i-sense

EPSRC IRC in Early Warning Sensing Systems for Infectious Diseases

Annual Report 2015/2016

EPSRC
Pioneering research and skills

Foreword

Going Viral: Building the Digital Future of Public Health

Ebola and Zika have exposed the world's vulnerability to emerging infectious diseases and the urgent need for early warning systems to protect patients and populations. Since we began in October 2013, i-sense EPSRC researchers have built the research foundations of a new generation of digital sensing systems that aim to detect outbreaks much earlier than ever before. We are linking traditional public health efforts with the millions of symptoms reported on the web each day, often before people visit their doctors. We are also engineering new mobile phone-connected diagnostic devices to help 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.

Strong partnerships with end users are central to our vision. From the very outset we have been working closely with Public Health England, clinicians, industry, patients, policy makers and the public to ensure we build technologies that meet their needs.

Research highlights include advanced models of Twitter and Google data to estimate the prevalence of flu, moving towards a commercialisation route for the IDRIS biomarker discovery platform for bacterial infections, a pilot study of mobile devices for HIV, advanced nanomaterials for early infant diagnosis of HIV and a new partnership with the Africa Centre to link newly diagnosed individuals to HIV care in South Africa. Our platform diagnostic technologies have also recently been piloted for Ebola in Uganda. Central to all our work is an ongoing ethics project on public trust, to ensure we develop these technologies responsibly.

I'm very proud of our brilliant team who have won national awards, fellowships, published high impact papers and leveraged funding. These achievements reflect a collective research excellence and commitment to impact across the five partner universities. Our Education Alliance's training programmes are growing the skills of our bright young researchers to become future leaders, and our Partnership Resource Fund is creating international networks of excellence and a new spirit of engagement with the public.

We hope you enjoy reading about our progress and plans for the future. As the health needs of developed countries begin to merge with the traditionally unmet needs of developing countries, we have a remarkable opportunity to build early warning systems for the common good.

Professor Rachel McKendry
Director of i-sense

i-sense in Numbers

Postdoctoral Research Associates: employed by i-sense on core Projects

15 Research Associates

Direct Leveraged funding: Funding received by i-sense members since launch. Total leveraged funding in excess of £30M.

£5 Million Direct Leveraged Funding

27 Prizes

Prizes awarded to i-sense members since launch, including the Society for Biomaterials Clemson Award, the UCL Provost Spirit of Enterprise Award, international fellowships and poster prizes.

24 Publications

Publications including in *Science*, *Scientific Reports* and *Nature Nanotechnology*

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About i-sense

The aim of i-sense is to detect outbreaks of infectious disease earlier than ever before to protect patients and populations.

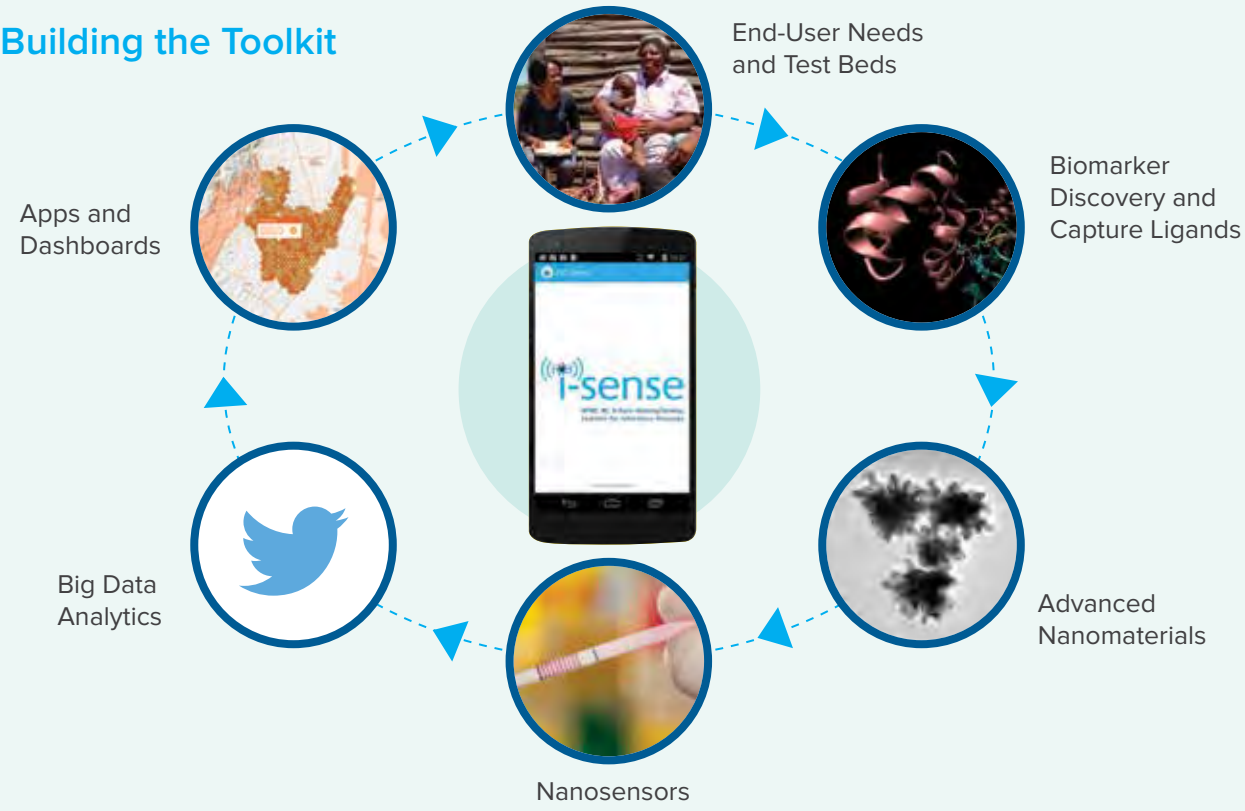
We will achieve this by engineering a new generation of low-cost, early-warning sensing systems. These systems will exploit web information, such as search engine queries and social media posts, in combination with mobile phone-connected diagnostics to widen access to testing in home settings.

Our Core Research Programme brings together our collective expertise in disruptive sensing systems – spanning from end user needs, to biomarker discovery, biomimetic capture ligands, advanced nanomaterials, low power sensors with wireless connectivity, big data analytics, apps and dashboards, and the creation of test beds to evaluate our technologies in the UK and developing countries.

It is focused around four core Projects: 1) A Systems Level Perspective of End-user Needs; 2) Influenza; 3) Bacterial Infections and 4) HIV. In addition, we have an Exploratory Projects funding stream to seed new projects across the consortium, an Education Alliance to increase training of our young researchers and a Partnership Resource Fund to build international networks of excellence, engage with industry and the public.

i-sense is a five year, £11M EPSRC-funded Interdisciplinary Research Collaboration (IRC). It brings together a strong team of biochemists, chemists, physicists, engineers, computer scientists, microbiologists, statisticians, bioinformaticians, architects, philosophers, clinicians and epidemiologists from across UCL, Imperial College London, London School for Hygiene and Tropical Medicine, Newcastle, Surrey, Public Health England, the NHS and industry. i-sense is one of three EPSRC IRCs funded to build critical mass in disruptive sensing systems for healthcare.

Building the Toolkit



Influenza

In the 2015 Cabinet Office National Risk Register Pandemic Influenza represents the most significant civil emergency risk to the UK population. In comparison to circulating seasonal flu, emerging strains of influenza are of particular concern due to the potentially severe response. For example, where patients were hospitalised during the 2003 H5N1 outbreak, 60% of cases resulted in death.

The best approach to control any outbreak is to identify the source of infection at the earliest stage possible. We are developing the tools to create an early warning system for flu by combining symptoms reported on the web with mobile phone-connected diagnostic tests. Influenza was a brand new area of research for the team and the EPSRC asked us to expand this work.

Public Health Needs

We are working closely with Public Health England (PHE) to better understand how i-sense technologies could strengthen national surveillance of seasonal and pandemic influenza.

