



ANNUAL REPORT

2024

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Letter from our Director

Dear Colleagues and Partners,

Our Kavli Institute continues to make significant strides in our mission to bring the physical sciences into the cell. This year we welcomed another exceptional statutory professor, Nynke Dekker, who is leading cutting edge research programmes in Biophysics.

This last year has also seen us launch our inaugural K.A.R.D projects, with seed funding to support bold, innovative ideas from young postdoctoral researchers and students through proof-of-concept funding.



In December 2023, we were privileged to host our second Kavli Lecturer, Dame Kate Bingham, who delivered an engaging and informative presentation on strategies for securing vaccines during the pandemic. This event further highlighted our commitment to impactful science communication.

We also had the pleasure of showcasing our work during the first visit of our Scientific Advisory Board. The feedback we received was invaluable, helping us to identify both our strengths and areas for improvement. Our early career fellows contributed to the visit and continue to shine, promoting our interdisciplinary connections which are becoming increasingly robust. This is evident in the growing number of interdisciplinary grant applications and publications featuring multiple Kavli authors across different departments.

Additionally, we were honoured to host Kavli Foundation President Dr. Cynthia Friend and Director of Life Sciences Dr. Amy Bernard. Their visit included a tour of the institute and presentations from our scientists. They provided us with valuable insights into the Kavli Foundation's research priorities, future funding strategies and took part in a lively question and answer session. We look forward to continuing to grow links with the Foundation as we progress our interdisciplinary research collaborations across traditional disciplines to tackle the challenges of our time.

I hope you enjoy reading this year's Annual Report, a compilation of contributions from our researchers.

With warm regards,

Professor Dame Carol V. Robinson Founding Director / Kavli INsD, Oxford

*Cover photo: Kavli Staff Annual Photoshoot 2024

A Year of Notable Milestones



KAVLI FOUNDATION SCHOLAR

We thank the Kavli Foundation, USA for the opportunity to host our first <u>Kavli Scholar</u>, Vladyslav Kim from Ukraine. Vladyslav will be studying for a D.Phil under the supervision of Kavli Oxford's Professor Vladyslav Vyazovskiy. He outlines his project below.

"I am looking to explore the relationship between subjective passage of time and sleep homeostasis in mice. Sleep is a

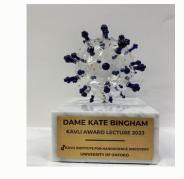
homeostatically regulated process, that is, the longer you stay awake, the greater the sleep pressure. Nevertheless, it remains inconclusive what constitutes the longer waking bout; I am interested in subjective experience of the bout, assuming that it is a subjective experience of time accumulating temporal information that consequently modulates sleep pressure. Sleep homeostasis is mainly reflected in the EEG changes throughout sleep, so mice will be implanted with EEG electrodes to record neural activity throughout the experiment. Time perception is estimated using an interval timing procedure with touchscreen chambers, which were used by my co-supervisor Dr Linus Milinski, a postdoctoral researcher at the Department of Physiology, Anatomy and Genetics, Oxford, specialising in the cortical effects on sleep-related brain activity and build-up of sleep pressure. I am honoured to be a member of Kavli Oxford's Professor Vladyslav Vyazovskiy's Group and am very grateful for the opportunity granted by the Kavli Foundation, making my studies possible!"



KAVLI OXFORD HOSTED 2ND LECTURE AWARD CELEBRATING DAME KATE BINGHAM

On 5th December 2023, Kavli Oxford held the <u>2nd Kavli Lecture Award</u>, honouring Dame Kate Bingham for her incredible work in science and innovation. A former Oxford biochemistry student and Managing Partner at SV Health Investors, Dame Kate has been instrumental in launching 24 new drugs and

leading the UK Vaccine Taskforce during the COVID-19 pandemic. In her talk, "Harnessing Scientific Innovation to Benefit Patients," she shared insights into the biotech industry's challenges and the importance of teamwork, especially for women in science. The event included a Q&A with students prior to her presentation. Following her lecture she was presented with a beautiful glass SARS-CoV-2 structure, crafted by the Department of Chemistry's Terri Adams. The evening concluded with a reception under the institute's colourful Christmas tree.



