UNIVERSITY OF BIRMINGHAM

Centre for Systems Modelling & Quantitative Biomedicine

CENTRE FOR SYSTEMS MODELLING AND QUANTITATIVE BIOMEDICINE

Annual Report 2022

Contents

About SMQB

Transforming lives through quantitative biomedical and clinical research

Established in 2019, the Centre for Systems Modelling and Quantitative Biomedicine (SMQB) is a leading interdisciplinary group of research innovators with backgrounds in mathematics, computer science, physics and biomedicine. Passionate about delivering transformative research, the SMQB seeks to impact upon lives, through contributing measurable advances to healthcare and medicine.
Within the SMQB basic and translational research are valued equally, with members encouraged to follow their curiosity and see where it takes them. For our work to be truly impactful we must pioneer new ways of working that bring communities together. Students, researchers, patients and the public, philanthropists, hospitals and clinics, industry and venture capital, policy makers and regulators forming a single ecosystem within which transformative research challenges are co-created and then solved for societal benefit.

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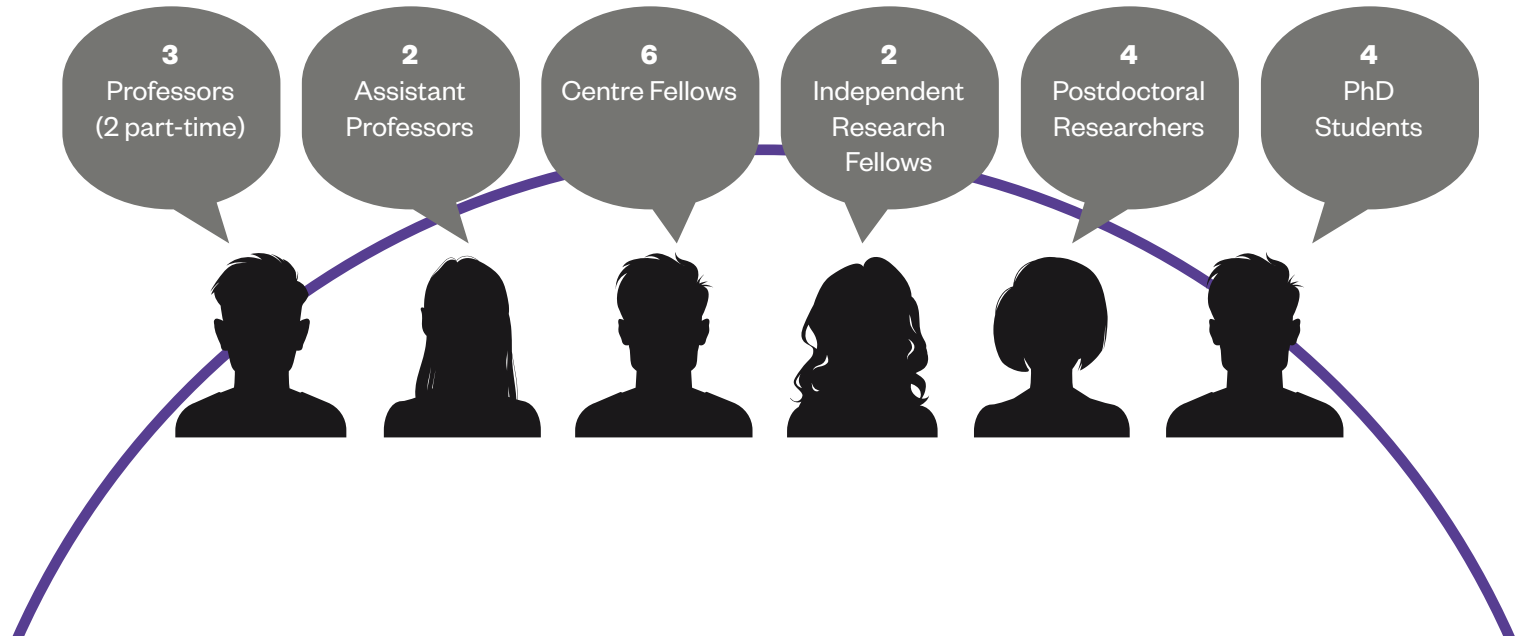

Foreword from the SMQB Director

2022 was an exciting year for the SMQB as we emerged from many of the challenges of the pandemic. It was pleasing to see so many of the team develop as researchers and to deliver outstanding outputs and impact. Everyone has been working hard on exciting projects, with many leading to high-profile publications; highlights of which are included in this report. Several members were also involved in exciting knowledge exchange activities, including partnerships with patient groups and industry. I was especially pleased that we were finally able to host an in-person exhibition showcasing the work of our fabulous Artists-in-Residence, the first of whom worked with us on research projects back in early 2020.

As an interdisciplinary centre spanning mathematics, computer science and medicine we are motivated by creating the environment and opportunities for cross-disciplinary research and enabling novel insights into challenging problems in biomedical and clinical research. As well as continuing to support new and emerging collaborations between quantitative, biomedical and clinical sciences, a personal highlight for me in 2022 was securing £1.2M funding from the EPSRC to establish a Network+ in responsible innovation for neurotechnology. Focussing on developing novel technologies that move diagnosis and management from hospital to non-hospitals settings, an initial partnership of over 50 organisations spanning academia, industry, healthcare, charities and non-governmental organisations (NGOs) has rapidly grown to over 100 partners. Testimony to the importance of this rapidly emerging area.

Finally, I wanted to acknowledge the fantastic support the Centre receives from our professional services team: Dr Rebecca Ward as Centre Manager, Dr Debbie Marsden as Senior Research Manager, Rebecca Wycherley as Senior Administrator and – until recently – Dr Caroline Gillett as Communities Engagement Manager. I say "until recently" as Caroline has recently transitioned into an academic role, as Assistant Professor in Patient and Public Involvement and Engagement. A fantastic example of the career development that we take so seriously within the SMQB.

Professor John Terry

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The Research Incubator

SMQB's flagship research incubator is inspired by business equivalents but repurposed for the specific needs of co-designing and co-creating interdisciplinary 'seedcorn' projects which address a biological or healthcare challenge using mathematical and computational approaches.

It is a six-month focussed period of research, where investigators from complementary disciplines (typically a biomedical or clinical scientist, and a quantitative discipline), are paired with one or more of our Centre Fellows. Centre Fellows provide the critical expertise needed to take the project from concept to delivery and by the end of six months teams will have produced results suitable for both first publications and onward funding.