Professor Richard Pebody heads up the national flu surveillance at PHE, one of the most advanced public health systems in the world. PHE brings together multiple data sources including GP and hospital cases and symptoms reported to NHS 111. Richard has identified three key priority areas for i-sense: (i) To explore if web data such as Twitter and Google can help to identify flu in the community; (ii) To investigate the use of web data to assess the impact of health interventions such as vaccination programmes; (iii) To develop home use tests that would help support interventions, such as antivirals and vaccines.

Looking ahead, in 2016-17 PHE will evaluate our advanced modelling of Twitter data for national surveillance for the first time. We are also developing target product profiles for flu self tests and modelling their cost-effectiveness for the National Pandemic Flu Service.

Tracking Flu with Google.org

In 2009 Google pioneered the use of search queries to track the spread of influenza. Google Flu Trends used flu-related queries typed into their search engine, similar to 'I have a fever' and 'flu symptoms' to map flu activity in near real-time. The original Flu Trends model was reported to overestimate flu activity. i-sense researcher, Dr Vasileios Lampos, a computer scientist at UCL, joined Google as a visiting researcher in 2014 to improve their influenza modelling techniques.

Since then, we have been able to significantly improve the original Google models and make more accurate flu estimates, during peak flu seasons in the US from 2008 to 2013. In the future, we hope to improve their models by bringing together various other user-generated data sources (e.g. social media, search query logs, mobile phone logs).

The i-sense digital disease surveillance group has successfully acquired access to a private Google Health Trends API, which offers anonymised and aggregate statistics for geo-located search queries related to flu.

Lampos, V., Miller, A.C., Crossan, S. & Stefansen, C. 'Advances in nowcasting influenza-like influenza rates using search query log' *Scientific Reports* **5**, 12760 (2015).

The Power of Web Data: Identifying Flu Outbreaks

Each day millions of people self-report their symptoms online and, in the UK, it is estimated that more than 72% of all internet users search for information about health.

We have developed advanced modelling methods for different web data sources including social media and search engine posts and mapped the location of users to identify flu hotspots. We are currently focusing on improving these data models, determining the demographics of users, and our pilot study of real-time Twitter analytics will be evaluated by PHE to strengthen national flu surveillance. Future work will explore the relationship between physical events, interventions and online behaviours, and modelling methods to infer causality rather than simply correlation.

i-sense Flu

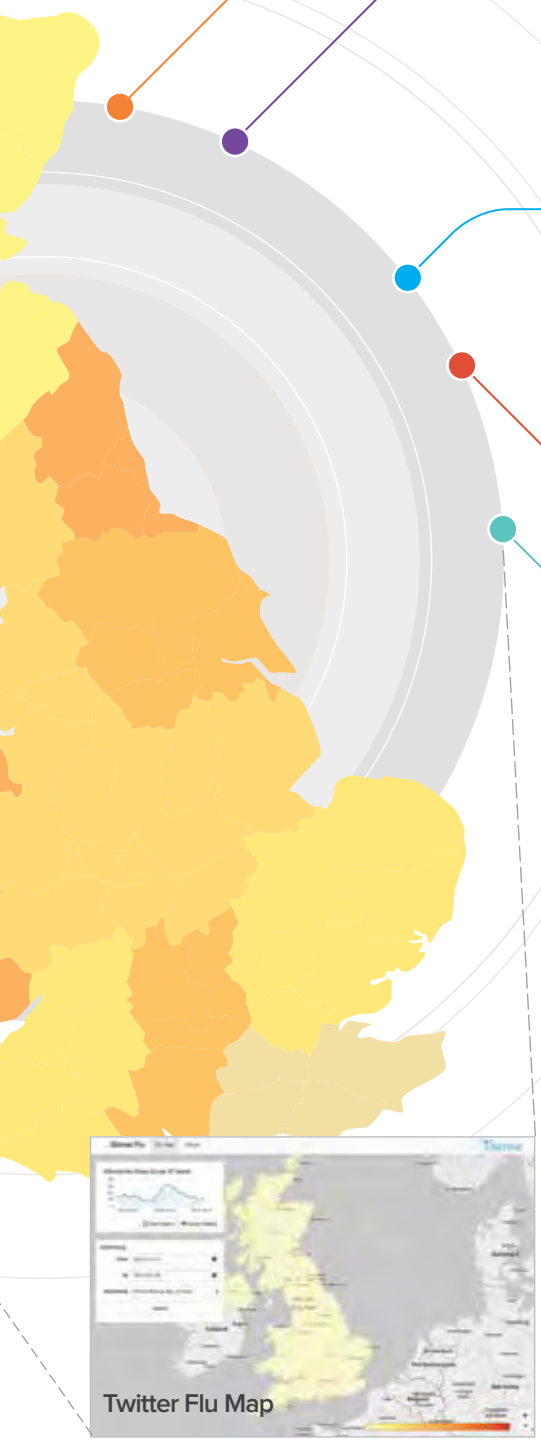
Traditional influenza surveillance is only able to look at cases that reach hospitals or GPs. Set up during the 2009 pandemic, Flusurvey, the UK's biggest crowd-sourced study of influenza, uses self-reporting from the community to rapidly monitor flu.

In collaboration with i-sense, flusurvey.org.uk volunteers were offered a swab to use at home, to confirm if their symptoms are caused by a flu virus or not. This pilot study involved 52 nasal swabs, which were analysed at a PHE central laboratory where they confirmed 17 cases of influenza and other respiratory viruses. Verifying cases of a particular virus is a crucial part of efforts to spot a pandemic flu outbreak and Flusurvey data feeds into national surveillance programmes. i-sense researcher Clare Wenham also used Flusurvey data to study the effectiveness of the 2015 flu vaccine.

Image courtesy of London School of Hygiene and Tropical Medicine

i-sense and Flusurvey ran 5 UK focus groups in order to address issues of recruitment, retention and representativeness and received numerous public feedback in order to improve the Flusurvey website and app (UK version now in development).

Wenham, C. & Edmunds, J. 'How effective is this year's flu vaccine' *BMJ Blogs* (2015).



Twitter Flu Map

How Effective is the Flu Vaccine?

Researchers have proven the effectiveness of a flu vaccination programme by analysing millions of Tweets and Bing search queries. The UK, in an effort to reduce the spread of influenza, and recognising that children are key factors in its transmission, launched the Live Attenuated Influenza Vaccine (LAIV) campaign for school children in England, during the 2013/14 influenza season.

In this study, i-sense researchers led by Professor Ingemar Cox at UCL, together with PHE and Microsoft extended previous data modelling approaches to analyse influenza-like illness (ILI) rates in the LAIV target vaccinated locations as well as a broader set of control locations across England. Their findings show that there was a reduction in ILI rates in the vaccinated areas, suggesting the LAIV campaign had a positive health impact.

This supported findings from traditional health surveillance data and demonstrates how data generated by Internet users can be successfully used to assess the impact of health interventions.

Lampos, V., Yom-Tov, E., Pebody, R. & Cox, I.J. 'Assessing the impact of a health intervention via user-generated Internet content' *Data Mining and Knowledge Discovery* **5**, 1434-1457 (2015).

Self-Diagnose on your Phone

Early stage research is underway to create the first self-test for flu for the National Pandemic Flu Service. Systematic reviews of current lateral flow flu tests shows that they are not very sensitive, often misinterpreted, and the test is not connected to healthcare systems – so the results are easily lost.

UCL researchers in Professor Rachel McKendry's team are developing an app linked to a smartphone camera to automatically analyse, interpret and connect commercial flu tests results to healthcare systems. Through a new partnership with Becton Dickinson, the i-sense app is being evaluated with their commercial tests. Pilot studies show that we can detect very low pg/ml levels of flu within minutes. Location sensors in the phone mean results can help to identify disease 'hotspots'.

A Biobarcode for Flu

A paper microfluidic test that resembles a barcode is being developed by i-sense researchers at UCL to detect up to 200 biomarkers in parallel. The barcode results would be impossible to read by eye, but can be interpreted using our smartphone app. In the future, such a biobarcode could be used to identify the cause of a fever and distinguish between seasonal and pandemic flu strains.

