE

Sourcing data

Online activity generates vast volumes of data in direct or indirect ways. This data is essential to our research and can come from posts on social media, such as Twitter or Facebook, or through web searches. i-sense researchers obtain this data through collaborations with Google and Microsoft, as well as from our own collection pipeline (Twitter).

Health data, such as the rate of a disease in specific geographies or parts of the population, is obtained through collaborations with two health agencies; Public Health England and the Royal College of General Practitioners.

i-sense researchers are using the latest privacy preserving tools, where deanonymisation is not possible, to help build public trust in our early warning systems.

Influenza surveillance from web search

The i-sense research group at the Department of Computer Science in UCL in collaboration with colleagues in Public Health England responsible for respiratory disease surveillance have been looking into improving methods of using online user data for health surveillance.

A common criticism of using web search data for monitoring the prevalence of influenza-like illness is that some query terms may be strongly correlated with influenza, but have no meaningful link to illness. For example, because flu is seasonal (commonly occurring during winter), it is not uncommon for terms such as 'Christmas' to have a high correlation.

These challenges have been overcome by proposing a novel query selection approach, which combines time series modelling with a semantic interpretation of search queries, discarding many of the confounding ones.

This method has been described and evaluated in a recent paper that was presented at one of the top Computer Science conferences, WWW '17. Work has now begun on applying such models to locations where historical health reports are limited or non-existent. Our live flu monitoring tool, the Flu Detector (fludetector.cs.ucl.ac.uk), uses these models for estimating flu rates in England. Preliminary work undertaken between UCL and Public Health England to evaluate the performance of this online tool compared to existing Public Health England influenza surveillance systems are encouraging, with further work planned.

Assessing the impact of health interventions

Traditional health surveillance schemes are based on data collected from people that use healthcare services. However, large parts of the population may not necessarily visit a general practitioner or a hospital. In this case, user activity, obtained via online resources, could complement traditional syndromic surveillance schemes.

For example, a statistical framework was previously developed for using social media and web search data to assess the population impact of a pilot vaccination programme against influenza in England. A new paper, which is currently under review, shows that we can also obtain important insights using social media on various other factors of a vaccination campaign. For example, analysis showed that vaccinating primary school children with influenza is a more effective strategy than vaccinating secondary school children to reduce flu in the general population. This information could be used to complement traditional metrics.

Mining user characteristics to stratify disease models

Understanding user profiles from mining online content could provide important insights for public health organisations.

i-sense researchers have been working on models for automatically classifying social media users based on their socio-economic status and occupation.

This work has been presented in top-tier conferences in computational and information retrieval. Future work will consider utilising such models to stratify flu estimates in England.

Sharing our research

In February 2017, we co-organised a one day workshop on 'Mining Online Health Reports' at the 10th International Conference on Web Search and Data Mining.

At the workshop, new peer-reviewed papers were presented and i-sense researchers had the opportunity to engage with leading researchers in the area of computational health.

These researchers are also acting as co-editors on a special issue focusing on the same topic that will be published by the *Journal of Medical Internet Research*.

Most recently published paper:

Lampos, Zou and Cox (2017). *'Enhancing Feature Selection Using Word Embeddings: The Case of Flu Surveillance'. WWW '17*, pp. 695–704.

Smart about flu detection

By Dr Stephen Hilton, UCL

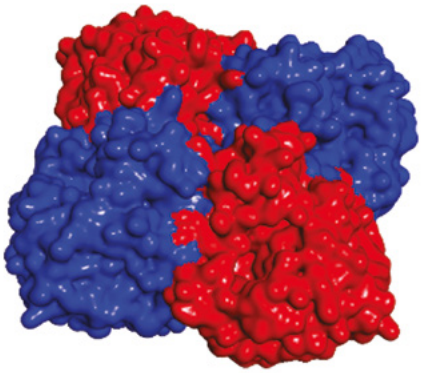
i-sense researchers are developing a low-cost mobile phone spectrometer, which enhances the ability of phone cameras to accurately read results on point-of-care tests for influenza.

In particular, the mobile phone spectrometer will be able to recognise the viral target protein, tetrameric neuraminidase, that the antiviral drug, Tamiflu, binds to in order to relieve symptoms.

A spectrometer is helpful in reading lateral flow tests because it is able to use light to detect the presence of the virus. The level of light varies depending on whether there is a presence or absence of the virus.

By using 3D printing to produce the spectrometer, manufacturing the device can cost as little as £5 per unit. This approach also means that the device can be readily adapted to a wide range of mobile phones and easily modified as technology advances.

This work is part of an Exploratory Project that brings together i-sense researchers Dr Matthew Penny, Dr Michael Thomas, Professor Molly Stevens, Professor Rachel McKendry and Dr Stephen Hilton.



Viral target protein, tetrameric neuraminidase

The tech behind our tests

By Candice Keane, UCL

Diagnosing the flu with a mobile app

Researchers in the McKendry group at UCL are developing and evaluating a mobile app to be used for readout of influenza A and B test strips in collaboration with Becton Dickinson.

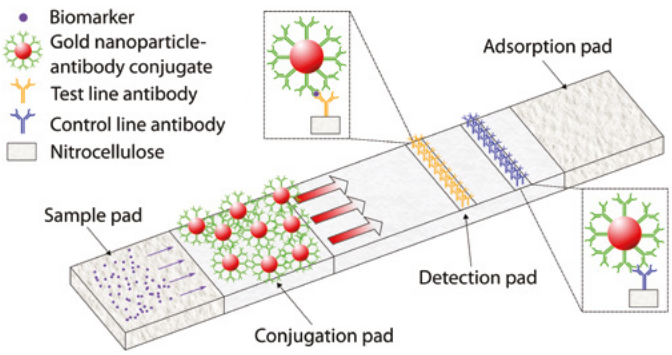
A small pilot study demonstrated good consistency between the reader and app for the detection of influenza in both panel and clinical samples.

The tiny tech used in self tests

Developments are being made towards designing an in-house lateral flow test that can more rapidly and accurately detect influenza using gold nanoparticles.

Experiments have demonstrated that influenza A nanobodies (antibody fragments) that can access hidden clefts on viruses bind well to flu nucleoprotein. This binding is important for improving test sensitivity.

Future work will examine how these robust nanobodies can be incorporated into novel mobile phone-connected, rapid tests for diagnosing influenza.



The value of rapid influenza testing in a pandemic

By Dr Peter J White, Imperial College London

The challenge of diagnosing and treating influenza

An Exploratory Project involving Imperial College London, UCL, and Public Health England examined the value of rapid testing for influenza in a pandemic, using data from the influenza pandemic of 2009 to 2010 collected by general practitioner-based surveillance and the National Pandemic Flu Service.

A challenge in treating influenza is that many different infections can cause influenza-like symptoms, whilst treatment is only effective against illness caused by the influenza virus.

Due to this, general practioners may be reluctant to prescribe treatment based on symptoms (so patients with influenza do not get treated), deterring patients from seeking care. Alternatively, many patients with influenza-like illness who receive treatment will not benefit from it, whilst over use depletes the national stock-pile.

A point-of-care test that could quickly and accurately diagnose influenza could encourage patients to seek care and general practitioners to prescribe treatment.

Challenges for creating an influenza rapid test

- Sufficient sensitivity: low chance of producing a false negative result
- Sufficient specificity: low chance of producing a false positive result
- Cheap enough to be cost-effective for use by the NHS
- Easy and quick to use

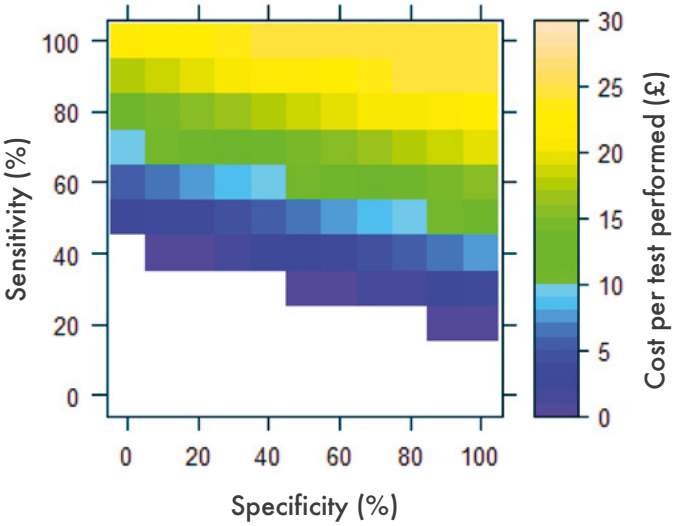
By considering these factors, an analysis was conducted to enable manufacturers to determine whether a potential test is likely to be commercially viable.

The value of a rapid flu test to the NHS

The example result shown (below) considers use of the test in a scenario in which general practioners prescribe to patients who test positive for influenza and not to patients who test negative. It was assumed that patients who test positive have an increased probability of taking the treatment as they are more confident that they have influenza infection and will benefit from treatment.

In this example, a 'perfect' test, with 100 per cent sensitivity and 100 per cent specificity, has a value of around £28 per test. A test with 80 per cent sensitivity and 80 per cent specificity would be worth around £20.

This work involves i-sense members Dr Nathan Green, Professor Andrew Hayward, Dr Peter J White, Dr Ellen Fragaszy, Dr Perrine Pelosse, Professor Christl Donnelly, and Dr Richard Pebody.