We kick off the projects with a two-day retreat facilitated by Professor John Terry and supported by colleagues from our professional services teams. The retreat features dedicated sessions built around research planning, IP, impact and business engagement, public involvement and engagement and research finance. Teams are awarded a budget of up to £10K to cover essential costs, as well as a proportion of time of at least one Centre Fellow.

Since 2020 we have embedded an Artist in Residency programme within the incubator. Our residents are artists and creative practitioners who collaborate with our researchers on the projects to bring on board new perspectives and insights, whilst developing exciting, novel creative outputs responding to the research.

The incubator was established by John Terry at the University of Exeter in 2016. Since then, 46 project teams have delivered 33 publications, 4 patent applications, and over £10M of onward funding secured. In partnership with the EPSRC Network+ N-CODE, we will expand the incubator during 2023 with a focus on emerging neurotechnologies.

Seedcorn Projects 2022

In 2022 we funded four new seedcorn projects through the research incubator. These saw us build new collaborations across the university with colleagues in Biomedical Sciences, Computer Science, Institute of Applied Health Research, Institute of Clinical Sciences, Institute of Metabolism and Systems Research, Institute of Microbiology and Infection, Mathematics and Pharmacy. The groups first met at the two-day retreat held in Solihull in June.

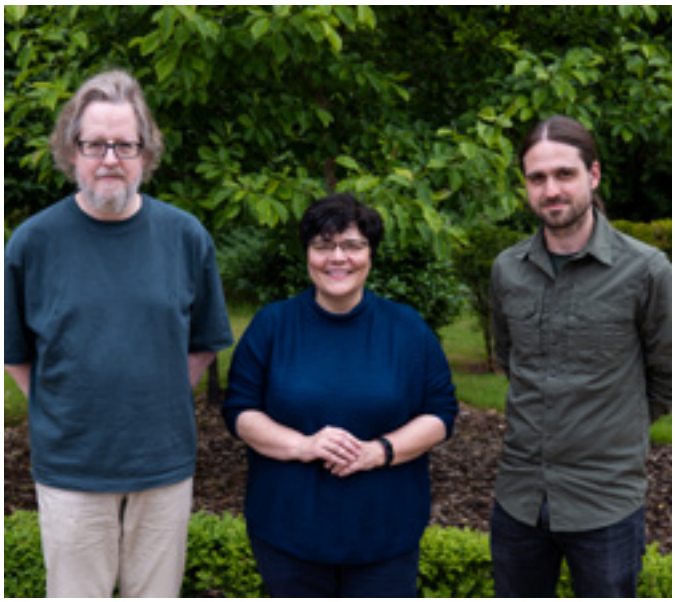
Seedcorn photos credited to Hayley Salter

Improving ocular drug delivery using mathematical modelling of the eye

Degenerative diseases of the optic nerve and retina including age-related macular degeneration and diabetic retinopathy lead to permanent and irreversible blindness. Currently, retinal diseases can only be treated by invasive, painful and risky injections directly into the back of the eye. Developing less invasive, effective and patient-friendly therapies was a priority for this project. Building on previous work to develop novel eyedrop technologies, mathematical modelling was incorporated to develop more efficient approaches to improve dosing strategies.

In the experimental part of the project, the team demonstrated how the cell penetrating peptide (CPP) allows topical ranibizumab (RBZ) to penetrate the cornea. Mathematical modelling developed by Centre Fellow Dr Paul Roberts is being used to further explain the mechanistic underpinnings of the experimental data, which is hoped will lead to improved dosing regimens in the human eye.

Exploring the metabolic fingerprint of pituitary tumours



Tumours in the pituitary gland usually present with debilitating headaches, visual deterioration, and dysregulation of the normal pituitary hormone secretion. Treatment options include surgery, radiotherapy or drugs, which are frequently unsuccessful. Developing our understanding of pituitary tumourgenesis and how metabolic pathways are altered was a priority for this project. The ultimate aim that improved prognostic biomarkers and of molecular therapeutic targets will positively impact on patient outcomes. Centre Fellow Dr Leandro Junges, has worked with the investigators, using NMR spectroscopy to quantify metabolite concentrations in different classes of pituitary tumours. Quantitative methods were used to identify metabolic differences between these tumours, focussing on metabolite concentration, tumour invasiveness and proliferation potential in the most common types of pituitary tumours. This quantification will permit better understanding of the metabolic pathways involved in tumour development and progression, and so support the development of more effective treatment strategies.

Using Artificial Intelligence Based Application to Support Leprosy Ulcer Care and Treatment by Community Health Workers

In countries such as India, Nepal and Nigeria, leprosy remains endemic, and accessing local healthcare is often challenging for people. Community health workers are frequently the primary care providers and often lack the specialised knowledge to effectively manage leprosy ulcers. Developing a mobile application to provide evidence-based advice on caring and treating ulcers was a priority for this project.
Facilitated by Business Engagement, the project team worked with Birmingham-based tech company B13 Technology to develop a protype of the App. Using mobile phone pictures of patient ulcers, Centre Fellow Dr Alexander Zhigalov used image analysis and machine learning algorithms to develop a classifier of ulcer severity to incorporate within the App. The Ulcer Care App passed the initial prototyping stage and is now being tested by several healthcare workers in Nepal coordinated by Dr Onaedo Ilozumba. This App not only provides a treatment plan based on the classifier of ulcer severity, but also collects vital demographic information, and so enable further personalisation of treatment in the next iteration.

Switching off Efflux: a multi-disciplinary approach to understanding and overcoming antimicrobial resistance

Antimicrobial resistance (AMR) is an urgent threat to global health and discovering new antibiotics has proved extremely challenging. Many antibiotics function by accumulating within bacterial cells and disrupting intracellular processes, and one key source of bacterial resistance comes from efflux pump proteins. These transmembrane proteins expel antibiotics from the intracellular environment and reduce their efficacy. Developing methods for circumventing these protection mechanisms is an active area of research, and mathematical models to advance our understanding of these mechanisms was a priority for this project. Centre Fellow, Dr Danny Galvis has focussed on the relationship between cellular permeability and rate of efflux at different stages in the growth cycle of bacterial populations. This built on previous work showing that membrane permeability changes drastically throughout the growth cycle and so knockout of prominent efflux pumps may be more effective at some points in the growth cycle. They developed mathematical model of Gram-Negative bacteria incorporates known biology and has been shown to replicate key findings. The model predicts that the kinetics of pump protein efflux play a critical role in determining the accumulation of drugs.