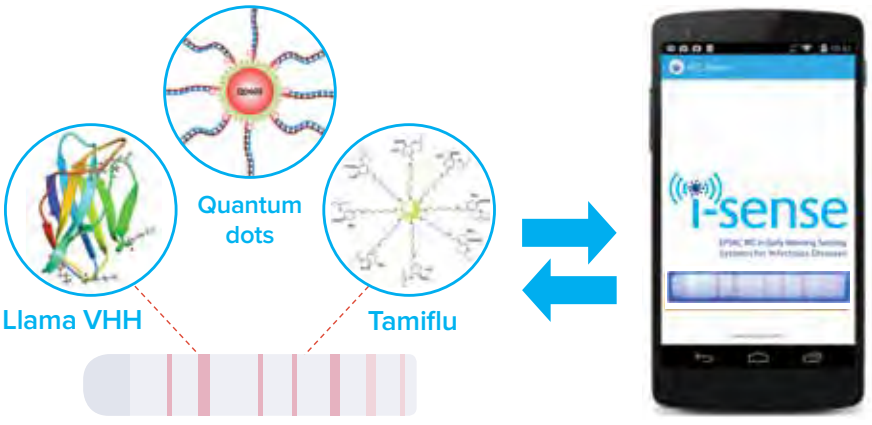
These platform technologies are also being developed for HIV and Ebola.

Howes PD, Chandrawati R, Stevens MM Colloidal nanoparticles as advanced biological sensors. *Science* (2014) 346(6205):1247390.

Novel Capture Materials

We are exploring a range of advanced nanomaterials for ultra-sensitive detection of flu:

Quantum Dots: Fluorescent materials are the fundamental basis of the most sensitive bio-diagnostic and imaging techniques. In our work, we use fluorescent semiconductor nanoparticles ('quantum dots') as a core technology for producing novel diagnostics for infectious disease detection. Our team, led by Professor Molly Stevens at ICL have created first generation projects focused on direct unamplified detection of target nucleic for flu, and we demonstrated excellent proof-of-principle assays. As a second generation we are using enzyme-assisted amplification to bring the limits of detection into a clinically appropriate range to produce rapid and high performance flu diagnostics.



Nanobodies represent an important new class of advanced nanomaterials, offering advantages over conventional monoclonal antibodies due to their small size, ability to access hidden clefts on viruses, and remarkable temperature and pH stability. Combining experimental and molecular modelling approaches, we are developing novel nanobodies against flu nucleoprotein, one of the most conserved and abundant proteins in the virus.

Novel Tamiflu-derivatives are being created that target neuraminidase proteins on the outer surface of the flu virus. An initial six-month Exploratory Project demonstrated a simple, scalable, gram-scale chemical synthesis of ligands. In the second phase, these will be combined with a fluorescence assay to detect clinically relevant levels of influenza using a mobile phone-connected spectrometer.

Systems Level Perspective of End User Needs

The role of Flagship 1 is to evaluate the systems level performance characteristics required for our early-warning sensing systems based on an understanding of end-user needs and existing clinical and surveillance diagnostic practices. This work is central to i-sense and outcomes feed into our Core Flagship Programmes on flu, bacteria and HIV as well as Exploratory Projects and Partnership Resource Funding calls.

Dare to Dream

We are conducting systematic reviews of the current UK and global landscape of early warning systems and point-of-care diagnostics, and results will be published soon. The UK surveillance system is globally respected and provides a template for other countries but inherent delays between sending samples to specialist laboratories, waiting for results and follow up appointments, often results in ongoing transmission of infections in communities (e.g. HIV and MRSA) and delays in responding to emerging threats (e.g. pandemic influenza).

There are increasing national and international drivers to dramatically improve our capacity to rapidly detect and respond to infectious disease threats by examining a variety of new data sources, including social media, widening access to testing in the community and a drive for innovative real-time surveillance.

"Dare to dream" interviews were conducted by Professor Rosanna Peeling's team with key stakeholders to identify where new diagnostic technologies would be of significant value. The research highlights the need for surveillance-connected tests at the community level and in the home. We will design our point-of-care tests to meet ASSURED criteria – 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 rapid treatment, and Robust, for example not requiring refrigerated storage, Equipment-free and Delivered to those who need it.

We are developing target product profiles for each Flagship. Potential benefits of self-tests include increased access to testing, convenience and autonomy, particularly for people living in marginal communities, faster access to treatment and reduced burden to health centres in a pandemic.

However, two notable challenges of self-testing are linkage to care and possible loss of data, causing gaps in disease surveillance.

Within i-sense we are exploiting the connectivity of phones to build online HIV care pathways in the UK and South Africa. This approach is being extended to other disease areas, including a flu self-test and MRSA tests for care home settings. Looking ahead, we aim to exploit our collective knowledge of different disease areas to develop open-platform technologies that can respond to any novel pathogen. We will also be looking at new ways to accelerate diagnostic development and the adoption process.

Building Public Trust in Early Warning Systems

We have teamed up with UCL Philosopher, Dr James Wilson to examine the key ethical and regulatory challenges for early warning sensing systems. This study examines how to build and maintain trust in these systems from two interlinked perspectives: first from the patients and citizen's perspective, and second, from a systems design perspective, examining the incentives necessary to establish trust in i-sense's systems. Three focus groups were conducted to understand different attitudes towards i-sense technologies and analysis of this data is now underway.

Saving Lives and Livelihoods

i-sense is working to protect patients and populations from the threat of infectious diseases.

Patients could benefit by gaining faster access to treatment and follow-up care, thus speeding recovery and reducing the risk of suffering and death.

Populations could benefit from the reduced spread of infection and antibiotic resistance.

The NHS and global healthcare providers could benefit from more cost-effective care, improved stewardship of antimicrobials and informed intervention programmes.

Public health could benefit from timely, targeted efforts to control disease spread.

Mobile Revolution

7 billion mobile phone subscriptions *(ITU)*

3 billion internet users *(ITU)*

500 million Tweet per day (80%) on mobiles *(Twitter)*

72% of people search online for health information *(Pew Research Centre)*

100 billion app downloads *(Apple Apps Store)*

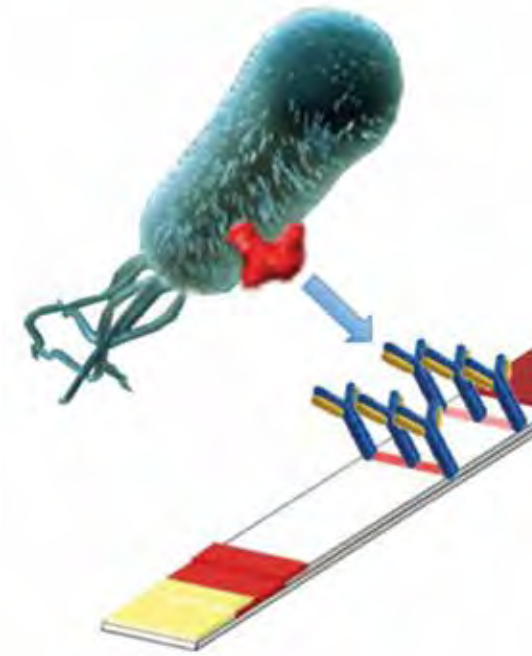
$14 trillion Internet of Things market by 2022 *(Cisco)*

Bacterial Infection

Dame Sally Davies, Chief Medical Officer described antimicrobial resistant infections as a "ticking time bomb" and Jim O'Neil, Chair of the UK Government's Review on antimicrobial resistance, reports an estimated human and economic cost of 10 million extra deaths by 2050 and a cost to the global economy of $100 trillion[1].

A key challenge is that current diagnostics tests can take up to several days to perform. Therefore, patients tend to be administered a broad-spectrum antibiotic, even for viral infections and this can fuel resistance. i-sense researchers are developing mobile phone-connected diagnostics tests to improve the early detection and identification of bacterial infections, including MRSA, *C. difficile* and *E. coli*.