Flagship 3: Bacterial infections

Overuse of antibiotics has resulted in bacteria developing resistance to currently available antibiotics, and we are now faced with a real threat of the antibiotics pipeline running dry. Flagship 3 is working on rapid sensor systems to detect and identify bacterial infections and antibiotic resistance mechanisms.

Where do we go from here? Developing diagnostics for bacterial infections

By Dr Chris Johnson and Professor Anil Wipat, Newcastle University

Resistance to treatment

Since the golden age of antibiotics we have continued to underestimate the genetic capabilities of the bacteria we have been trying to kill.

A key challenge of diagnostic tests is that current technologies may take several days to perform. Due to such delays, patients are often prescribed broad-spectrum antibiotics, which has led to an increase in antibiotic resistant bacterial infections.

One of the ways we can help to stop the misuse of, and continued resistance to, antibiotics is by building rapid diagnostics that not only identify the bacteria causing the infection, but also inform us of its antimicrobial resistant profile.

i-sense researchers are developing mobile phone-connected diagnostic tests to improve early detection and identification of bacterial infections, including MRSA, *C. difficile* and E. *coli*.

The i-sense vision of delivering technologies suitable for point-of-need detection of antimicrobial resistant genes is based on complementary technologies, isothermal nucleic acid amplification combined with rapid sensor systems based on optical, electrical or, in a new and exciting development, optoelectronic detection coupled with mobile phone technology.

Designing diagnostics for antimicrobial resistance

Due to their speed, simplicity and sensitivity, isothermal amplification techniques are now establishing themselves as a clear point-of-need alternative to traditional polymerase chain reaction methods. They allow the rapid identification of antimicrobial resistant genes and can be adapted to a simple lateral flow format (similar to a pregnancy test) for point-of-need applications.

The ability to detect antimicrobial resistant genes quickly and specifically at the point-of-need would be a potential game-changer in the battle against antimicrobial resistance. It would allow general practitioners to prescribe the correct antibiotics at the point-of-need, based on ultrasensitive antimicrobial resistance tests rather than simply patient symptoms, helping to turn the tide in our favour in the ongoing battle against antimicrobial resistance.

The aim of i-sense Flagship 3 is to develop tests with superb sensitivity that are suitable for all environments, that provide rapid results, and that are appropriate for end-user needs, particularly those in rural and remote locations.

Computing and diagnostics

Recent developments in technology, computing and instrumentation have had a major impact on medicine and are changing the relationship between patients and the healthcare system. For diagnostics in particular, we are seeing the emergence of point-of-need sensor technologies that are based on molecular information, such as DNA sequence data.

To keep up with the sheer size and complexity of data being collected, it is necessary that the data is sent to a central repository, where it is analysed, integrated and the diagnosis returned.

Researchers in i-sense are making developments in distributed computing, particularly cloud computing, that are now making this model possible. Data can be streamed from the point-of-need device over the Internet to a Cloud server where a workflow can be executed to return the diagnosis. These workflows can also potentially include human decision makers, in addition to computational data analytics.

This new model of point-of-need operation offers many exciting opportunities. In the future, health data networks will offer the ability to integrate information from point-of-need devices with personalised healthcare data, as part of the diagnostic decision making process.

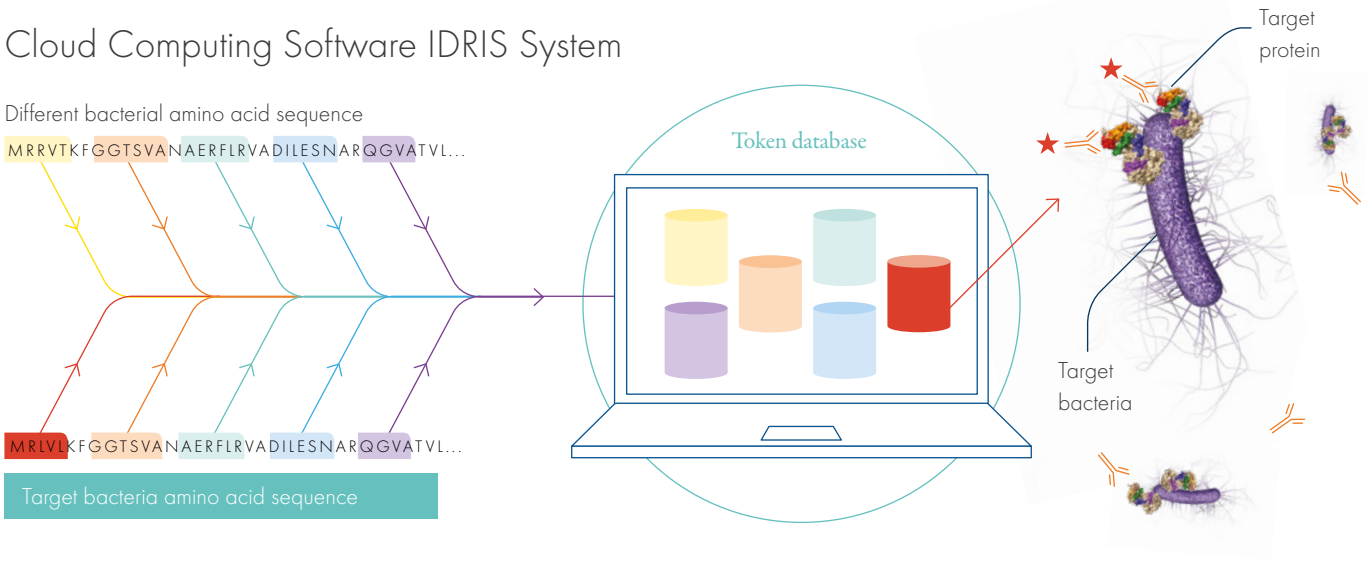
Moreover, since data from multiple point-of-need devices can be assimilated in Cloud servers, these diagnostic decisions can be made in the context of data emerging from other devices, such as other point-of-need systems, smartphones and data from social media. This form of distributed data integration will have major implications for epidemiology, offering the scenario of real-time monitoring of infectious disease outbreaks.

Although some significant steps have been made towards a more integrated healthcare system, there are still some challenges with storing large amounts of data, as well as the need to address social and political related challenges, such as data sharing and security.

If this network model of patient monitoring and healthcare decision support can be achieved, with central data aggregation, this will open the door to a much more reactive and dynamic approach to patient care.

Discovering unique biomarkers for *C. difficile*

By Dr Chris Johnson, Newcastle University



The process of finding suitable affinity reagents for emerging infectious disease threats can take months or even years. So, to help speed the process up, the i-sense team at Newcastle University have developed a novel bioinformatics cloud computing-based system called IDRIS, to predict biomarkers for a given group of organisms from genome sequencing data.

These biomarkers can be used to generate novel monoclonal antibodies (mAbs), with the potential to recognise all target organisms with little or no cross-reactivity to non-target organisms.

Using IDRIS for diagnostic development

Clostridium difficile infection continues to be a significant economic healthcare burden. Clostridium difficile (*C. difficile*) includes both pathogenic (toxin-producing) and non-pathogenic strains, and although both strains can colonise their hosts, only toxin producing strains are associated with disease.

Current testing protocols for clostridium difficile infection in the UK are based on guidelines from the Department of Health, who advise that organisations adhere to a two-step testing algorithm.

Due to concerns about the performance of the commonly used glutamate dehydrogenase immunoassay, i-sense have sought to design a diagnostic test for clostridium difficile infection that could replace this test in a typical two-step algorithm.

Identifying new biomarkers for *C. difficile*

IDRIS was used to identify a unique biomarker for *C. difficile*, present in all *C. difficile* strains sequenced to-date. The biomarker resides in the surface-layer, a highly abundant paracrystalline structure that surrounds the *C. difficile* cell.

mAbs were raised against a peptide corresponding to the unique amino acid sequence of the biomarker. Antibody characterisation revealed one of the antibodies, mAb521, could recognise all known *C. difficile* surface layer types, and showed negligible cross reactivity with other bacteria typically found in stool samples.

By using targeted antibody design through harnessing the power of IDRIS we have generated a mAb that has the potential to demonstrate species specific recognition of *C. difficile* and a UK patent application has been submitted.

The next step is to assess the performance of mAb521 against clinical samples in a study planned in collaboration with Public Health England.

Pushing the limits

By Dr Neil Keegan, Newcastle University and Professor Ciara O'Sullivan, Rovira i Virgili University

i-sense researchers from Newcastle University and Rovira i Virgili University, wish to push the limits of next generation molecular diagnostics using isothermal amplification approaches.

Analysing current tests

Current state of the art commercial level technologies for molecular diagnostics, such as the Cepheid GeneX-pert® and Roche cobas® Liat® real-time polymerase chain reaction systems, are excellent and sophisticated point-of-care solutions, but currently incur a high cost for the benchtop reader and complex cartridges.