View from a Centre Fellow, Dr Daniel Galvis

I have been involved in many seedcorn projects during my five years as a Centre Fellow, first at the University of Exeter and now here at the University of Birmingham. Each project has been a distinct journey, with unique problems to tackle and many opportunities to learn. Each project has had a similar framing: a six-month project in a foreign biomedical question, with new collaborators, propelled by the intensive planning retreat, with the goal of producing a foothold for the development of ambitious research. Yet, no two projects have ever been alike. I have worked on biomedical questions spanning cellular ageing, propulsion in archaea, diabetes, stress after major surgery, the intersection of epilepsy and other mental health conditions, and antimicrobial resistance. And I have employed quantitative techniques spanning mathematical modelling and analysis, optimisation, molecular dynamics simulation, network science, and data science. I have at once taken on the role of a teacher and also of an eager student. And I have become adept (or journeyman at least) in developing a shared language with biologists and clinicians across diverse fields.

Currently, I am working with Sara Jabbari and Jessica Blair on a project to better understand how bacteria react to antibiotics at different stages in the population growth cycle. This question is critical for optimising drug efficacy against bacteria and for mitigating the effects of microbial resistance to antibiotics. We began with what seemed like a simple question, to produce a model that accounts for the permeability of bacterial cells to a drug (influx) and the removal of drug by the bacteria (efflux) across the growth cycle. However, through many discussions, attempts to generate suitable mathematical models, and poring over the data, we have uncovered myriad questions still to be answered. Over the six months, we have developed a model and started writing up a manuscript. But more importantly, we have identified critical unasked questions and formed a new collaboration with great potential.

Ultimately, the success of these seedcorn projects comes down to the enthusiasm of people working on them. For the Fellows, it requires curiosity, a desire try new things, and a willingness to spend a great deal of time out of one's depth. For the PIs, it requires an open mind and the patience to answer many questions sometimes many times. I have thoroughly enjoyed working on these projects, and I have seen first-hand the benefits they bring to both Fellows and PIs alike.

Work with SMQB on a seedcorn project

"This opportunity is open to academic or clinical researchers across the University of Birmingham and the associated hospital trusts. We are looking for teams of interdisciplinary researchers who have a hypothesis and initial data but need the input and quantitative skills provided by our SMQB Centre Fellows to drive forward the project. If you have an idea that you would like to discuss, please get in touch."

Dr Rebecca Ward, Centre Manager

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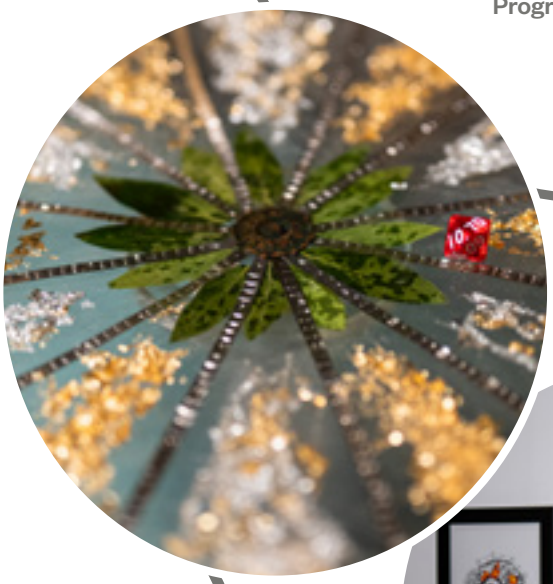
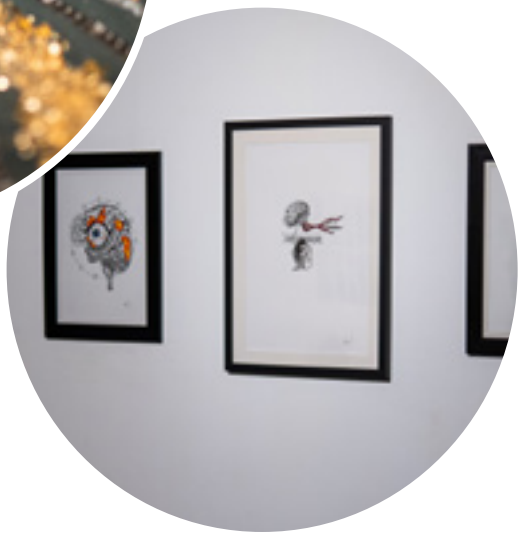
Lore + (Dis)order Exhibition

After the disruption of the pandemic, we were thrilled to be able to finally showcase the creative outputs of our Artist in Residence programme in a gallery setting within Digbeth's cultural quarter in September 2022. Our sciart exhibition 'Lore + (Dis)order' brought together the work of eight artists who have collaborated with SMQB researchers and interdisciplinary collaborators between 2020-2022. Many of the artworks were created by lived experience artists and/or in consultation with patient groups. We had a fantastic launch night with lots of public visitors, as well as a series of linked online events and in-person workshops.

"It was so encouraging to see how the exhibition lifted barriers by creating an environment where conversations about health and research, as well as the role of science and art within society could take place quite naturally. All around the gallery, I heard questions and stories being exchanged in a way that felt very different, equitable and inspiring."

– Dr Caroline Gillett, Artist in Residence Programme Manager.

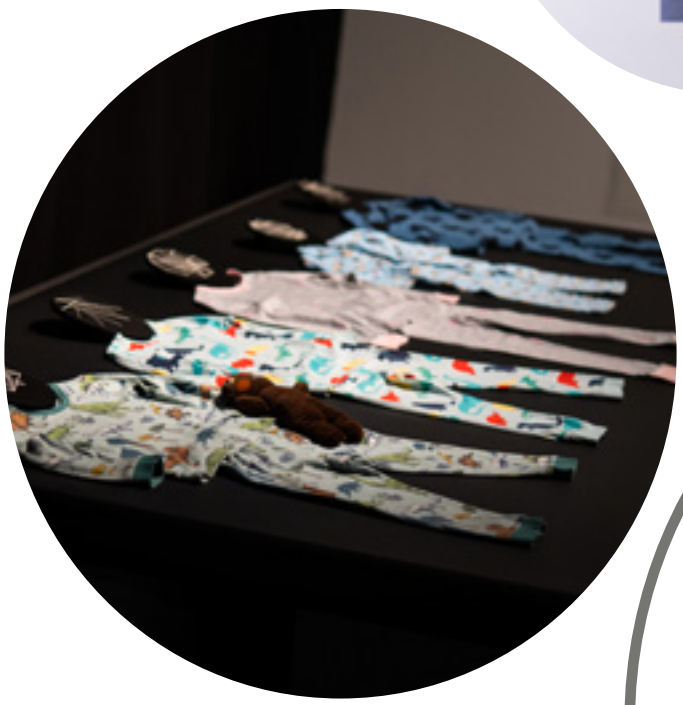




"It was a truly inspirational evening which highlighted the power of art to explain complex scientific concepts to the public. It reinforced to me how fortunate we are to work in a broad-based university with an integrated campus which facilitates interactions between different disciplines."