Our approach combines innovations in biomarker discovery and capture ligands with low power microelectronic chips for wireless signal transmission of results. In 2015, following the guidance of our Advisory Board, we made the strategic decision to focus on testing of bacterial infections in care homes and we plan to conduct a pilot study in 2018.



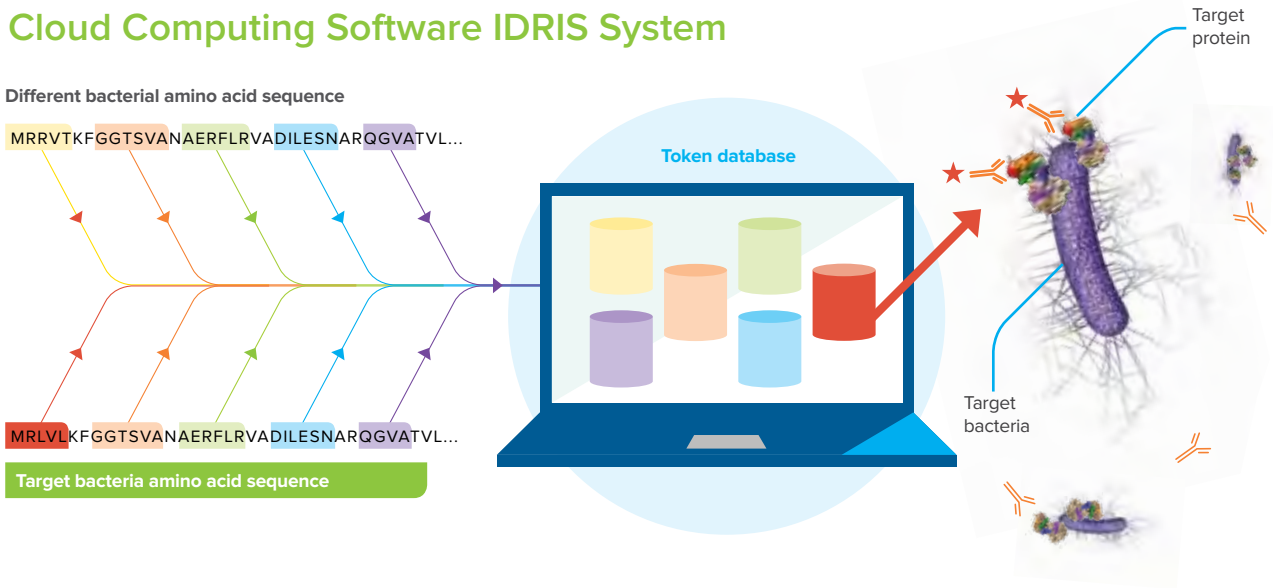
Biomarker Discovery

To help identify the capture molecules for these tests, we have developed novel software that harnesses the huge amount of genetic data available for bacteria.

A novel cloud-based computing system, called IDRIS has been built by the Newcastle team, under the direction of Professor Anil Wipat. IDRIS rapidly processes genome sequence data to identify highly conserved amino acid "patches" present in proteins located at the surface of the target bacteria. These patches of amino acids, referred to as tokens, then guide the development of a variety of capture molecules for incorporation into diagnostic sensors.

Targeting tokens on surface-exposed proteins overcomes the need for complex sample handling and improves the speed and ease of use of diagnostics tests by non-expert staff in care home settings. Version 3 of the system is currently being road-tested and the i-sense team is working with Newcastle University's Research Enterprise Services and the Partnership Resource Fund to explore a route to commercialisation and the possibility of establishing a spin out company.

Cloud Computing Software IDRIS System



Care Homes

MRSA colonisation levels among residents in care homes in the UK have been indicated to be greater than 20% and subsequent infections can have serious and, in some cases, life-threatening consequences. Early detection and the application of appropriate treatment is therefore very important. In 2016 we have commissioned a report from researchers at the Brighton and Sussex Medical School to assess the need for rapid diagnostic tests for bacterial infections in care homes, including MRSA and *C. difficile*, in order to identify further opportunities for i-sense technologies.

Novel Capture Ligands

In addition to conventional antibodies, a range of novel molecules are being investigated for capturing whole bacterial cells, including smaller, potentially more efficient peptide and DNA aptamers.

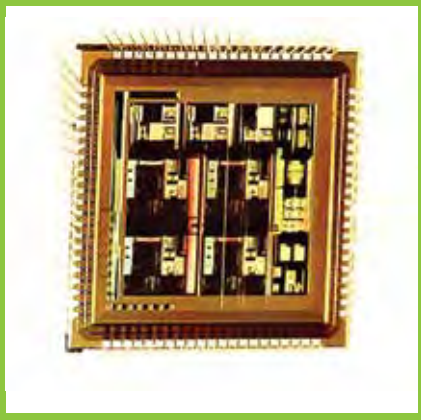
The IDRIS system has already been used to identify a token within a surface exposed protein, found in all *C. difficile* species. Monoclonal antibodies directed against this token have demonstrated species-specific recognition of *C. difficile* – paving the way to develop more sensitive and specific diagnostic tests.

The Newcastle University team, led by Dr. Neil Keegan and Prof. Anil Wipat, have recently won an MRC Confidence in Concept Award to support the translation of these *C. difficile* antibodies and a patent application is now in progress.

Miniaturised Sensors

Sensor technologies, including impedance-based lateral flow tests, and MEMS are being integrated with mobile phones. Miniaturisation is key to enabling these tests to be done at the point of care.

UCL researchers led by Professor Andreas Demosthenous have developed a tiny CMOS potentiostat, to replace the large bench-top machine used in the laboratory to read out electrochemical diagnostic tests. The first chip was fabricated in November 2015 and testing has been completed.

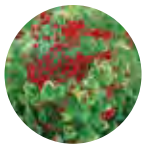


The chip has now been connected to capacitive biosensors, which are read using an electrical signal. Researchers are currently working on an improved version of the chip with optimised performance and real-time extraction of sensor impedance.

Researchers at UCL led by Prof. Rachel McKendry are also investigating an antimicrobial susceptibility test that works in minutes, based on newly discovered mechanical vibrations, produced by living bacteria. This early stage research utilises micromechanical cantilevers, which resemble tiny diving boards, to capture bacteria in the patient samples to be tested.

Patil, S.B., Manuel V., Webb, B., Mazza, G., Pinzani, M., Soh, Y., McKendry, R.A. & Ndieyira, J.W. 'Decoupling competing surface binding kinetics and reconfiguration of receptor footprint for ultrasensitive stress assays' *Nature Nanotechnology* **10**, 899-907 (2015).

1. Jim O'Neill, 'Antimicrobial Resistance, Tackling a crisis for the health and wealth of nations' *The Review on Antimicrobial Resistance* (2014).



HIV & Ebola

HIV-1 is a formidable virus, continually changing, mutating and evolving. The molecular diversity of the virus found in a single HIV-1-infected patient is greater than the diversity of annual influenza infections worldwide, posing a significant challenge to diagnosis of HIV. The World Health Organisation estimates that more than 35 million people are currently living with HIV. An estimated 100,000 people in the UK are HIV-positive but one in five are unaware of their status.

Early diagnosis of HIV plays a critical role in access to antivirals before their immune system is irreversibly damaged. In the wake of recent legislation to allow HIV home testing in the UK, we are working with local and global partners to widen access to HIV self-testing and developing mobile phone-connected tests to ensure patients are rapidly diagnosed and linked into care pathways.

The recent Ebola outbreak in West Africa further highlighted the urgent need for point-of-care tests to prevent and control epidemics, and we have been able to extend technologies developed within i-sense, to look at immunity in Ebola survivors.