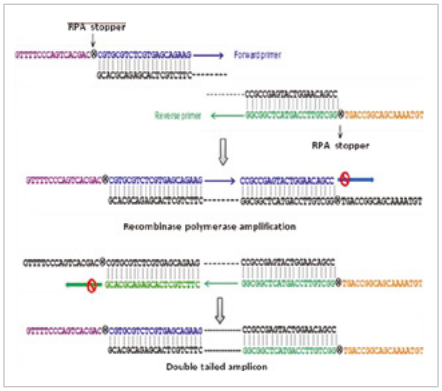
As an alternative method the Alere™ i system uses isothermal amplification (nicking enzyme amplification) at 59°C, simplifying the system as no thermal cycler is required. This system also relies on cartridge based sample preparation and an optical fluorescence benchtop reader. These systems can provide results in approximately 15 to 30 minutes in optimised assay formats.

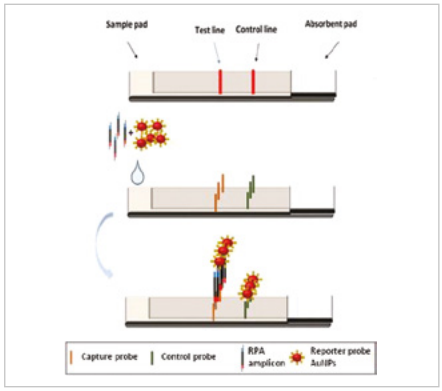
Building paper-based tests

The team at i-sense aim to create a simple sample-in-result-out system using cheap paper-based approaches that require limited infrastructure, are user-friendly, quick to manufacture and provide accurate results. Such tests are crucial for the emerging field of personalised medicine, for which companion diagnostics are essential. The tests are also well suited for infectious organism detection and antimicrobial resistance screening in the UK and resource limited settings.

i-sense researchers and international collaborators have reported on the development of a point-of-care nucleic acid lateral flow test for the direct detection of isothermally amplified DNA.

In our approach, the recombinase polymerase amplification method was modified slightly





and we were able to detect the amplification of DNA in less than 15 minutes at a constant temperature of 37°C.

The use of the tailed primers obviates the need for hapten labelling and consequent use of capture and reporter antibodies, whilst also avoiding the need for any post-amplification processing for the generation of single stranded DNA. This presents an assay that can facilely find application at point-of-care.

i-sense test design

The image above visualises the nucleic acid lateral flow assay, which clearly resembles the rapid diagnostic immunoassay formats, but with the promise of achieving much higher sensitivity levels.

The incorporation of polymerase stoppers within the engineered tailed primers facilitates the production of duplex amplicons flanked by single stranded tails (left panel).

In lateral flow detection the tailed duplex amplicon is captured by a nucleic acid capture probe complementary to forward strand tail, whilst the amplicon is detected via a nucleic acid containing reporter probe complementary to the reverse strand tail (right panel).

While there is a long way to go to realise sample-in-result-out paper based assays, the team have taken the important first steps towards realising this vision.

Jauset-Rubio, M., Svobodová, M., Mairal, T., McNeil, C., Keegan, N., El-Shahawi, M. S., Bashammakh, A. S., Alyoubi, A. O., O'Sullivan, C. K. *'Aptamer Lateral Flow Assays for Ultrasensitive Detection of ß-Conglutin Combining Recombinase Polymerase Amplification and Tailed Primers.' Analytical Chemistry* (2016); DOI: 10.1021/acs.analchem.6b03256

Jauset-Rubio, M., Svobodová, M., Mairal, T., McNeil, C., Keegan, N., Saeed, A., Abbas, M. N., El-Shahawi, M. S., Bashammakh, A. S., Alyoubi, A. O., O'Sullivan, C. K. *'Ultrasensitive, rapid and inexpensive detection of DNA using paper based lateral flow assay.' Scientific Reports*, 6, 37732, (2016); DOI: 10.1038/srep37732

Mobile health in care homes

By Professor Jackie Cassell, Jo Middleton, and Stefania Lanza, Brighton and Sussex Medical School

What makes communication enabled diagnostics useful in real life? A clear focus is to meet the needs of potential users of tests for MRSA and *C. difficile*, who work in complex landscapes.

Residential and nursing care homes are a priority population for i-sense. These homes, where many vulnerable individuals live in close proximity, are particularly susceptible to outbreaks of respiratory or gastrointestinal disease.

i-sense researchers at Newcastle University worked in collaboration with Brighton and Sussex Medical School to undertake a study designed to explore and address usability challenges in a care home setting for a largely hidden and vulnerable population.

The study looked at the current use of point-of-care tests, and aimed to understand how these tests could potentially be used to help decision making for *C. difficile* and MRSA, the benefit to healthcare professionals in using such tests, and at what points in care should these tests be used.

As many health and social care professionals flow in and out of residential and nursing care homes to attend to residents, the study used Normalization Process Theory (normalizationprocess.org) to explore these questions and establish a foundation for future piloting and implementation in i-sense.

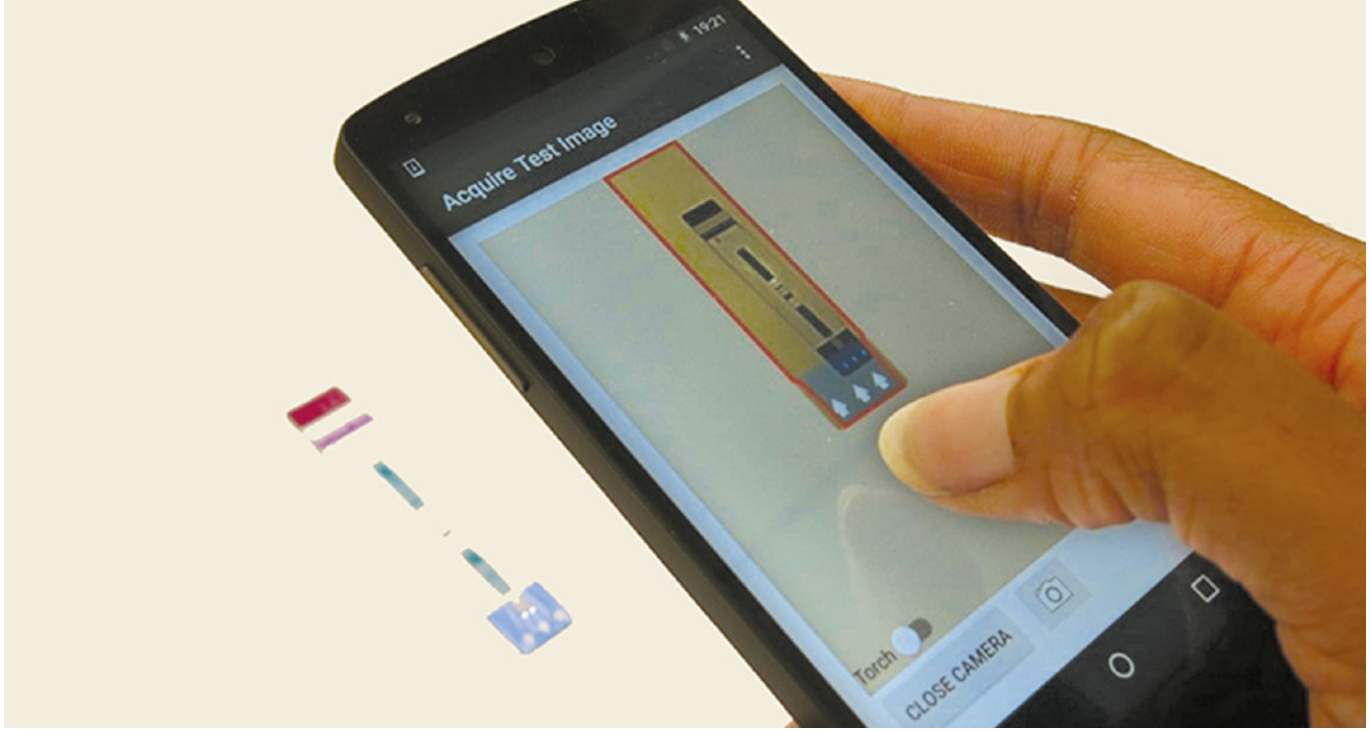
Potential users of communication enabled diagnostics in residential and nursing care homes include general practitioners, care home staff, paramedics, community nurses and health protection practitioners. The study interviewed members of all these groups across a range of residential and nursing care homes types and locations.

The work, currently being prepared for publication, demonstrated multiple and often contradictory perspectives on the use of these tests. A key consideration was what action would be triggered, and timing in relation to visits or other episodes of care was a key issue. While mobile communications were welcome, existing communication technologies were very variable and often surprisingly dated. Engagement with this complex range of potential users in residential and nursing care homes will be critical to successful introduction of future tests.

Flagship 4: HIV and Ebola

“Early diagnosis of HIV and Ebola is crucial for effective treatment and care. Flagship 4 are dedicated to developing new, urgently needed point-of-care tests to prevent and control epidemics.”

Professor Molly Stevens, Imperial College London



Online support for HIV testing and care

By Dr Jo Gibbs, Professor Ann Blandford, Dr Pam Sonnenberg, and Dr Aneesha Singh, UCL, and Professor Claudia Estcourt, Glasgow Caledonian University

Developing online pathways to support HIV

We live in a world where mobile and online resources are increasingly becoming the first point of contact for people seeking health information.

In 2015, Public Health England reported that more than 101,000 people were living with HIV in the UK and more than 6,000 people were infected with HIV that year alone.

i-sense researchers believe that there is an important role for apps and online interventions, particularly for prevention, early diagnosis, referral to care and ongoing management [of HIV].