– Professor David Adams, Pro-Vice-Chancellor and Head of College of Medical and Dental Sciences.

Images credited to Hayley Salter



"The artist in residency scheme has opened the eyes of our researchers as to what is possible when you bring the perspectives of people with different backgrounds together to focus on a key challenge. The artworks we present here are one legacy of these projects, and their impact on the evolution of the research being undertaken is another."

– Professor John Terry, Director of the SMQB

Research Highlights

Since SMQB was established in October 2019, our researchers have collectively applied for over £20M and been awarded £6.5M in research funding. For 2022, SMQB applied for £5.6M and was awarded £2.5M in funding. We have published 28 papers over the year, and we are proud to share some of this year's research highlights.

Dr Debbie Marsden,
SMQB Senior Research Manager

Understanding how sleep is impacted by neurological and neurodevelopmental conditions using personalised brain networks from EEG data

Poor sleep has a negative impact on children's quality of life and is detrimental to child development. Sleep disturbances are commonly reported in children with neurological and neurodevelopmental disorders (NNDs) including epilepsy, autism spectrum disorder (ASD), and attention-deficit/hyperactivity disorder (ADHD). However, the relationship between NNDs and sleep is still poorly understood, especially when such conditions coexist. Throughout 2022 Dr Leandro Junges has been funded by the Waterloo Foundation to explore functional brain networks calculated from clinical EEG (a measure of the brain's electrical activity). His work explores features of these networks in wakefulness and sleep, and how they are affected by the interplay of epilepsy and autism/ADHD symptomatology. He has also explored the contributing factors of plasticity and brain development by estimating the robustness of these networks to reconfiguration. Improving our understanding of the relationship between brain networks and NDDs in wake and sleep can underpin the development of new computational tools to support management of sleep quality in children with brain conditions.

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Information and Communication Technologies (ICT) Public Engagement Champion

In March it was announced that Professor John Terry had been named an EPSRC ICT Public Engagement Champion. Working with Dr Caroline Gillett, the £167K award will deliver a programme of activity over two years to equip a diverse group of young people with digital skills confidence and to inspire a greater interest in the real-world application of ICT for creative problem solving around health-related societal challenges.

Working with the School of Computer Sciences, it will also aim to increase the public engagement skills and experience of ICT researchers involved in delivery of the project.

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Perturbations in Epilepsy Workshop

In April Dr Isabella Marinelli and Dr Aravind Kumar Kamaraj organised Perturbations in Epilepsy, our first in person workshop following the restrictions of the pandemic. The two-day event focused on the physiological factors known to affect the likelihood of seizures in epilepsy including sleep, hormones, and stress and examined our mechanistic understanding of the interplay between brain networks, seizure likelihood and these physiological triggers. Importantly we were grateful for the insight from two people with lived experience of epilepsy who shared their experiences of seizure triggers and their hopes for what research could do to improve their quality of life.

World-leading researchers presented keynote talks, including Dr Victor Ferastraoaru (Montefiore Medical Center, Albert Einstein College of Medicine, USA), Dr Clare Anderson (Monash University, Australia), and Professor Shakila Thangaratinam (University of Birmingham). On the second day there was a facilitated discussion session where all participants shared and discussed innovative ideas to take the field forward. This series will continue in 2023 with a second event to explore how we can predict or prevent seizures through long-term monitoring of seizure triggers using smart devices.

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Isabella Marinelli presents at the International Conference for Technology and Analysis of Seizures (ICTALS)

The ICTALS conference (International Conference on Technology and Analysis for Seizures) brings together scientists and clinicians using quantitative methods to analyse seizures and better understand and treat the disorder.

At the 2022 conference in Bern Switzerland, SMQB Research Fellow Dr Isabella Marinelli spoke about modelling the impact of candidate mechanisms underlying common circadian distributions of epileptiform discharges and her work to investigate the physiological drivers that underline rhythms of epileptiform activity. Isabella secured a London Mathematical Society Travel Grant to present at the conference.

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Cross-campus networking in neuroscience

CHBH
CENTRE FOR HUMAN BRAIN HEALTH

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Centre Fellows Dr Leandro Junges and Dr Alexander Zhigalov organised an interdisciplinary networking event in October between SMQB and colleagues in the Centre for Human Brain Health (CHBH) and the Institute for Mental Health (IMH) to discuss opportunities for research in the field of neuroscience. Introductions from the three directors Professors John Terry, Andrew Bagshaw (CHBH) and Matthew Broome (IMH) set the scene for a series of flash talks from a selection of researchers at each centre with different and complementary backgrounds spanning mathematics, psychology, physics and computer science discussing their broad range of research interests in the field of neuroscience. The successful event stimulated synergy between teams, identified common research interests and opportunities for future multidisciplinary collaborations. The round-table discussions developed actionable strategies around topics like funding opportunities, including the SMQB Research Incubator and ongoing communication across research teams.

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Developing technologies that enable diagnosis and management of neurological conditions in the community (N-CODE)

In October we launched N-CODE, the £1.2M EPSRC-funded Network+ led by SMQB director Professor John Terry, in collaboration with co-Is from Birmingham (Prof Alexandra Sinclair, IMSR), University of Warwick, University of Plymouth and Imperial College London. This new initiative by EPSRC to help form new interdisciplinary research communities will see SMQB and N-CODE support the development of technologies that shift the emphasis of diagnosis and management of neurological conditions from hospital to the community and help set a research agenda and fund novel feasibility studies.

We secured £1.7M in matched funding from the network partners from across academia, industry, hospitals, private healthcare, charities, social enterprises and policy makers. Together, we will work collaboratively though a variety of funded activities to develop digital solutions for the many challenges faced by people with neurological conditions and those responsible for their care. The Network launched with an online networking event and will be facilitating events in areas of emerging interest and funding proof of concept studies through sandpits, study groups and the Research Incubator.