Harnessing Mobile Phones to Stop the Spread of HIV: An International Collaboration

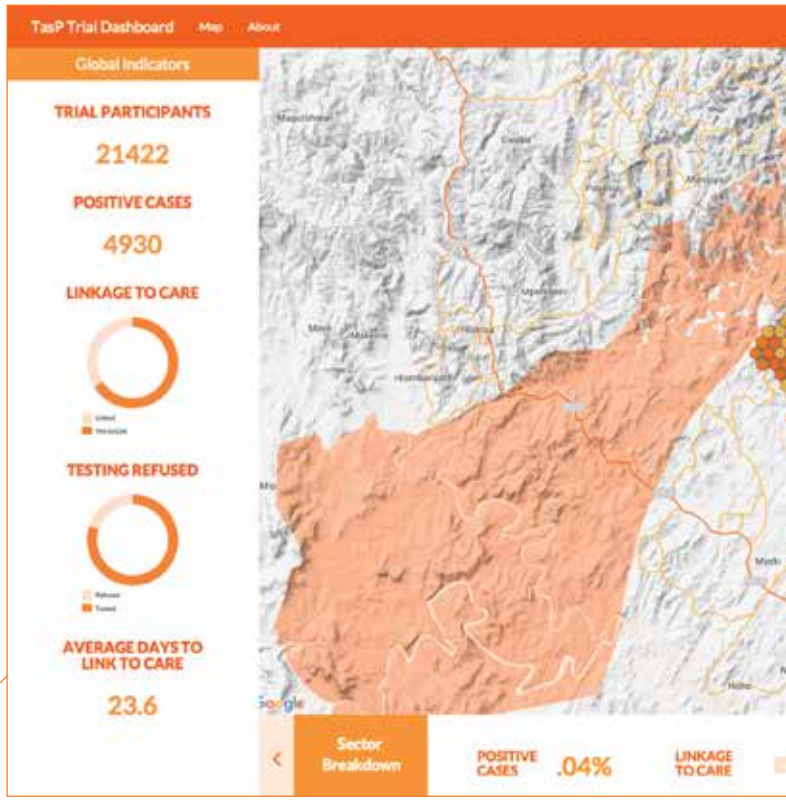
i-sense has teamed up with the Wellcome Trust Africa Centre for Health and Population Studies and The Bartlett Centre for Advanced Spatial Analysis (CASA) at UCL to harness the power of mobile technologies and link newly diagnosed HIV patients to treatment.

The research builds on a major Treatment as Prevention (TasP) trial in Kwazulu-Natal, South Africa, involving more than 24,000 participants to assess the impact of home-based HIV testing and immediate treatment for the newly diagnosed, on reducing HIV incidence.

We developed a real-time digital dashboard to track the progress of the trial, identify areas where further support is needed and target interventions to improve linkage to care. The dashboard also serves to demonstrate the work of the Africa Centre, and promote data exploration by its staff and visitors, and it will be presented at this year's International AIDS Conference in Durban. Researchers will also recruit a small sample of volunteers from the TasP trial to assess the impact of i-sense's mobile phone app, to record HIV test results.

South Africa has the highest burden of HIV infection worldwide. This project represents a crucial first step in assessing the impact of i-sense's emerging technologies in developing countries, and tackling the global challenge of HIV.

Tracking TasP trial in Kwazulu Natal, South Africa



Detection of Ebola Antibodies in Human Survivors

Lateral-flow based diagnostic technologies developed within i-sense have been extended to Ebola virus, following the outbreak in West Africa.

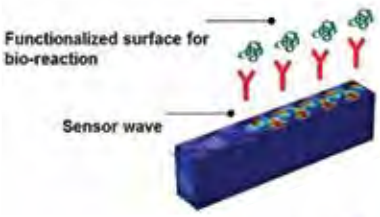
In this project, ICL and UCL researchers developed a mobile phone-connected immunity test to detect the immune response of survivors in Uganda to the Ebola Virus.. This work was made possible by i-sense student Polina Brangel who collaborated with Dr Leslie Lobel from Ben-Gurion University of the Negev and Dr John M Dye from the US Army Medical Research Institute of Infectious Diseases.

The novel assay is based on a lateral flow test strip combined with a smartphone app. A pilot study of 123 sera samples, obtained from previously Ebola-infected patients and non-infected controls, exhibited 96% sensitivity, 100% specificity and 97% correlation with the standard lab-based tests. Overall, this assay is rapid, robust, simple and portable and has the potential to be used as an essential tool for on-site diagnostics and patient management during, and after, Ebola outbreaks.

Listening to Viruses

i-sense researchers at UCL and UCLH are working with diagnostics company OJ-Bio to pioneer mobile diagnostics for HIV, based on low-cost surface acoustic wave components found in every mobile phone. The collaboration leverages on an NIHR i4i Award and OJ-Bio have developed a disposable USB-like sensor chip which can be inserted into a hand held detector and the results wirelessly sent to a mobile phone. A recent i-sense pilot study of 30 HIV-infected patient plasma samples showed high 100% sensitivity and specificity based on multiplexed antibody detection. Finite element models of the shear horizontal wave propagation along the sensor surface are being developed for ultrasensitive detection of the p24 HIV antigen.

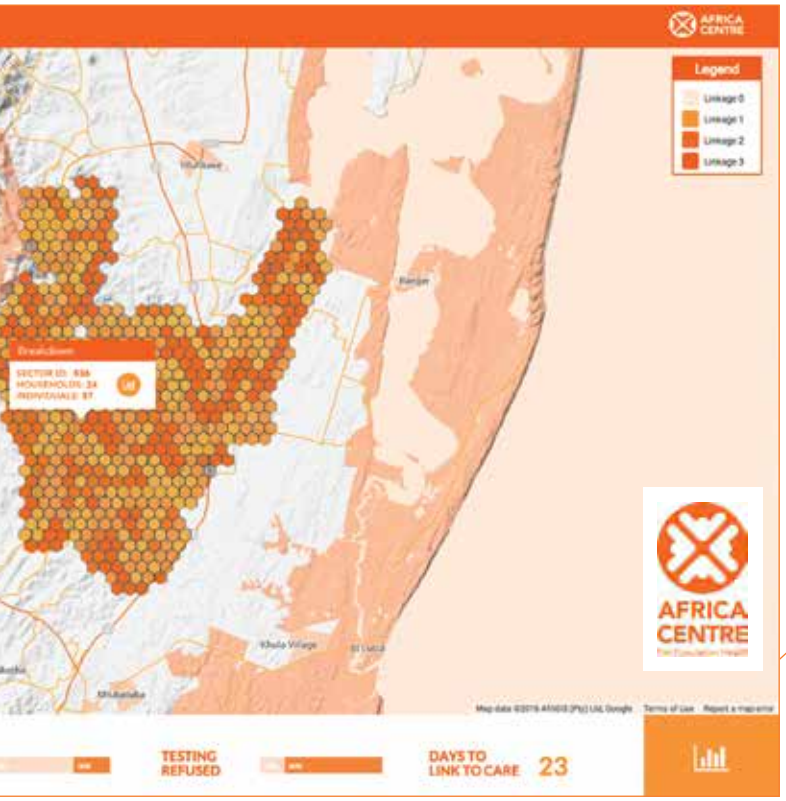
Detection of HIV biomarkers on SAW sensors



Left: Finite element analysis models determine waves launched on the SAW surface sensor chip.

Right: OJ-Bio's prototype SAW detector and disposable, single-use sensor chip.

Brookes, J.C., Bufacchi, R., Kondoh, J., Duffy, D.M. & McKendry, R.A. 'Determining biosensing modes in SH-SAW device using 3D finite element analysis' Sensors & Actuators: B. Chemical 234, 412-419 (2016)

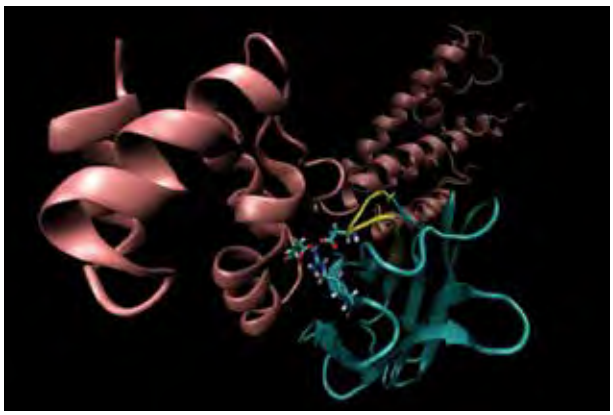


Nanoparticle-Nanobody Constructs for Early HIV Diagnosis

Early HIV detection in the community is problematic, as tests typically rely on antibody detection. These antibodies cannot be detected until approximately one to six months after exposure. Moreover, antibody detection is sometimes inaccurate, for example in infants, where their mothers' antibodies may cause false-positive results.

i-sense researchers at UCL and QVQ have developed a library of novel nanobody capture ligands to detect p24, one of the earliest and most conserved biomarkers of HIV. We find that these small antibodies, one tenth the size of conventional antibodies, show strong pM binding, broad specificity to 50 HIV-1 subtypes worldwide and temperature stability up to 90°C. Lead candidates will be taken forward for clinical evaluation studies on a range of diagnostic platforms.