Apps can provide an important link between technology, a person testing for or already diagnosed with HIV, and healthcare professionals.

In a collaboration between UCL and Glasgow Caledonian University, i-sense researchers are developing a user-centred online pathway for HIV, called iSHOP. The pathway starts from testing for infection through to either long-term prevention or management and engaging in care.

These studies have found that the functionality of available online resources to support HIV differs widely and many fail to meet the basic health care needs of people testing for or living with HIV, such as developing confidence in their ability to conduct a self-test reliably and receiving results in a sensitive way that supports them to move forward.

It was also found that many resources create stigma around HIV and provide information that is not accurate or supported by evidence.

Project highlights

The Exploratory Project has had a successful year, with highlights including welcoming Human Computer Interaction Research Associate, Dr Aneesha Singh, presentations and publications at both international and national conferences, and involvement of two Masters students in projects for their dissertations.

Expanding the potential of iSHOP

In January, the group, which includes Dr Jo Gibbs, Professor Ann Blandford, Dr Pam Sonnenberg, Dr Aneesha Singh, and Professor Claudia Estcourt, secured further funding through a Partnership Resource Fund application, which has allowed for expanding the project scope.

The expanded scope includes integrating iSHOP with the existing, award winning, eSexual Health Clinic and linking the eSexual Health Clinic with the HIV self-test reader app being developed within i-sense. The team are currently finishing user studies and will shortly be starting software development of the new eSexual Health Clinic.

Llamas helping fight HIV

By Dr Eleanor Gray, Dr Jenny Brookes, and Professor Rachel McKendry, UCL

Using nanobodies for early detection

Early stage HIV detection in the community is problematic as tests typically rely on the detection of antibodies. These antibodies are difficult to detect until approximately one to six months after exposure.

The prevention of HIV and other infectious diseases is a global priority and driving force for the continued development of advanced nanotechnologies capable of diagnosis at point-of-care.

i-sense members at UCL have explored the potentially important role llamas and their family (camelids) could play in developing tools to detect early stage HIV.

This research looked into how well i-sense camelid nanobodies (antibody fragments) bind to the p24 antigen, an important protein found in the early stages of HIV infection.

Nanobodies are one tenth of the size of antibodies, allowing them to more easily access hidden parts of proteins. They are also stable in temperatures up to 90°C making them suitable for varying environments.

These antibodies have high affinity to worldwide subtypes and fast on rates, making them ideal for rapid diagnostic tests.

Collaborating across disciplines and institutes

By collaborating with L'Institut de Biologie Structurale at Grenoble and QVQ in the Netherlands, an x-ray crystal structure was determined for the new nanobody 59H10, which binds with high affinity to p24.

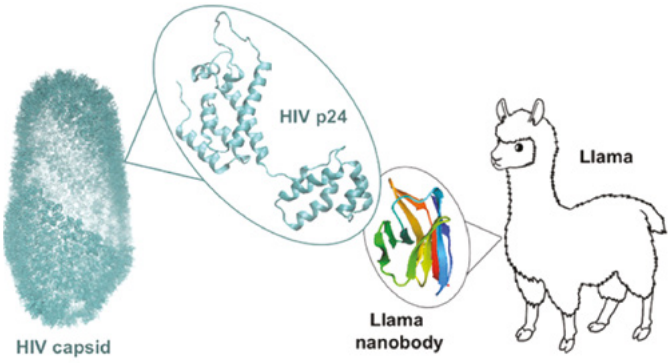
The research characterised the relationship between nanobody 59H10 and p24 (pictured to the right) to pin-point the binding properties important in understanding the molecular process needed for the design of suitable components of diagnostic tests.

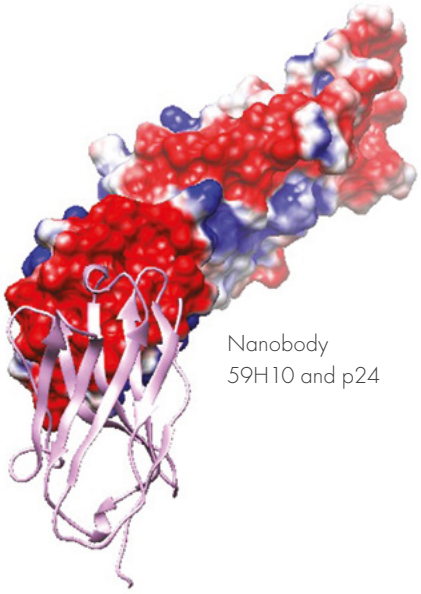
The experimental research was supported by computer science, where simulations were run to determine how well i-sense nanobody 59H10 binds to p24 compared to other nanobodies with varying properties.

The atomic coordinates for these simulations can be found on the Protein Data Bank (pdb code 5O2U) as deposited by i-sense collaborators Winfried Weissenhorn, Christophe Caillat and Theo Verrips.

The crystal structure combined with functional studies, including ELISA and biolayer interferometry, and atomistic investigation using molecular simulations determine how and why these nanobodies interact with an important HIV biomarker.

These findings are important in designing biosensors for the development of future diagnostic tests.





Nanobody 59H10 and p24

Gray, E.R., Brookes, J.C., Caillat, C., Turbe, V., Webb, B.L., Granger, L.A., Miller, B.S., McCoy, L.E., El Khattabi, M., Verrips, C.T., Weiss, R.A., Duffy, D.M., Weissenhorn, W., McKendry, R.A. *'Unravelling the molecular basis of high affinity nanobodies against HIV p24: in vitro functional, structural and in silico insights.'* ACS Infectious Diseases (2017); DOI: 10.1021/acsinfecdis.6b00189

Developing patents for new diagnostic tools

By Dr Mike Thomas, Colleen Loynachan and Professor Molly Stevens, Imperial College London

i-sense researchers at Imperial College London filed a UK patent application to cover the production and use of core-shell catalytic metal nanoparticles in amplified lateral flow testing.

The team has shown how these nanomaterials enable simple and rapid testing for HIV in lateral flow assays. This work constitutes a major success within Flagship 4, in which they engineered a methodology to construct monodisperse catalytic particles using a seeded synthesis. This methodology produces nanoparticles that retain high catalytic activities following facile antibody conjugation and during clinical sampling.

The test, which uses llama antibodies made by the McKendry group at UCL, includes an amplification step that triggers a colour change at the test line when small quantities of p24 are present, even during very early stages of HIV infection. The improvements have increased sensitivity for this lateral flow design. This surpasses the current industrial gold standard for lateral flow rapid tests used at the point-of-care.

Although tested initially on HIV, the patent application covers a range of diseases in demand of innovative diagnostic tools targeting low level protein detection in complex fluids.

Tiny tech for next generation tests

By Dr Vijay Chudasama, UCL

i-sense researchers at UCL and Imperial College London have been working together to understand the chemistry behind nanoparticle-antibody conjugation to improve biomarker detection in point-of-care tests for protein based disease biomarkers.

The work introduced the protein modification expertise of the Chudasama group at UCL into i-sense and coupled it with the extensive knowledge of fluorescent nanoparticles present within the Stevens group at Imperial College London. Additional expertise was sought from the Heeney group at Imperial College London, whose novel fluorescent polymers are being employed as the reporter module for the current work.

The novelty of this project has led to many challenges at the practical level, often necessitating last minute changes and innovative solutions, but has improved our overall understanding of nanoparticle-protein conjugation.

Future work hopes to see further progress in the area and make truly significant improvements to the way researchers attach protein ligands to nanoparticle surfaces.

This Exploratory Project is a collaboration between i-sense researchers Dr Vijay Chudasama, Dr Daniel Richards, Dr Chris Wood, Dr Mike Thomas, Dr Adam Creamer, Ye Wang, Dr Philip Howes, João Nogueira, Professor Martin Heeney, and Professor Molly Stevens.