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The UNiTY Trial to evaluate the clinical and cost effectiveness of IVF versus IUI for unexplained infertility

Assistant Professor Meurig Gallagher has been funded though the NIHR Heath Technology Assessment (HTA) Programme as the Healthcare Sciences sub-study lead for the £1.8M UNexplained InfertiliTY treatment Trial (The UNiTY Trial) which commenced in October. The randomised controlled trial, led by Professor Jackson Kirkman-Brown (IMSR), will compare the outcomes of one cycle of in vitro fertilisation (IVF) with three cycles of intrauterine insemination (IUI), a less invasive and cheaper alternative treatment for couples with unexplained infertility. Diagnosis of the male partner is a key factor in assessing suitability for IUI. Meurig will lead the work to investigate the variations in how male factors are assessed across the clinical partners involved in the trial, both at diagnostic and the therapeutic stages of treatment. This will comprise the creation and storing of videos of the male sperm sample at each site for Quality Assurance. These videos will be analysed with Meurig's FAST software to enable further evaluation of male factor markers in microscopy such as flagellar beat which may be prognostic indicators for treatment.

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Advanced Brain Stimulation approaches for treating depression and anxiety

In December, Centre Fellow Dr Alexander Zhigalov organised and hosted a webinar on Advanced Brain Stimulation approaches for treating depression and anxiety. Depression and anxiety are among the most common mental health problems worldwide. The existing drug-based therapies often have negative side effects and are ineffective in around 30% of cases. Non-invasive brain stimulation is a promising alternative to pharmacological treatment. The webinar bought together experts across the field of brain stimulation who discussed their latest work to better understand new and emerging approaches for treating depression and anxiety.

Alexander was also part of a team led by Dr Isabel Morales-Munoz (Centre for Human Brain Health) who were recipients of a Wellcome Mental Health Data Prize for their work in the prevention of persistent high levels of depression across adolescence and young adulthood. The team will build a digital tool using machine learning models that will reliably predict combinations of active ingredients that are associated with a lower risk of depression.

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'Shape-shifting' implanted medical device to provide blood pressure monitoring outside of hospital

Dr Atif Shahzad, lead for SMQB's Medical Sensors and Wearable Technology research theme is part of a European Union consortium grant awarded €4.4million in December for the SMARTSHAPE project to focus on developing an implantable medical device for continuous blood pressure monitoring. Working with Professor Liam Grover, Heath Technologies Institute and colleagues at the Smart Sensors Lab at the University of Galway where he holds a fractional appointment, Atif will work to formulate an innovative biomaterial and a microsensor that can be curled up, introduced into the body through a minimally invasive procedure, and 'opened up' when placed at body temperature to take a predefined shape to provide blood pressure monitoring.

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Publications spotlight

Differential routing and disposition of the long-chain saturated fatty acid palmitate in rodent vs human beta-cells

Rodent and human β-cells are differentially susceptible to the lipotoxic effects of long-chain saturated fatty acids but the factors accounting for this are unclear. Dr Patricia Thomas and collaborators at the University of Exeter and Newcastle University studied the intracellular disposition of the fatty acid palmitate in human vs rodent β-cells and presented data that reveals new insights into the factors regulating β-cell lipotoxicity.

In rodent β-cells, palmitate accumulates in the Golgi apparatus at early time points whereas, in human cells, it is routed preferentially into lipid droplets. This may account for the differential sensitivity of rodent vs human β-cells to "lipotoxicity" since manoeuvres leading to the incorporation of palmitate into lipid droplets is associated with the maintenance of cell viability in both cell types.

This paper was published in Nutrition & Diabetes, DOI: 10.1038/s41387-022-00199-y

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Mathematical models of retinitis pigmentosa: The trophic factor hypothesis

Retinitis pigmentosa (RP) is the term used to denote a group of inherited retinal-degenerative conditions that cause progressive sight loss. Individuals with this condition lose their light-sensitive photoreceptor cells, known as rods and cones, over a period of years to decades; degeneration starting in the retinal periphery, and spreading peripherally and centrally over time. RP is a rod-cone dystrophy, meaning that rod health and function are affected earlier and more severely than that of cones. Rods degenerate due to an underlying mutation, whereas the reasons for cone degeneration are unknown. A number of mechanisms have been proposed to explain secondary cone loss and the spatio-temporal patterns of retinal degeneration in RP.

One of the most promising is the trophic factor hypothesis, which suggests that rods produce a factor necessary for cone survival, such that, when rods degenerate, cone degeneration follows.

In this paper, Centre Fellow Dr Paul Roberts formulated and analysed mathematical models of human RP under the trophic factor hypothesis. These models were constructed as systems of reaction-diffusion partial differential equations in one spatial dimension and were solved and analysed using a combination of numerical and analytical methods. The models predict the conditions under which cones will degenerate following the loss of a patch of rods from the retina, the critical trophic factor treatment rate required to prevent cone degeneration following rod loss and the spatio-temporal patterns of cone loss that would result if the trophic factor mechanism alone were responsible for retinal degeneration.

The paper was published in the Journal of Theoretical Biology, DOI: 10.1016/j.jtbi.2021.110938

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Publications spotlight

Non-invasive imaging could replace electrodes in epilepsy surgery planning

In February, Centre Fellow Dr Daniel Galvis, Dr Wessel Woldman (Epilepsy Research UK Emerging Leader Fellow) and Professor John Terry published results from a study with colleagues from the University of Melbourne in Australia. Data demonstrated that magnetoencephalographic (MEG) imaging can be used to produce a dynamic map of the whole brain during a seizure and this non-invasive technique has shown potential in helping clinicians plan epilepsy surgery. Surgery can be an effective treatment for the one third of people with epilepsy who are resistant to medication, but it is under-used due to the challenge of accurately identifying the specific brain regions involved in seizures.

At present these regions are most commonly identified by implanting electrodes on the surface of the brain and monitoring brain activity. This is highly invasive not to mention expensive and is limited to monitoring only a small number of networks underlying the implanted electrodes. In this proof-of-concept study, the researchers worked with 12 people with epilepsy to reveal the sources of their seizures using non-invasive MEG imaging. From these data a computer model of the whole brain was constructed, which enable virtual surgeries to be performed. The model, called virtual intracranial EEG (ViEEG), provides a 'real time' picture of brain areas involved in generating seizures. The team was able to show that, using their technique, they could identify distinct characteristics such as hyper-synchronised rhythms, clear transitions from background 'normal' activity to the seizure state, and patterns caused by the seizure spreading through the brain.