Researchers from ICL and UCL are closely collaborating with the Nanomaterials Laboratory at Seoul National University, to develop ultrasensitive diagnostics for the detection of p24 at very low concentrations in the body. The team at ICL is using advanced nanomaterials, including quantum dots and highly active, catalytic nanoparticles to engineer colorimetric and fluorescence-based assays. The incorporation of nanobodies of high stability and specificity towards p24 onto these nanoparticles is being explored, using site-specific mutation and modification. This will create precisely designed nanoparticle beacons for use in these diagnostic assays.



Molecular dynamics simulation of nanobody 59H10 binding to p24 HIV antigen.

Exploratory Projects

The £2M Exploratory Projects programme is designed to close the expertise gaps in the i-sense consortium by bringing in new partners from collaborating institutions. Exploratory projects are intended to be short, high-risk, new collaborations (up to 24 months), between two or more partners from the i-sense institutions to complement the Core Research Programme. Following two funding calls for new partners, i-sense have launched ten multidisciplinary, collaborative projects to date, totalling almost £1.1M, with 6 funded this year to address Digital Disease Detection.

Second Call: Digital Diseases Detection – Building the Toolkit (2015)

Smart Detection of Influenza: The Chemical Interface Between the Virus and Mobile-Phones. Dr. Stephen Hilton (UCL) with collaborators from ICL.

Advancing HIV Self-Testing: Developing an NHS-based Online Clinical Pathway and System to Link Self-Testers into Appropriate Services and Surveillance. Dr. Pam Sonnenberg and Dr. Jo Gibbs (UCL) with collaborators from PHE and QMUL.

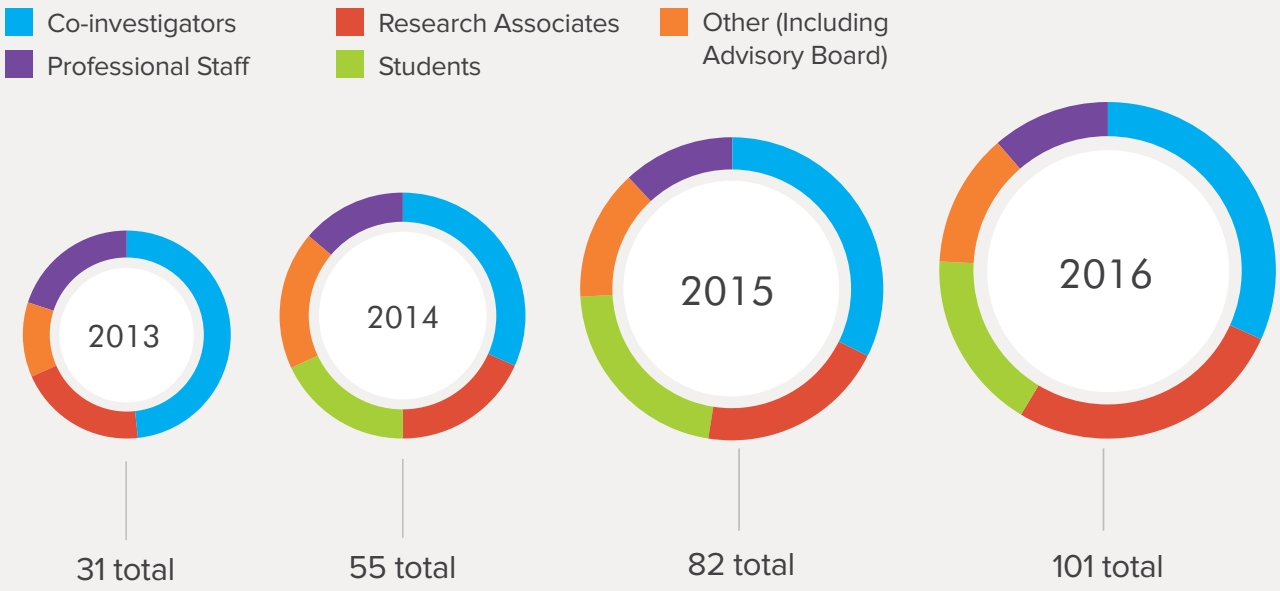
Highly Controlled Nanoparticle-Antibody Conjugates for Next-Generation Point of Care Diagnostics. Dr. Vijay Chudasama (UCL) with collaborators from ICL.

A Technical Framework for Enabling and Supporting Data Donors for Medical Research. Professor Ingemar Cox (UCL) with collaborators from ICL.

Developing Target Product Profile of Flu Self-Tests: How Could They Increase The Cost-Effectiveness of the National Pandemic Flu Service and of the Management of Seasonal Flu. Dr. Peter White (ICL) with collaborators from UCL and PHE.

Exploiting Microfluidics and Printing Technologies to Rapidly Detect MRSA in Nasal Swabs. Professor Kenny Dalgarno (UNEW) with collaborators from PHE and UCL.

The i-sense Network



Education Alliance

The i-sense Education Alliance has been created to introduce new teaching and training courses in order to grow the interdisciplinary skills of our students and researchers.

This programme is overseen by the Education Alliance Board, led by Newcastle's Neil Keegan, and has representatives from across the i-sense partner institutions. This unique programme is designed to prepare and inspire students and researchers for future careers, developing and disseminating new sensing systems to solve global healthcare challenges. It provides a supportive and exciting environment for postdoctoral researchers and students, creating new working cultures and building relationships between teams in universities.

Communication and Networking

The second Education Alliance event, held in November 2015, was a 2-day workshop, which focused on building the students and postdocs' networking and communication skills and was held at Imperial College London.

The group learnt how to maximize their personal profile, build networks and communicate their research effectively to a non-academic audience. At the end, everyone produced lay brochures of their research as part of a scientific communication competition – we had some great entries!

As part of this event, the wider i-sense network was invited to attend the seminar "Diagnostics from Bench to Bedside: A Fragmented Pathway" given by diagnostics leader, Professor Rosanna Peeling. The seminar focused on diagnostics development, evaluation, policy development and implementation.

Future workshops will address data security and career development.

Preparing a Global Health response

Professor Rosanna Peeling and Dr Penny Wilson from Innovate UK recently led an interactive workshop on open platform technologies and global health regulations. i-sense students and researchers were challenged to come up with solutions to three central issues for academics working within industry, that could impact the development of open platform technology. As part of this event, they were exposed to a simulated global health emergency and asked to pitch their diagnostic technologies in response to the challenge. This enabled them to better understand the complexities of a global health response and place their technologies into a real-life context.

Building skills:

26 researchers

26 researchers attended courses over the past year to improve their academic and business skills.

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.

Our initiatives include a series of workshops, funds to support visiting researchers, flexible funding to leverage through partnership and broad dissemination of our research through our website and communication channels, policy and public engagement activities.

The work is overseen by a Partnership Resource Fund Board, led by Professor Vince Emery. The Board is made up of i-sense members and external partners, including Peter Dobson (Oxford Begbroke Science Park), Mike Short (Telefonica O2), Sue Dunkerton (Knowledge Transfer Network) and Simon Lusignan (Royal College of GPs).

We are aiming to build on our national and international partnerships through flexible funding opportunities: Our Mobility Fellowships, Knowledge Transfer Grants and Outreach Grants. Funding applications will be reviewed by the Partnership Resource Fund Board, but final approval will be given by the i-sense Management Committee.