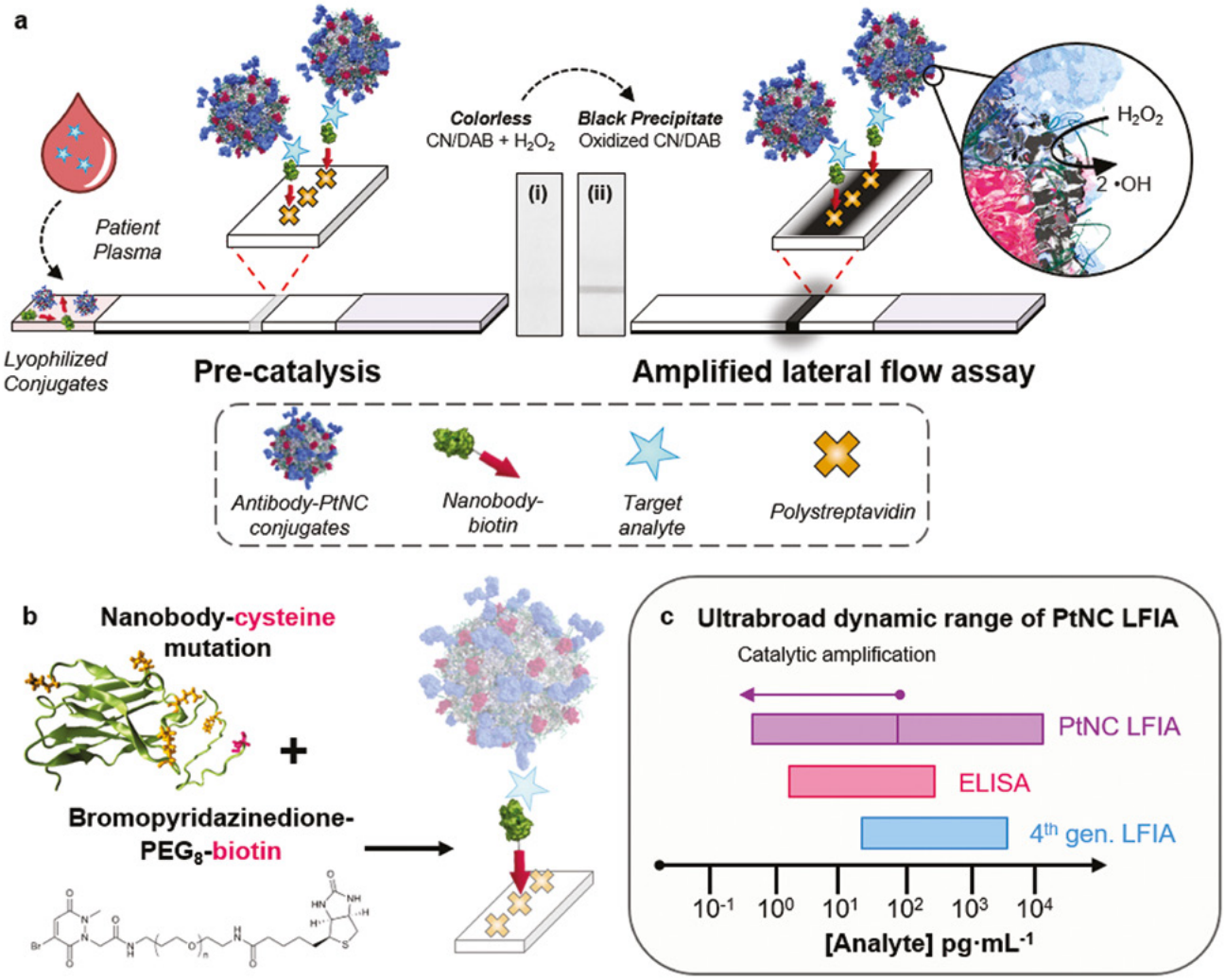
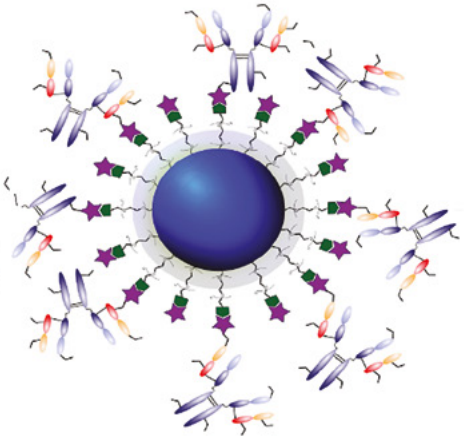


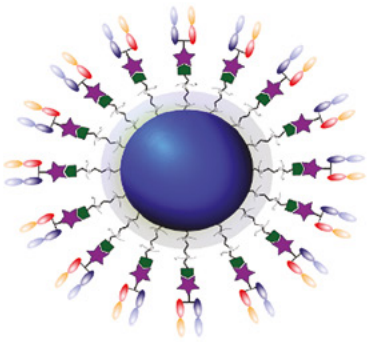
Figure 1. (a) Scheme showing amplified LFIA, where functionalised Pt nanocatalysts (PtNC) and biotinylated nanobody fragments are mixed with a plasma or serum sample. In the presence of a target, PtNCs become biotinylated through complexation with the target, and rapid high affinity biotin-streptavidin binding enables a [target] dependent deposition of PtNC at the test line. PtNCs bound at the test line catalyze the oxidation of CN/DAB (4-Chloro-1- naphthol/3,3´-Diaminobenzidine, tetrahydrochloride) substrate in the presence of hydrogen peroxide producing an insoluble black product which is clearly visible with the naked eye. (b) Scheme for site-selective chemical modification of a nanobody with an exposed cysteine mutation (red), where lysine residues are highlighted in orange on the structural model (left), and cartoon of oriented elements at the streptavidin test line. (c) Schematic comparing the dynamic ranges of 4th generation LFIA, ELISA, and PtNC LFIA.

Current technology

– Non-oriented arrangement
– Sub-optimal antigen binding
– Significant surface crowding



Our aim



+ Oriented ligands
+ Optimal binding
+ Flexible
+ Translatable

Working across disciplinary boundaries

These are stories from projects, training and collaborations in the UK and overseas.

Digital diagnostics for those hardest hit by HIV

By Dr Kobus Herbst, AHRI, Dr Valérian Turbé, Dr Maryam Shahmanesh and Professor Rachel McKendry, UCL

Collaborating with South Africa

i-sense researchers recently secured translational funds to develop mobile phone-connected HIV tests, which link to online prevention and medical care, for use in South African communities hardest hit by HIV.

The £600K m-Africa collaboration is a two-year project, funded by the Medical Research Council Global Challenges Research Fund, and led by Professor Rachel McKendry at UCL and Professor Deenan Pillay at Africa Health Research Institute (AHRI).

The aim of the project is to evaluate the feasibility of introducing mobile phone-connected tools to improve access to HIV testing, as well as linkage to care, in low and middle-income countries. The KwaZulu-Natal province of South Africa is being used as a test bed, where our major collaborator, AHRI, is located.

South Africa is the country most affected by HIV; almost seven million people are living with HIV and 300,000 new cases of HIV occur each year. The province of KwaZulu-Natal is particularly affected. Forty-five per cent of women attending antenatal clinics have HIV and only half of all people diagnosed with HIV receive care within the following year.

We will be working with different end users in KwaZulu-Natal to understand how simple paper-based diagnostic tests (lateral flow tests) that use mobile phones for readout, can fit into and help reduce the load on the local healthcare system.

Understanding our end-users

Initial studies, based on population surveys ran by AHRI, highlight social trends related to the HIV situation in the region. These include the high levels of unemployment, as well as mobility and stigma around HIV, particularly in hard to reach groups, such as men. These findings will help shape the design of the online care pathway.

An ethics application has been put forward to run focus groups with the local population, and key informant interviews with health care workers that will help us gain further information to refine the design of our tools, and understand how they will fit into the HIV testing, prevention and treatment landscape.

Additionally, questions about ownership and usage of smartphones have been added to the routine questionnaire used by AHRI fieldworkers.

Adapting our technology for the user

The ultimate aim is for our apps to read out HIV test results within minutes and also to interpret already available HIV tests, automatically linking results to a doctor and helping people receive the rapid and regular care that they need.

Our interdisciplinary team has made progress in the design of mobile applications, with the initial focus on developing an image recognition module, using the mobile phone camera to automatically interpret the results of a lateral flow test. The app will also use machine-learning to classify pictures taken of test results into three categories; positive, negative, and invalid.

A library of images of the tests currently used by AHRI has recently been built (5000+ pictures of tests taken in the field) to train the model, and a system has been put in place for AHRI field workers to take pictures of the tests they will administer daily, thereby constantly increasing the size of the library and helping to refine the model. An accuracy of 96 per cent was achieved on an initial proof-of-concept model, which will now be optimised and retrained using the new library.

A workflow facilitating smooth synchronisation and backing up was adopted and will allow for the mobile device to sync to a dedicated server when in range of WiFi.

The p24 lateral flow assay developed within i-sense will soon be piloted at AHRI, using approximately 100 patient samples. This pilot study will initially focus on assessing the levels of non-specific binding affecting the readout of negative samples. The reason for this is that non-specific binding could vary (in nature and levels) between patient samples from the UK and South Africa.

Finally, a joint i-sense and m-Africa workshop is being organised for late 2018 with the aim to explore the needs and existing capacity for mobile health technologies to support linkage and retention in public HIV programmes.

These technologies are being developed for HIV in the first instance, but they can be applied across a range of infections and medical conditions and quickly integrated into the community, empowering patients to manage their own health.

Cutting edge explorations

By Christine Wang, Imperial College London

During my four-month i-sense Mobility Fellowship at the Molecular Foundry, Lawrence Berkley National Laboratory in California, I aimed to explore the dynamic interactions of nano interface technology, which is crucial in building biosensing systems, such as lateral flow tests, for the early detection of infectious diseases.

To achieve this, we used in situ liquid cell transmission electron microscopy, which enables real-time visualisation of nano systems, while remaining at nanometer-scale resolutions. This method was used to investigate i-sense related projects by exploring real-time interactions between ligand-functionalised gold nanoparticles and the whole influenza virus, as well as investigating the recognition kinetics of HIV-1 biomarker, capsid antigen p24, and antibody modified nanoparticles in a microscopic lateral flow format that enables single particle resolution.