The paper was published in Nature Communications DOI: 10.1038/s41467-022-28640-x

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New insight in patient response to surgical disruption in life-saving hormones

Major surgery and critical illness produce a potentially life-threatening systemic inflammatory response, which is counterbalanced by changes in adrenocorticotrophic hormone (ACTH) and cortisol. The body's stress response system, known as the hypothalamic-pituitary-adrenal (HPA) axis, controls the production of these hormones as a vital part of patients' response to surgery, but research by Dr Daniel Galvis, Dr Eder Zavala and collaborators at the University of Bristol have found that there is no simple graded HPA response to cardiac surgery.

Their research shows cardiac surgery causes major dynamic changes in concentration of ACTH and cortisol, as well as their pattern of secretion. They developed a mathematical model of HPA axis activity that predicts the physiological mechanisms responsible for different patterns of cortisol secretion. It was found that the HPA axis response can be classified into one of three dynamic phenotypes: single-pulse, two-pulse and multiple-pulse dynamics which may reflect individual differences in how people respond to this type of stressor. These patterns may reflect underlying physiological

differences in each person's HPA axis, but inflammation caused by surgery also appears to be contributing to changes in at least one of these patterns, the single pulse phenotype, suggesting that patients showing this dynamic could be experiencing the greatest inflammatory response to cardiac surgery. The different patterns of HPA axis response could reflect different underlying physiological changes in adrenal sensitivity, cortisol production and turnover.

"We now need further studies to investigate whether and how these patterns are correlated with clinical outcomes. This will be critical in establishing whether we can use the patterns to identify and classify post-surgical risk. Our research also shows the existing model used for diagnosis and prognosis after major surgery and critical illness may not be giving us the full picture. Improved diagnostics based on individual responses could lead to a better, personalised diagnosis and targeted interventions."

Co-author Dr Daniel Galvis, SMQB Centre Fellow.

The paper was published in the Journal of The Royal Society Interface, DOI: 10.1098/rsif.2021.0925

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We gratefully acknowledge the funding from the following organisations who support the work of the SMQB.

Training and Development

PhD Students

PhD training and development of early-career academic staff are key activities for SMQB. In addition to our contribution to education through the new MSc Biomedical Innovation launching September 2023, we offer a high-quality interdisciplinary research opportunities for postgraduate research students, summer students and skills training for Early Career Researchers. The MSc will provide an innovation-inspired education for enhanced employability in the MedTech sector.

Current SMQB PhD students are conducting research which bridges mathematical, computational, experimental and healthcare research:

Sophie Mason is a multidisciplinary PhD student funded through the School of Mathematics Alumni Scholarship scheme under the co-supervision of Professor John Terry, Dr Leandro Junges and Dr Andrew Bagshaw (Centre for Human Brain Health). Her current research focuses on studying fMRI and EEG data to understand how different human chronotypes manifest in different functional networks. Her PhD thesis title is 'Dynamic Graph Theoretic Markers of Human Chronotype.

Rosie Evans is working under the supervision of Dr Meurig Gallagher. Her research is focused on endocrinology and mathematical modelling, with a particular interest in parameter identifiability and model reduction through matched asymptotic analysis.

Professor John Terry, Dr Leandro Junges and Professor Viktor Jirsa jointly supervise Gwen Harrington. Her research is focused on dynamic network models to better understand why some surgeries for epilepsy are successful, whereas other fail.

Peter Kissack joined SMQB in September 2022 and is working under the supervision of Dr Wessel Woldman and Dr Samuel Johnson (School of Mathematics). His work focuses on the mathematical modelling for epileptic seizure prediction.

Peter Kissack

Rosie Evans

"SMQB has focused on my development, both in terms of knowledge and communication skills, through help with successful applications for multiple summer school programs, in the fields of sleep and neuroscience."

Sophie Mason, final year PhD student.

"I have been looking into how brain plasticity after surgery can impact surgical results. This is an interdisciplinary project that involves mathematics, computer science and neuroscience. I have had the opportunity to take additional courses within the department of mathematics as well as training to use high performance computing."

Gwen Harrington, PhD Student

MSc Biomedical Innovation

Our MSc Biomedical Innovation programme brings together talented students from a variety of backgrounds to focus on innovating new technologies that advance human health. Embedded within an exciting ecosystem spanning academia, hospitals and the medical technology (MedTech) industry, we develop innovators and entrepreneurs who have a real impact on society.

This flagship programme launches in September 2023 with a planned cohort size of 6-12 students. Working in teams of 3 or 4, students will follow a structured programme that enables them to identify unmet biomedical or clinical needs and to invent novel solutions to those needs. Working in close collaboration with industry partners, including venture capital, the programme will build a natural pipeline of early-stage ventures that will drive reputation and impact for the University.

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Engagement with Industry

A strategic priority for the SMQB is to generate knowledge exchange in partnership with industry. To enable this, we have been involved in a range of activities including the running of a taster course in Biomedical Innovation, participation in the Innovate UK ICURe programme, involving industry in workshops and meetings, as well as large-scale joint research projects funded by the NIHR and Research England.

Investing in early-stage partnerships and training the next generation of researchers with the tools to develop coherent, sustainable, and impactful partnerships are key to deliver on this strategy. Here we present two case studies:

BioInnovation Taster Course

In advance of launching the new MSc in Biomedical Innovation in Autumn 2023, Dr Atif Shahzad worked with colleagues from the Health Technology Institute (HTI), to deliver a 6-week crash-course in Biomedical Innovation during summer 2022. Designed to provide basic skills in needs-led innovation in healthcare through experiential learning, 22 participants received training on clinical need discovery, patient journey mapping, design thinking and ideation, stakeholder engagement, and fundamentals of health technology business development. This helped establish connections with clinical, academic and external key stakeholders and laid the foundation for delivering such training in Birmingham that will be instrumental in the success for the new MSc programme.