Workshops

i-sense have already held three successful workshops, bringing together interdisciplinary teams of experts to discuss the global risks and challenges of pandemic influenza, the need for point-of-care diagnostics for bacterial infections and, more recently Zika diagnostics needs.

One exciting outcome of the bacterial infections workshop was leveraged funding for i-sense scientists at Newcastle University and Imperial College to participate in a successful €18m large-scale European Commission Horizon 2020 project, aiming to increase diagnostic capability in the area of paediatric bacterial infection.

Zika Diagnostics Workshop 2016

In the wake of WHO declaring Zika as a Public Health Emergency of International Concern on 1st Feb 2016, Professor Rosanna Peeling ran a workshop with leading experts from the London School of Hygiene and Tropical Medicine to explore the diagnostic needs for Zika and how i-sense researchers might respond to a global health emergency. Rosanna was joined by Professor Laura Rodrigues who spoke on her experiences working with Zika-infected patients in Brazil and Dr Adam Kucharski who highlighted the transmission patterns of Zika and its spread across island populations. This workshop provided researchers with a rare opportunity to hear from global experts on Zika and emerging infectious diseases, with experience in the field. The talks sparked some lively discussions on how we might respond to future disease threats and the need for rapid, open-platform diagnostic technologies.

Flexible Funding

The i-sense Partnership Resource Fund and Education Alliance have announced three new funding calls over the past year.

Two Knowledge Transfer Grants were awarded, totalling £76k, with the aim of supporting the translation of i-sense technologies into products and practices. Anil Wipat and Neil Keegan from Newcastle University, received funding to explore commercialisation routes for the 'IDRIS' system. Professor Jackie Cassell and her team from Brighton and Sussex Medical School were awarded for an initial scoping exercise, which will assess the need for rapid diagnostic tests for bacterial infections in a care home setting.

i-sense Mobility Fellowships were awarded to 5 successful applicants, totalling £25k. i-sense and UCL students Isabel Bennett and Ben Miller will work with nanophotonic pioneer Professor Aydogan Ozcan and his group at UCLA, and Christine Wang from Imperial College will join the Molecular Foundry at Berkeley, a global leader in nanoscience research. We have also awarded Fellowships to researchers from École Polytechnique Fédérale de Lausanne (EPFL) and the University of Melbourne to come and work with the i-sense group.

Future workshops will include an i-sense industry workshop in 2016 and a joint HIV workshop with the Africa Centre in 2017.

Communications and Engagement

Website: The i-sense website **www.i-sense.org.uk** has nearly 2500 unique visitors a month and more than 40,000 unique visits to date. You can visit the site for more information on the research projects, news, events and funding opportunities in this Annual Report.

We have a strong social media presence – now 360 followers on Twitter and a recently launched Facebook page. We have plans to expand our social media strategy with new mediums in 2016. You can follow i-sense on Twitter **@isenseIRC** and like our Facebook page **i–sense EPSRC IRC**.

Public engagement: Over the past year i-sense has opened up a wider dialogue with the public, London public office, business leaders, and schools enabling us to both disseminate, and gain feedback, on our research in order to ensure we are creating technologies that people need, and want to use.

Most recently, i-sense teamed up with UCL Enterprise to run an exciting Rosalind Franklin app competition to empower and recognise Women in STEMM. We received over 170 registrations and 70 applications from across the country. High profile judges and speakers included Baroness Martha Lane Fox, and Rosalind Franklin's sister, Jenifer Glynn. Following this, i-sense Director Rachel McKendry, who led the competition, was interviewed for a Women in Business feature in the Financial Times on academia as a driving force for technology entrepreneurship.


Women in Business

Academia develops technology to boost entrepreneurial talents

We have featured in several high-profile films around innovative and interdisciplinary EPSRC-funded healthcare research; Calum McNeil in the Royal Society of Medicine and ITN "Doctors of the Future" series and Rachel McKendry in the EPSRC Healthy Nations film.

We have secured funding from the Wellcome Trust to run an activity at Einstein's Garden in August 2016, as part of the Greenman Festival in Brecon Beacons, Wales. This fun and interactive stall will show the public how we can use their digital technologies to rapidly test and track infectious diseases.

Talks

80 talks were given on i-sense research in the UK and internationally by i-sense members in 2015-16.

Highlights include Ingemar Cox's opening talk at the ECDC ESCAIDE conference, Rosanna Peeling's Closing Plenary at the UK Diagnostics Forum on Disruptive Technologies and Rachel McKendry's Institution of Engineering and Technology (IET) Annual Lecture.

11 Conference posters and papers were presented nationally and internationally.

Prizes


UCL Provost Spirit of Enterprise Award (2015), Rachel McKendry, UCL


IEEE Signal Processing Society Sustained Impact Award and Runner-up Lloyd's Science of Risk Prize, Ingemar Cox, UCL, 2015


International Clostridium Difficile Symposium (ICDS) Young Investigator Grant, Beth Lawry, UNEW, 2015


Catalan Aguar Beatriu de Pinós Fellowship, Claudio Parolo, UCL, 2015


Clemson Award for Basic Research from the Society for Biomaterials, Molly Stevens, ICL, 2016


President's Award and Medal for Excellence in Research- Outstanding Research Team, Stevens Group, ICL, 2016


Global Health Innovation Student Challenges Competition, Harriet Gliddon, ICL, 2016


UCL Electrical and Electronic Engineering Cisco Poster Prize, Evdokia Pilavaki, UCL, 2016


Marie Sklodowska Curie Individual European Fellowship, Philip Howes, ICL, 2016


Wellcome Trust Society Ethics Fellowship, Benedict Rumbold, UCL, 2016

Policy

In 2015/2016 i-sense researchers have been influencing policy in the following ways:

- Rosanna Peeling Co-chair the WHO Platform Technologies Initiative to accelerate the development, of diagnostics, therapeutics and vaccines for emergency preparedness.
- Rachel McKendry on Steering Group for Cross Council Antimicrobial Resistance Initiative
- Calum McNeil a panel member for cross-Council innovation and collaboration grants on antimicrobial resistance.
- Molly Stevens was on the Advisory Board that steered the Royal Society Review of UK Research Councils, which led to the "Ensuring a successful UK Research Endeavour" report, to advise on determining the future research funding landscape in the UK.
- Rosanna Peeling on WHO global consultations on Zika outbreaks and member of the Advisory group to develop Target Product Profiles for Zika diagnostics
- Rachel McKendry joined opinion leaders at the Prime Minister's Council for Science and Technology (CST) to discuss the convergence between materials, bio and digital technologies.
- Rachel McKendry represented EPSRC-funded research at the Parliamentary Office of Science and Technology (POST) event held at the House of Commons, Westminster.
- Anne Johnson, Ingemar Cox and Rachel McKendry joined Wellcome Trust Director Jeremy Farrar for the *Digital Phenotypes – Health research in the digital age?*
- Rosanna Peeling a member of the European Commission Horizon 2020 Prize for AMR
- James Wilson joins National Data Guardian Panel to build trust in the use of data across health and social care.
- i-sense group at UCL hosted a lab and site visit for Carol Monaghan, an MP and member of the Science & Technology Select Committee

Publications

Maruani, A., Richards, D.A. & Chudasama, V.
'Dual modification of biomolecules' Org. Biomol. Chem (2016)

Brookes, J.C., Bufacchi, R., Kondoh, J., Duffy, D.M. & McKendry, R.A.
'Determining biosensing modes in SH-SAW device using 3D finite element analysis' Sensors & Actuators: B. Chemical 234, 412-419 (2016)

Gliddon, H., Howes, P.D. & Stevens, M.M.
'A nucleic acid strand displacement system for the multiplexed detection of tuberculosis-specific mRNA using quantum dots' Nanoscale 8, 10087-10095 (2016).