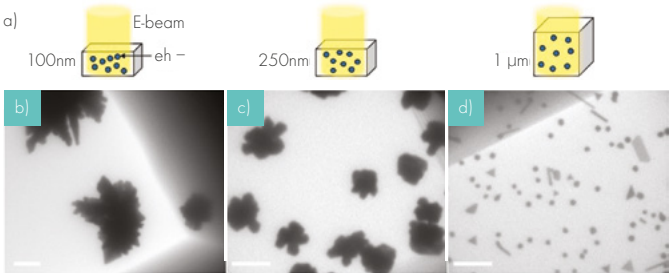
We achieved successful liquid cell assembly by physical adsorption of the biomolecules on the Silicon Nitride window, and visualised the strong antigen-antibody interactions. Several parameters such as the size of gold nanoparticles and flow rate were optimised, however, the binding processes were interfered by the electron-water interactions that caused bubble formation, liquid depletion and electron beam induced protein denaturing effect.

Beyond the current results, we have further investigated the use of varying liquid thickness and anticipate that the use of liquid cell transmission electron microscopy may assist the search for an optimised growth condition, as well as unveil the mechanism of metal nanocrystal growth in aqueous solution (shown on the right).

The output of such a novel and cutting edge exploration of these phenomena could be significant in the design and establishment of biosensing platforms for influenza and HIV.

This Mobility Fellowship has provided a great opportunity to further explore i-sense projects and work overseas with great research teams at the Foundry.

Christine Wang is a PhD student in the Stevens group at Imperial College London



e)

Spacer	Growth rate	Morphology	Structure
100nm	Fast	Sharply branched/dendritic	Polycrystalline
250nm	Medium	Branched	Twinned
1 µm	Slow	Prisms and rods	Faceted/twinned (rods)

Testing our tiny tech

By Ben Miller, UCL

My i-sense Mobility Fellowship aimed to increase the sensitivity of gold nanoparticle and fluorescence-based microfluidic paper analytical devices, exploring paper membrane transparency, nanoparticle selection, and readout methods.

The project formed links between the McKendry (UCL) and Ozcan (UCLA) groups with the aim of future collaboration on optical device design.

As part of the Mobility Fellowship, a smartphone attached reader was developed for lateral flow tests, employing a background subtraction technique that was also a result of this Fellowship. The reader was produced at UCLA and will be tested back at UCL.

The opportunity to go and work in a different lab, with a slightly more electrical engineering based approach helped me to look at the project from a different perspective, gaining new insights.

I was able to greatly improve my knowledge of optics, and the process of designing a smartphone optical device. I had the opportunity to work with and learn from people with different backgrounds and experience.

On a personal note, it was brilliant to visit America for the first time, and get a chance to see some of the beautiful scenery in California.

Ben Miller is a PhD student in the McKendry group at UCL.

Science in sunny Sydney

By Lucia Massi, Imperial College London

My i-sense Mobility Fellowship was a five-week placement at the Centre for Advanced Macromolecular Design at the University of NSW in Sydney, Australia.

The main aim of the placement was the acquisition of polymer chemistry skills for the development of an enzyme-responsive polymer-based platform for enabling earlier HIV detection, there by finding a way around the need to store the enzymatic components long-term in adverse conditions.

The proposed innovative approach aimed to combine nanomaterials and lateral flow design from the Stevens group at Imperial College London with smartphone detection capabilities from the McKendry group at UCL.

By using RAFT polymerisation techniques, a library of block copolymers has been successfully synthesised and their ability to self-assemble into nanostructures has been investigated.

Cross-linking strategies have been studied with the aim of conferring enzyme-responsive properties. Future studies will address the response of the system to HIV-1-protease and detection capabilities.

From a scientific point of view, this has been an amazing experience that allowed me not only to achieve the proposed project aims but also to broaden my skills, be in contact with a different scientific environment and start useful collaborations for my future career.

From a personal point of view, I had the opportunity to explore the amazingly beautiful and sunny Australia and meet extremely interesting people.

Lucia Massi is a PhD student in the Stevens group at Imperial College London

From UCLA labs

By Isabel Bennett, UCL

I was awarded an i-sense Mobility Fellowship to spend two months in Professor Aydogan Ozcan's group at UCLA, California.

The project was to develop a mobile phone-connected diagnostic tool to measure antibiotic susceptibility of bacteria, specifically for uropathogenic E. *coli*, which cause urinary tract infections.

I worked with Professor Ozcan to come up with a novel strategy involving a fluorescent indicator to provide specificity for uropathogenic E. *coli*.

As someone with a biochemical background, it was interesting to immerse myself in a group that was mostly engineering and photonics focussed. Although challenging, working with other disciplines was a highlight of my time at UCLA.

In addition, the opportunity exposed me to some of the challenges faced when initiating a new project in a lab with unfamiliar facilities and regulations.

Regardless of the obstacles, the project continues back in London, and the testing of a mobile device should happen in the near future.

Isabel Bennett is a PhD student in the McKendry group at UCL.

Protecting pregnant women and infants from sexually transmitted infections

By Dr Harriet Gliddon, UCL

Over a two-month placement at the World Health Organization's Department for Reproductive Health and Research, I was a member of a team working towards the elimination of mother-to-child transmission of HIV and syphilis.

Mother-to-child transmission of HIV and syphilis remain significant causes of perinatal morbidity and mortality, but can easily be prevented by screening pregnant women and providing appropriate treatment. Untreated maternal syphilis results in significant adverse pregnancy outcomes, such as spontaneous abortion, stillbirth, foetal death, preterm birth, low birth weight, neonatal death and congenital syphilis (i.e. syphilis infection of the neonate).

Antenatal screening followed by treatment early in pregnancy effectively treats the pregnant woman and prevents congenital syphilis in infants. Treating a pregnant woman for HIV can reduce the likelihood of mother-to-child transmission of HIV from 15-45 per cent to less than five per cent. The World Health Organization has prioritised the elimination of mother-to-child transmission of HIV and syphilis, and several countries have now achieved validation of elimination of mother-to-child transmission for HIV and/or syphilis, including Cuba, Belarus and Thailand.

My role at the World Health Organization involved literature searches and end-user engagement in order to collate data on the performance of rapid diagnostic tests that simultaneously detect antibodies to HIV and Treponema pallidum, the cause of syphilis. The advantages of these dual HIV/syphilis rapid diagnostic tests include lower manufacturing costs, streamlined procurement, minimised storage needs, simplified training for healthcare professionals, a single finger prick required for testing, and shortened time for results.

After completing my internship at the World Health Organization, I was contracted to perform a systematic review to evaluate data on the operational performance of these dual HIV/syphilis rapid diagnostic tests, which will contribute to the establishment of the World Health Organization guidelines for the use of the tests in field settings. The systematic review appraises the available evidence on the operational performance, cost-effectiveness and acceptability of dual rapid diagnostic tests. I recently presented this work at a World Health Organization Sexually Transmitted Infections Guideline Development Group Meeting.

This work was made possible by my supervisor at the World Health Organization, Dr Melanie Taylor, who gave me the opportunity to work with her in this exciting field, and Professor Rosanna Peeling who supported and guided me throughout the process.

Dr Harriet Gliddon was a PhD student in the Stevens group at Imperial College London and is currently a Postdoctoral Research Associate in the McKendry group at UCL.

Empowering new leaders in Uganda

By Dr Polina Brangel, UCL

After a successful first workshop in 2015, this year we ran the second in a series of workshops conducted at the Uganda Virus Research Institute.

The programme was designed with the aim to empower, train and teach participants about the technology used in rapid diagnostic tests for viral infectious diseases.

This year we were joined by 15 enthusiastic local participants, including young researchers, graduate students and lab technicians.

Throughout the programme participants were provided training on theoretical and laboratory background for lateral flow immunoassay development and validation.

Each participant experienced the different development steps of lateral flow immunoassays, including; materials selection, labeling agents (nanoparticles) surface functionalisation, and determination of the limit of detection of the technology.

In addition, the course also provided practical experience with different lateral flow-based assays, which are commercially available today.

This second workshop was part of a Mobility Fellowship that was awarded with the aim to better engage researchers from low and middle income countries on novel rapid diagnostic strategies and technologies.

The programme benefited i-sense through the engagement with an important on-field institute that investigates and provides the forefront response to a wide range of emerging diseases that are within the scope of the i-sense agenda.

Dr Polina Brangel was a PhD student in the Stevens group at Imperial College London and is currently a Postdoctoral Research Associate in the McKendry group at UCL.

Education Alliance

The i-sense Education Alliance has been created to introduce new teaching and training events in order to grow the interdisciplinary skills of our students and early-career researchers. Led by Dr Neil Keegan and supported by a team of representatives across i-sense partner institutions, the unique programme is designed to inspire and prepare our members for their future careers.

As well as the York retreat in collaboration with Flagship 1 (see page 10), the Education Alliance also recently supported the all IRC conference on 28 and 29 June 2017.

The two-day conference, titled the Future of Healthcare Technology, was a wonderful opportunity to bring together the three EPSRC funded Interdisciplinary Research Collaborations (IRC) in Bath.

Professor Vince Emery, Senior Vice-President (Global Strategy and Engagement) and Professor of Translational Virology at University of Surrey,and i-sense Partnership Resource Fund lead says "Two things struck me at the conference; the first was the amazing progress that all three EPSRC funded IRCs have made over the last four years, and the second was the wealth of talented young researchers we have attracted to be part of these IRCs.

"I felt quite uplifted after two days of exciting presentations and discussions."

As the first of its kind, the conference focused on the latest developments in healthcare technologies, central to the core theme of each research group.