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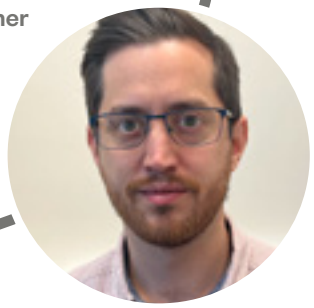
Understanding the commercial opportunities for products that aim to improve male fertility treatment

Testing market-fit of ideas emerging from research is an important part of the translational pathway. Dr Meurig Gallagher, Assistant Professor, was awarded a prestigious Innovate UK Innovation-to-Commercialisation of University Research (ICURe) award to understand the commercial opportunity for products that aim to improve male fertility treatment. Providing training in developing value propositions and business models, the ICURe scheme enables teams of university researchers to conduct conversations with stakeholders globally to further the commercial development of research ideas.

"ICURe gave me the opportunity to explore the commercially promising market and see where it sits, whether people think there is a genuine need and how to take that forward."

Dr Meurig Gallagher



Together with Professors Jackson Kirkman-Brown MBE (Centre for Human Reproductive Science) and Dave Smith (School of Mathematics), Meurig has developed software and a microfluidic device aiming to improve fertility outcomes by optimising how male fertility is measured.

The software (called FAST) tracks sperm tails and analyses the efficiency of their energy and metabolism, while a microchannel device extracts the strongest-swimming sperm from a sample via a microfluidic chamber. From Dec 2021 to March 2022 Meurig participated in over 80 international meetings with industrial leaders in fertility and with fertility clinics. This generated insights into the evidence and validation needed to bring the devices and software to the commercial market.

Following ICURe Meurig has boosted his industrial engagement further, engaging with companies Hamilton Thorne, Cooper Surgical, and Vitrolife to explore next stages. As a result, the team are exploring a number of further licencing and collaborative research opportunities with these internationally industry leaders.

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SMQB has established relationships with a diverse range of companies including Neuronostics, Garmin, Design Works, U-RHYTHM, SymPhysis, AuirGen and Merck.

Engagement with Industry

NIHR BioEP: From prototype to clinical evaluation

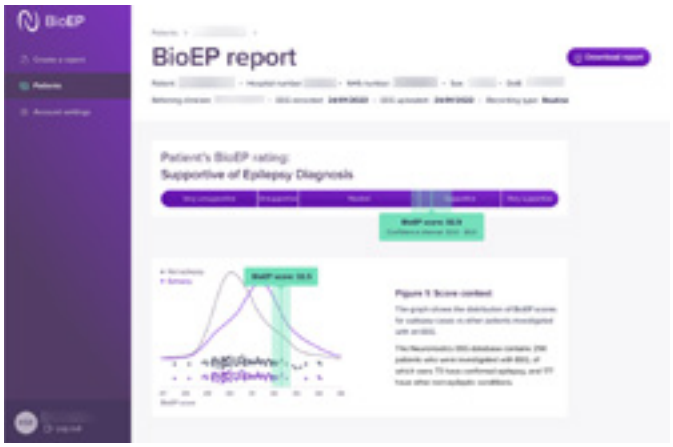
Funded by the National Institute for Health and Care Research (NIHR) Artificial Intelligence (AI) in Heath and Care award, researchers from SMQB worked with industry and clinical collaborators to deliver an NIHR Portfolio Study over 2021-2022. Working with multi-award-winning industry partner Neuronostics (co-founded by Professor John Terry and Dr Wessel Woldman), SMQB research fellow Dr Luke Tait, was part of the team validating and refining a set of candidate biomarkers for seizure susceptibility – called BioEP.

The study aimed to test the performance of these candidate biomarkers in a large-scale, multi-site retrospective study and assess their potential for decreasing diagnostic delay (which is often more than a year) and potentially misdiagnosis (which might be as high as 30% in non-specialist settings). In total, we secured 809 EEG recordings from 561 subjects (384 with epilepsy) from across eight different NHS sites.

Luke's work focused on an interesting subset of the cohort (N=250), for whom their first EEG was definitively clinically non-informative. By this we mean that the overall diagnostic yield was effectively equal to 0. In contrast, the application of the BioEP algorithm, applied to apparently normal parts of these EEG recordings, achieved a balanced accuracy of 67%. This is only a small decrease from the previously published results that this study built on, where an overall accuracy of 72% was achieved.

Critically, the NIHR Portfolio study has provided additional confidence in the BioEP algorithm and increased its applicability.

The next steps for this collaboration will be a prospective study that aims to assess its potential added value in a real-world clinical context.



The Neuronostics Platform which delivers a clinical report presenting the outcome of the BioEP algorithms.

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Development of a new EEG headset for home monitoring of epilepsy

Application for Research England Building on previous support from Innovate UK and the NIHR, a Research England QR Enhancing Research and Knowledge Exchange Funding Programme award of £40,000 enabled Dr Atif Shahzad and Professor Liam Grover (Healthcare Technologies Institute) to work with Neuronostics and its Lived Experience Group of 25 people with epilepsy on the development of an affordable and user-friendly EEG (electroencephalography) headset. Over the course of 3 months from January, the team developed a second iteration of the headset, focussing on evolving the electrodes which had been highlighted by users as uncomfortable and prone to leave marking on the scalp and forehead. Feedback from the user testing informed updates to design requirements and specifications and has led to subsequent grant applications to Innovate UK Biomedical Catalyst and the NIHR i4i Product Development Award to fully develop the system.

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Development of smart sensors with SymPhysis Medical

SymPhysis Medical is a start-up company based in Galway, linked to experts internationally. They develop innovative technologies that treat a range of chronic diseases, putting the patient experience at the forefront of design solutions to improve quality of life. Working with SymPhysis, Dr Atif Shahzad is developing a novel smart sensor to integrate in Symphysis Medical's Pleural Drainage device, called release. This smart drainage system will relieve pain during the drainage of malignant pleural effusions and provide independence and mobility to palliative care patients. These groundbreaking new medical technology products are expected to take a huge leap forward in prevention and patient independence.

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Implantable wireless sensing device for heart failure management

AuriGen Medical is an Irish electrophysiology and structural heart company dedicated to transforming the management of longstanding persistent atrial fibrillation by developing the first cardiac implant to treat both the stroke and arrhythmia risk associated with this devastating condition. Dr Atif Shahzad had an established collaboration with Aurigen and has co-developed an implantable wireless sensing device for heart failure management. This technology will reduce a significant burden on healthcare systems by reducing re-hospitalization in congestive heart failure. Combined with AuriGen Medical's Zenith device for cardiac arrhythmia treatment, this novel technology can prevent progression of heart disease by active monitoring in vulnerable patients.