Kostkova P., Brewer H., De Lusignan S., Fottrell E., Goldacre B., Hart G., Koczan P., Knight P., Marsolier C., McKendry R.A., Ross E., Sasse A., Sullivan R., Chaytor S., Stevenson O., Velho R. & Tooke J.
'Who Owns the Data? Open Data for Healthcare' *Front. Public Health* **4**, 2296-2565 (2016).

Preoțiuc-Pietro D., Volkova S., Lampos V., Bachrach Y. & Aletras N.
'Studying User Income through Language, Behaviour and Affect in Social Media' *PLoS ONE* **10**, e0138717 (2015).

Almeida, C., Howes, P.D. & Stevens, M.M.
'Tailoring Cellular Uptake of Conjugated Polymer Nanoparticles Using Modular Amphiphilic Peptide Capping Ligands' *Chemistry of Materials* **27**, 6879-6889 (2015).

Lampos, V., Miller, A.C., Crossan, S. & Stefansen, C.
'Advances in nowcasting influenza-like influenza rates using search query logs' *Scientific Reports* **5**, 12760 (2015).

Soh, J.H., Lin, y, Rana, S, Ying, J.Y. & Stevens, M.M.
'Colorimetric detection of small molecules in complex matrixes via target-mediated growth of aptamer-functionalized gold nanoparticles' *Anal. Chem.* **87**, 7644-7652 (2015).

Lampos, V., Yom-Tov, E., Pebody, R. & Cox, I.J.
'Assessing the impact of a health intervention via user-generated Internet content' *Data Min. Knowl. Discov.* **5**, 1434-1457 (2015).

Patil, S.B., Manuel V., Webb, B., Mazza, G., Pinzani, M., Soh, Y., McKendry, R.A. & Ndieyira, J.W.
'Decoupling competing surface binding kinetics and reconfiguration of receptor footprint for ultrasensitive stress assays' *Nature Nanotech.* **10**, 899-907 (2015).

Wenham, C. & Edmunds, J.
'How effective is this year's flu vaccine' *BMJ Blogs* (2015).

Yom-Tov, E., Cox, I.J., Lampos, V. & Hayward, A.C.
'Estimating the secondary attack rate and serial interval of influenza-like illnesses using social media' *Influenza and other Respiratory Viruses* **9**, 191-199 (2015).

Zhang C., Zhou S., Miller J.C., Cox I.J & Chain B.M.
'Optimizing Hybrid Spreading in Metapopulations' *Scientific Reports* **5**, 9924 (2015).

Yom-Tov E., Cox I.J. & Lampos V.
'Learning about Health and Medicine from Internet Data' *WSDM 2015*, 417-418 (2015).

Yom-Tov, E., Borsa, D., Hayward, A.C., McKendry, R.A. & Cox, I.J.
'Automatic Identification of Web-Based Risk Markers for Health Events' *J. Med. Internet Res*. **17**, e29 (2015).

Kappeler N.
'Cantilevers for biological monitoring: opportunities for classical and quantum physics' *Contemporary Physics* **56**, 186-201 (2015).

Langlois P.J., Neshatvar N. & Demosthenous A.
'Sinusoidal Current Driver with an Extended Frequency Range and Multifrequency Operation for Bioimpedance Applications' *TBioCAS* **9**, 401-411 (2015).

Looking Forward

Towards a World Class Centre of Excellence and Long-Term Sustainability

The next two years will see continued advances in our Core Research, Exploratory Projects and pilot studies with end-users. Highlights include the first evaluation of Twitter data for national flu surveillance with Public Health England, the implementation of HIV mobile diagnostic tests and real-time data dashboards with the Africa Centre, the first HIV NHS self-testing e-pathway, and a pilot study of bacterial diagnostic prototypes in care homes.

We have expanded our Partnership Resource Fund and hope to continue to fund innovative and exciting projects for development and translation as well as to welcome new skills and expertise into the i-sense consortium.

Our strong advocacy and engagement programme will include three future workshops – diagnostics for developing countries (with researchers and policy makers from PHE and DFID), an industry workshop and an all-IRC event with Sphere and Proteus IRCs as well as science festivals and new public-patient initiatives. Upcoming Education Alliance events include seminars on data security and career development training for our young researchers.

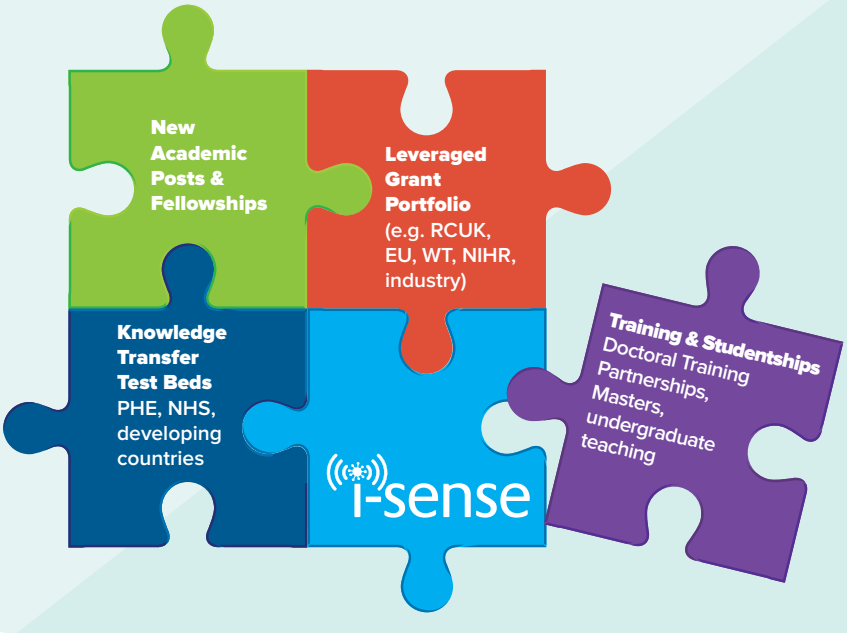
Our long-term aim is to grow a world class centre of excellence, and a pipeline of open-platform, deployable sensor technologies for real-time surveillance, to help build UK and global preparedness to any novel pathogen or novel strain of a known pathogen. To achieve long-term sustainability, we propose to leverage a broad portfolio of funding (including the Global Challenges Research Fund, EU, Wellcome Trust, Gates, NIHR, Innovate UK, industry) and secure new academic posts and fellowships. We will also grow our pilot studies into Knowledge Transfer test beds and bid for Doctoral Training Partnerships to support future leaders.

We are always open to new collaborations and feedback to help us achieve our vision so please do contact us to find out more.

With my very best wishes,

Professor Rachel McKendry
Director of i-sense

Long-Term Sustainability



Management Committee

Rachel McKendry,
Professor of Biomedical Nanotechnology, UCL and Director of i-sense.

Tania Saxl,
Strategic Operations Director and Deputy Director of i-sense, UCL.

Ingemar Cox,
Professor of Telecommunications, UCL Deputy Director and i-sense Flagship 2 lead (flu).

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

Calum McNeil,
Professor of Biological Sensor Systems, Newcastle University Deputy Director and i-sense Flagship 3 lead (bacteria).

Vincent Emery,
Pro Vice-Chancellor (International Relations) and Professor of Translational Virology, University of Surrey, i-sense Flagship 1 and Partnership Resource Fund lead.

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

Anne Johnson,
Professor of Infectious Disease Epidemiology, Chair and Vice-Dean, External Relations, UCL and i-sense Deputy Director.

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

Deenan Pillay,
Director of the Wellcome Trust Africa Centre for Health and Population Studies and i-sense Deputy Director.

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

Advisory Board

David Heymann (Chair), Professor of Infectious Disease Epidemiology, London School of Hygiene and Tropical Medicine and Chair of Public Health England.

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

Andrew Eland,
Engineering Director, Google.

Mike Short,
Vice President, Telefónica Europe.

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

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

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

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

Industrial and Clinical Partners

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Microsoft

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Health Research

The Newcastle Upon
Tyne Hospitals
NHS Foundation Trust
NHS

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UCL Institute of Biomedical Engineering

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BD

i-sense

EPSRC IRC in Early Warning Sensing Systems for Infectious Diseases

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