The three IRCs (i-sense, SPHERE, and Proteus) bring together:

- 11 leading UK universities
- £30M in funding from the EPSRC
- 200+ academics

Hannah Swinburne, PhD student, i-sense, Newcastle University says "The conference provided a great insight into the work of Proteus and SPHERE, with all three groups delivering interesting talks from both a scientific view and as demonstrations of how well interdisciplinary research can work.

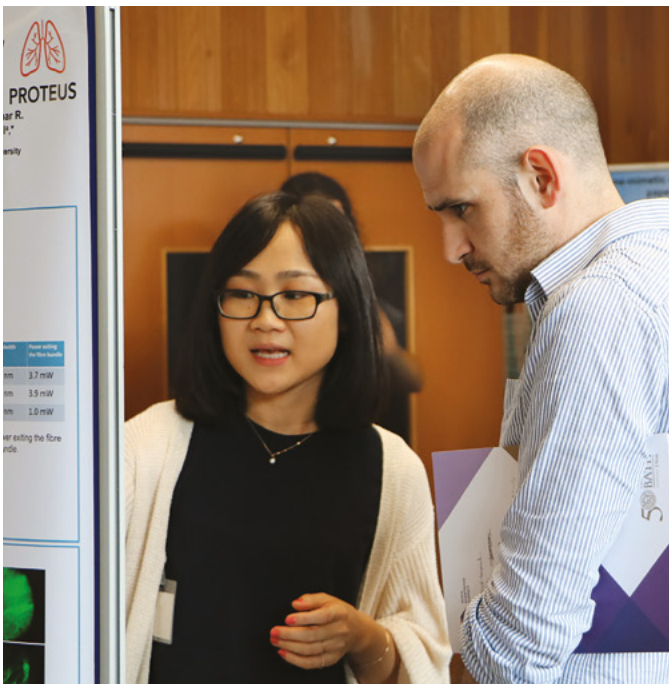
"As a student it was inspiring to hear the value each of the IRCs puts on the development of early career researchers."

As programmes of internationally acknowledged scientific and technological excellence, these IRCs have sufficient critical mass to make a real impact in areas of key future industrial relevance to the UK.

Candice Keane, PhD Student, i-sense, UCL says "It was great that despite coming from all different subject backgrounds and universities we were able to come together to organise a conference that highlighted all the progress we've made towards creating the next generation of healthcare technologies and seeing how this all ties into the EPSRC framework.

"It was also nice to showcase some of the outputs from the i-sense project and be afforded the opportunity to reflect on how far we've come."

The conference was made possible by the hard work of organisers across the three IRCs, including Dr Harriet Gliddon, Candice Keane and Evdokia Pilavaki from i-sense, UCL.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Speaking out about i-sense

By Erin Manning, i-sense Communications Officer

Llama Outbreak!

The Llama Outbreak Control Clinic was a key highlight of i-sense public engagement efforts in 2016. The event was part of Einstein's Garden at Greenman Festival in Wales, and made a second appearance during the 2017 Courtyard Festival in London. The clinic was set up to respond to a public health emergency that had descended upon the two festivals – a strange virus that was turning people into llamas!

Starting with life-sized llamas spotted around the festival, the llama disease started to spread with festival-goers unexpectedly being tagged with 'llama tails' (socks) and prompted to be tested at the control clinic. We were able to demonstrate to visitors how quickly and unpredictably an infectious disease can spread, particularly in mass gatherings, and explain the nanotechnology behind a simple lateral flow test.

If tested positive, visitors helped us track the outbreak by pinpointing where they may have come in contact with the virus so we could predict where it might spread. People were also keen to communicate their opinions and concerns around health data and have their face painted to look like llamas.

School day at St Josephs Primary School

As part of 2017 National Science Week, Professor Rachel McKendry and i-sense PhD student, Isabel Bennett, visited St. Joseph's Catholic Primary School in Maida Vale, London.

In front of an assembly of students from Year 2, Professor McKendry and Isabel discussed their backgrounds and what inspired them to get into scientific research.

Part of the aim of the event was to encourage young people to change their perceptions of what a scientist is – they are not always men in white coats with glasses and wild hair! Women are under-represented in science, and it is important to address gender stereotypes to encourage more girls to study science.

The work carried out to detect and track infectious diseases by the i-sense team was also introduced and an interactive activity about antibiotics and bacterial resistance was carried out with volunteers from different year groups.

The activity involved using balloons as a model for bacteria, with a wooden skewer acting as the antibiotic that could burst the bacteria. Some of the bacteria were made resistant using tape so they were no longer 'killed' by the antibiotic skewers. This activity was based on the PhD work carried out by Isabel using atomic force microscopy to study the effects of novel antibiotics.

The floor was then open to discussion, with many children asking questions, demonstrating an interest in the research discussed, and wanting to know more about what it means to be a scientist. Overall the event was well received by both the students and teachers.

Our communication channels

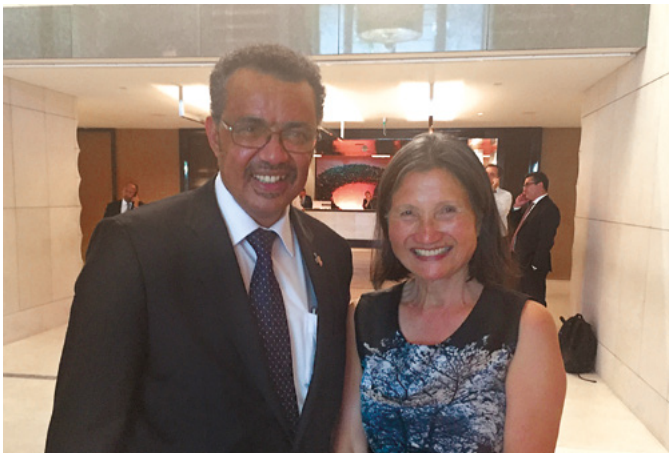
i-sense launched its UCL website in October 2013 and its main website (i-sense.org.uk) in October 2014. It now has more than 2,000 unique visitors every month and more than 75,000 unique visitors to date.

i-sense has a lot to say about the fantastic news and discoveries our researchers are doing. Our website is the key way we communicate our work with the general public, so this year we decided to give it a bit of a facelift. You can check out the fresh look and get more information on news, research highlights and case studies from the events and workshops at i-sense.

i-sense also has a strong social media presence with more than 470 followers on Twitter and constant engagement on our Facebook page. You can follow us on Twitter via @isenseIRC and like our Facebook page i-sense EPSRC IRC.

Talks and media appearances

Throughout the year, our team has given more than 80 talks nationally and internationally. Highlights included Professor Pam Sonnenburg and Professor Rachel McKendry speaking at NHS Digital Health, Professor Claudia Estcourt presenting the i-sense vision and online STI pathways at Innovate UK as part of the 'Healthcare of the Future' panel, the group at Newcastle University speaking in Malaysia at the Molecular Diagnostics and Biomarker Discovery conference and Professor Rosanna Peeling's talk on antimicrobial resistance at the World Health Assembly. Pictured below is Professor Rosanna Peeling with Dr Tedros Adhanom Ghebreyesus in Geneva on May 24 2017, the day he was elected Director General of the World Health Organization.



i-sense has also been lucky to have a number of mentions across media. This year the i-sense dashboard and Professor Deenan Pillay from the African Health Research Institute appeared on the *BBC One* documentary *The Truth About HIV*. Our work on the m-Africa collaboration was featured in the EPSRC's *Pioneer 18* magazine and UCL's Africa and Middle East newsletter, and our 'tiny tech' was highlighted in *The Evening Standard*.

Celebrating success

Every year, i-sense members work tirelessly to contribute to global health research. From the work of our Professors, to our early-career researchers and PhD students, there is always plenty to celebrate.

Kailey Nolan, UCL
i-sense Communications Officer, Kailey Nolan, won the 2016 UCL Provost's Award for Public Engagement. The judges were impressed by her work on the Llama Outbreak, as well as her dedication in promoting diversity and equality in science through the Rosalind Franklin Appathon.

Nayoung Kim, Imperial College London
i-sense member, Nayoung, won joint first place for the AWE William Penney Prize, which is an annual award to students on the MSc Advanced Materials course in the Department of Materials for the best project report.

Professor Rachel McKendry, UCL
i-sense Director, Professor Rachel McKendry, was named one of Grant Thornton's 100 Faces of a Vibrant Economy. Professor McKendry was awarded for her commitment to interdisciplinary research and engagement with policy makers and industry.

Jobie Budd, UCL
i-sense PhD student, Jobie Budd, was a poster prize winner at the all IRC meeting. The judges were impressed by Jobie's artistic talents as well as his ability to communicate his research in a simple yet informative way.

Dr Natascha Kappeler, UCL
In 2017, i-sense member Dr Natascha Kappeler took up a position as Lecturer and Senior Research Associate at the University of Applied Sciences and Arts Northwestern Switzerland FHNW.

Dr Philip Howes, Imperial College London
Dr Philip Howes received the Marie Skłodowska-Curie Fellowship within ETH Zürich to work on using microfluidics for disease diagnostics, which started in July 2016.

Dr Harriet Gliddon, UCL
Dr Harriet Gliddon received a number of prizes including the Student Award for Outstanding Achievement for her excellence in extramural activities that brings credit to Imperial College London. Dr Gliddon has also been awarded the Next Generation: Global Health Innovator Prize and Best Video Prize at the Imperial College Institute for Global Health Innovation Student Challenges Competition.