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Continuous measurement of steroid hormone levels using U-RHYTHM

U-RHYTHM is a portable device designed for high-frequency, minimally-invasive collection of subcutaneous interstitial fluid in daily life, including during sleep. Combined with novel ultra-sensitive assays, U-RHYTHM is the first technology to enable continuous measurement of steroid hormone levels in ambulatory humans. Assistant Professor Eder Zavala's research involves the mathematical modelling and analysis of these daily hormonal profiles to detect computational biomarkers of abnormality. This has allowed the characterisation of circadian and ultradian hormone rhythms in health and disease, and the development of computer algorithms to revolutionise the way that endocrine disorders are diagnosed and treated.

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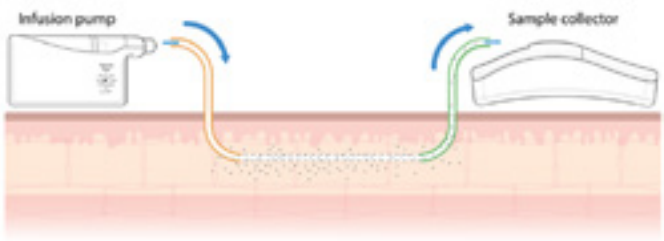

Into the Future

We will continue to develop our pipeline of activities, both focusing on training and development of students and researchers, as well as direct collaboration with SMEs and larger companies. The launch of our MSc in Biomedical Innovation in Autumn 2023 is an exciting opportunity to contribute to the training of the next generation of innovators and entrepreneurs.

The opening of the Precision Health Technology Accelerator on the Birmingham Health Innovation Campus provides a fantastic opportunity for the SMQB to help shape the creation of an ecosystem where academia, healthcare, industry and other key stakeholders co-create knowledge for societal benefit and impact.

Community Engagement

At the SMQB we believe involvement and engagement with public and patient groups is highly valuable, as these interactions can often help improve the quality and direction of research itself. From helping us to ask the right questions, through to improving the way we communicate and share our findings so that the maximum number of people can benefit from science discovery.

SMQB AMIGO

AMIGO - our Advisory Members Involvement, Guidance and Outreach group is a group of public volunteers who provide advice on how SMQB can best communicate with, engage and involve the wider public and patient groups in what we do. Our AMIGOs are a valued network of allies and the group consists of a diverse mix of members of the public and people living with different health conditions related to SMQB research areas.
If you would like to become an AMIGO please contact us at smqb@contacts.bham.ac.uk

Allies in Advocacy workshop

Supported by Research England QR funding, Dr Caroline Gillett and Dr Eder Zavala organised a co-creation workshop called 'Allies in Advocacy' in February. This two-day residential brought patients and members of the public from our AMIGO group together with mathematicians and computer scientists from across the University of Birmingham. Together all 40 diverse attendees undertook joint training on science communication and public engagement, helping mixed groups to subsequently work together to co-write, co-direct and even co-star in 'DIY' videos aimed at explaining complex terms such as 'mechanistic modelling' and 'network analysis' to a general audience with no specialist background.

These videos employed a storytelling approach which often made use of everyday analogies and lived experience perspectives to provide compelling testimonials for how and why these techniques, and the research they enable, make a difference in people's lives. This collaborative event exercised attendees creative talents to produce tangible resources which anyone can now use to improve other's understanding of common mathematical and computational approaches used in health research. Find out more and watch the videos yourself

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Image: www.thinkbigpicture.co.uk/

Purple Day

At SMQB we also passionate about working with other partners to raise awareness of the health conditions we study. One of our major research areas is in epilepsy and so we organised a campus event to mark Purple Day, the International Day of Epilepsy Awareness in March. Over 40 staff, students and member of the local community joined us for an afternoon of seizure first-aid training and short talks from lived experience advocates, charities, nurse specialists and of course SMQB researchers and other science collaborators. Even Old Joe got involved with purple illumination for the evening!

CoCoMad festival

We also took part at CoCoMad festival in Cotteridge Park in July, engaging hundreds of children and their families through our activity 'Machine Learning with Tigers!'. Dr Isabella Marinelli, Dr Paul Roberts and Dr Yingjing Feng proved it is never too early to engage young people with computational logic using a card sorting game which explored concepts like data quality, false positive and false negatives. Even adults joined in the fun to learn the 101 basics of machine learning!

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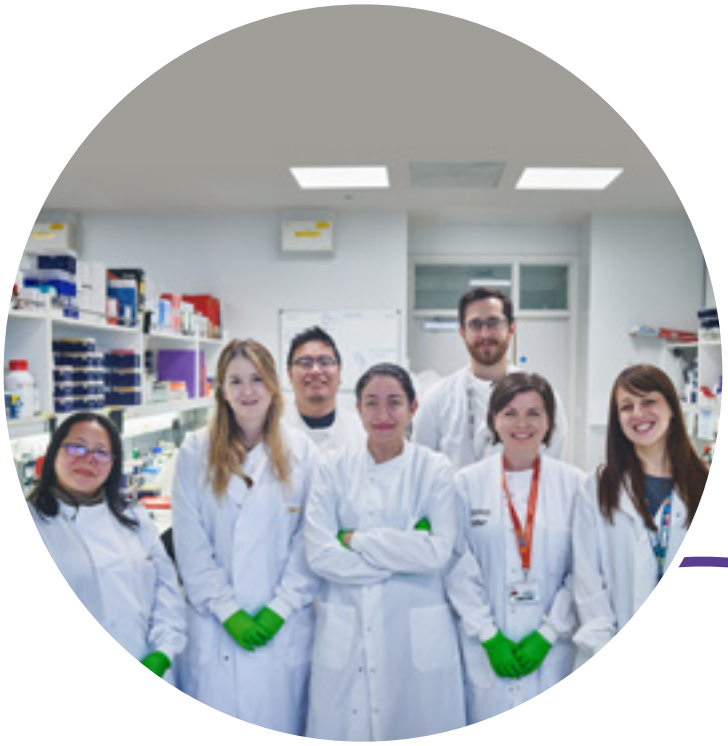

Visit from Diabetes UK

In November, we supported a special Diabetes Awareness Month visit from representatives of the charity Diabetes UK. Dr Patricia Thomas took visitors on a tour the labs and high-tech microscopy suites, answering questions and giving people the chance to get up close and personal with cutting-edge research in the field of diabetes.

"We've received some amazing comments from our guests who were all blown away to see what their support makes possible and grateful to know people like you are working so hard to make the future brighter for people living with diabetes."

– Faye Riley, Research Communications Manager at Diabetes UK

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