Dr Olivia Varsaneux, LSHTM
In 2016, i-sense member Dr Olivia Varsaneux took up a position as Epidemiologist, HIV/AIDS and Tuberculosis Section Surveillance and Epidemiology Division, Centre for Communicable Diseases and Infection Control, Infectious Disease and Prevention Control Branch, at the Public Health Agency of Canada, Government of Canada.

Dr Kristina Schlegel, UCL
After completing her PhD in 2015 as part of i-sense, Dr Kristina Schlegel secured a position with the GSK Future Leaders Programme and in 2017 joined GSK's first Medical Device spin-out, Galvani Bioelectronics, as Engineering Program and Alliance Specialist.

Isabel Bennet, UCL

i-sense PhD student, Isabel Bennett, won the presentation prize at the UCL Antimicrobial Resistance Network Event. Isabel presented her research using atomic force microscopy to investigate a novel antimicrobial peptide, tilamin, and its action on live bacterial cells.

Dr Subinoy Rana, Imperial College London

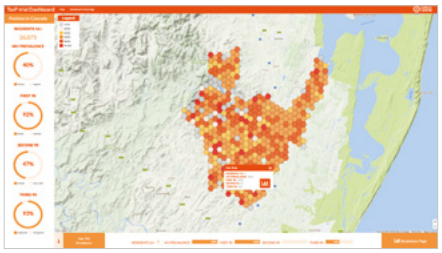
In September 2017, i-sense member Dr Subinoy Rana started a lectureship at the Newcastle University. Dr Rana was also awarded the Young Investigator's Meeting Travel Award from India Bioscience. He was previously a Postdoctoral Research Associate in the Stevens group.

Dr Neil Keegan, Newcastle University

This year, Dr Neil Keegan was promoted to the lead academic representing Newcastle University. Dr Keegan will also continue to lead the i-sense Education Alliance.

Professor Molly Stevens, Imperial College London

Professor Molly Stevens was awarded the 2017 Harrison Medal from the Royal Pharmaceutical Society. This prestigious medal is awarded every two years to a scientist who has made an outstanding contribution to pharmaceutical science and practice in pharmacy. Professor Stevens also won the 2016 Clemson Award for Basic Research from the Society of Biomaterials. This award recognises the Stevens group for having contributed to the basic knowledge and understanding of the interaction of materials with tissue.



The i-sense data dashboard

This year, i-sense Deputy Director, Professor Deenan Pillay, appeared on the *BBC One* documentary, *The Truth About HIV*, talking about the major Treatment as Prevention (TasP) trial in KwaZulu-Natal, South Africa. The piece featured the TasP Trial Dashboard created by the i-sense team at The Bartlett Centre for Advanced Spatial Analysis, UCL.

Dr Jo Gibbs, Professor Claudia Estcourt and Professor Pam Sonnenberg

During the 2016 Health and Wellbeing Awards night, run by the Royal Society for Public Health, Barts Health NHS Trust won the prestigious Technology and Health Innovation award and a Public Health Minister's Commendation. i-sense members Dr Jo Gibbs, Professor Claudia Estcourt and Professor Pam Sonnenberg were part of the winning team who developed the eSexual Health Clinic as part of the eSTI2 consortium.

The Stevens group, Imperial College London

The Stevens group were awarded the 2016 Imperial College President's Award and Medal for Outstanding Research Team for their activities and accomplishments in research.

Published papers

Turbé, V., Gray, E. R., Lawson, V. E., Nastouli, E., Brookes, J. C., Weiss, R. A., Pillay, D., Emery, V. C., Verrips, C. T., Yatsuda, H., Athey, D., McKendry, R. A. *'Towards an ultra-rapid smartphone-connected test for infectious diseases'* Scientific Reports *7,* Article number: 11971 (2017);
DOI:10.1038/s41598-017-11887-6

Ruiz-Sanchez, A. J., Parolo, C., Miller, B. S., Gray, E. R., Schlegel, K., McKendry, R. A. *'Tuneable plasmonic gold dendrimer nanochains for sensitive disease detection'* Journals of Material Chemistry B (2017);
DOI: 10.1039/C7TB01394A

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

Soh, J.H., Lin, Y., Thomas, M.R., Todorova, N., Kallepitis, C., Yarovsky, I., Ying, J.Y., Stevens, M.M. *'Distinct Bimodal Roles of Aromatic Molecules in Controlling Gold Nanorod Growth for Biosensing' Advanced Functional Materials* (2017) 1700523;
DOI: 10.1002/adfm.201700523

Kim, E., Howes, P.D., Crowder, S.W., Stevens, M.M. *'Multi-Amplified Sensing of MicroRNA by a Small DNA Fragment-Driven Enzymatic Cascade Reaction' ACS Sensors* (2017);
DOI: 10.1021/acssensors.6b00601

Lin, Y., Pashuck, E.T., Thomas, M.R., Amdursky, N., Wang, S.-T., Chow, L.W., Stevens, M.M. *'Plasmonic Chirality Imprinting on Nucleobase-Displaying Supramolecular Nanohelices by Metal–Nucleobase Recognition' Angew. Chem. Int. Ed.* (2017), 56, 2361;
DOI: 10.1002/anie.201610976

Wang, S.-T, Lin, Y., Hsu, C.-C., Amdursky, N., Spicer, C.D., Stevens, M.M. *'Probing amylin fibrillation at an early stage via a tetracysteine-recognising fluorophore' Talanta* (2017);
DOI: 10.1016/j.talanta.2017.05.015

Gray, E.R., Brookes, J.C., Caillat, C., Turbe, V., Webb, B.L., Granger, L.A., Miller, B.S., McCoy, L.E., El Khattabi, M., Verrips, C.T., Weiss, R.A., Duffy, D.M., Weissenhorn, W., McKendry, R.A. *'Unravelling the molecular basis of high affinity nanobodies against HIV p24: in vitro functional, structural and in silico insights.' ACS Infectious Diseases* (2017);
DOI: 10.1021/acsinfecdis.6b00189

Lampos, V., Zou, B., Cox, I.J. *'Enhancing Feature Selection Using Word Embeddings: The Case of Flu Surveillance' WWW '17 Proceedings of the 26th International Conference on World Wide Web* (2017);
DOI: 10.1145/3038912.3052622

Aletras, N., Tsarapatsanis, D., Preotiuc-Pietro, D., Lampos, V. *'Predicting judicial decisions of the European Court of Human Rights: a Natural Language Processing perspective.' PeerJ Computer Science* 2:e93 (2016);
DOI: 10.7717/peerjcs.93

Jauset-Rubio, M., Svobodová, M., Mairal, T., McNeil, C., Keegan, N., El-Shahawi, M. S., Bashammakh, A. S., Alyoubi, A. O., O'Sullivan, C. K. *'Aptamer Lateral Flow Assays for Ultrasensitive Detection of ß-Conglutin Combining Recombinase Polymerase Amplification and Tailed Primers.' Analytical Chemistry* (2016);
DOI: 10.1021/acs.analchem.6b03256

Lampos V., Aletras N., Geyti J.K., Zou B., Cox I.J. *'Inferring the Socioeconomic Status of Social Media Users Based on Behaviour and Language.' Advances in Information Retrieval. ECIR 2016. Lecture Notes in Computer Science, vol 9626. Springer, Cham* (2016);
DOI: 10.1007/978-3-319-30671-1_54

Management Committee

Professor Rachel McKendry, Professor of Biomedical Nanotechnology at UCL with a joint position at the London Centre for Nanotechnology and Division of Medicine, and i-sense Director.

Professor Ingemar Cox, Professor of Computer Science, UCL and i-sense Deputy Director and Flagship 2 lead (Influenza).

Professor Vincent Emery, Senior Vice-President (Global Strategy and Engagement) and Professor of Translational Virology, University of Surrey, and i-sense Partnership Resource Fund lead.

Professor Anne Johnson DBE, Professor of Infectious Disease Epidemiology and 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 Flagship 3 (Bacterial infections) and Education Alliance lead.

Professor Calum McNeil, Professor of Biological Sensor Systems, Newcastle University and i-sense Deputy Director.

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

Professor Rosanna Peeling, Professor and Chair of Diagnostics Research, London School of Hygiene and Tropical Medicine and i-sense Flagship 1 lead (System needs).

Professor Deenan Pillay, Director of the Africa Health Research Institute and i-sense Deputy Director.

Professor Molly Stevens, Professor of Biomedical Materials and Regenerative Medicine, Imperial College London and i-sense Flagship 4 lead (HIV and Ebola).

Advisory Board

Professor David Heymann (Chair), Professor of Infectious Disease Epidemiology, London School of Hygiene and Head of the Centre on Global Health Security at Chatham House.

Professor John Brownstein, Associate Professor of Pediatrics, Harvard Medical School, co-founder of HealthMap.

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

Andrew Eland, Engineering Director, Google.

Professor Christoph Gerber, Professor, Swiss Nanoscience Institute, University of Basel.

Professor Patrick Maxwell, Regius Professor of Physic and Head of the School of Clinical Medicine, University of Cambridge.

Professor Ciara O'Sullivan, Research Professor Nanobiotechnology and Bioanalysis Universitat Rovira i Virgili.

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

Industry and clinical partners

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