FIRST SEED-FUNDING AWARDED TO INNOVATIVE AND COLLABORATIVE INTERDISCIPLINARY PROJECTS PROPOSED BY EARLY CAREER RESEARCHERS

Since awarding <u>seed funding</u> to two innovative and collaborative interdisciplinary projects for early career researchers in November 2023, the Kavli Application for Research Development award (K.A.R.D) projects continue to progress.

L1CAM and Beyond: Targeting the Neuronal Extracellular Vesicle Code

"We have made significant progress in the isolation and characterization of extracellular vesicles (EVs) from both frozen postmortem brain tissue and iPSC-derived neuronal conditioned media. Using a combination of ultracentrifugation, filtration, and size exclusion chromatography, we have successfully isolated pure populations of EVs. The isolated EVs have been extensively characterized using various techniques, including western blotting, which confirmed the presence of several key EV marker proteins. Additionally, we employed NanoFCM, nanoparticle tracking analysis (NTA), and cryoelectron microscopy (cryoTEM) to assess canonical surface markers and EV morphology. Moreover, we have identified and screened multiple surface markers, including both common EV markers and brain cell-type-specific markers.

Our investigation into alpha-synuclein has revealed its presence within and on the surface of brain cell-derived EVs. We are currently analyzing its form (monomer vs. aggregate) using different antibodies across various neurodegenerative conditions. We have also completed two sets of native mass spectrometry on our EV samples, and data analysis is underway. A notable challenge we have encountered is the glycosylation of many proteins, which complicates our analyses; however, we are actively working to overcome this issue. Progress is ongoing, and we continue to refine our methods as we gather more data."

by Dr Suman Dutta (Clinical Neurosciences), Dr Corinne Lutomski (Chemistry) and Dr Stelios Chatzimichail (Physics)

In addition, building on their K.A.R.D Award, Suman Dutta was awarded the <u>ARUK</u> <u>Thames Valley Pilot Project award 2024</u> alongside Corinne and Stelios to further their study on 'Mapping protein pathways in brain EVs for targeted dementia therapies'.











Characterisation of Dopamine Neuron and Astrocyte Extracellular Vesicles in Parkinson's Disease

"Parkinson's disease (PD) is the second most common neurodegenerative disorder, mainly affecting individuals over 65, and is marked by the progressive loss of dopamine neurons. While the cause of this neuron loss is unclear, astrocytes are hypothesised to contribute to the progression of PD. Astrocytes and neurons communicate through their extracellular vesicles (EVs) and secretome, and this project set out to decipher the molecular messages which facilitate these communication pathways.

Using induced pluripotent stem cells (iPSCs), we successfully differentiated EV-generating dopaminergic neurons and astrocytes derived from both healthy and PD patient lines. Having achieved this, we then optimised our cell culture conditions for EV and secretome production, employing a cyclic dosing strategy which enabled us to collect without non-natural protein contamination whilst simultaneously maintaining the integrity of the differentiated cell lines. During this phase we also determined the cell counts required to obtain sufficient EVs for our proposed analyses. Having compared EV purification methods for our system, we ultimately opted for size exclusion chromatography (SEC) over ultracentrifugation (UC) due to the higher purity of resulting samples, and its ability to isolate secretome signalling proteins in parallel.

Following successful EV isolation from our iPSC-derived cell lines, they were validated via Western blot using the EV markers CD9, CD81, CD63 and syntenin. Interestingly, Western blot also revealed the additional proteins GM130, TSG101 and Cytochrome C in our samples, hinting at EV origins in the Golgi and endoplasmic reticulum. Nanoparticle tracking analysis (NTA) revealed comparable EV particle sizes across all samples in the range of 100 nm, however we expect that our pending cryo-electron microscopy (cryo-EM) experiments will provide further insights into PD-linked differences in EV size, structure, density of contents and membrane protein density. NTA did reveal that the PD-patient astrocytes release more EVs than their healthy counterparts, highlighting difference in molecular behaviour. Proteomics identified bulk protein differences in the EVs and secretome between the two cell lines, and between PD and healthy conditions, whilst nMS of the secretome hinted at localised differences between the systems. Direct analysis of EVs by nMS remains challenging, however we have obtained preliminary data to enable initial comparisons between PD and healthy cellular communication.

Turning our attention to communication between astrocytes and dopamine neurons, a lentivirus with mScarlet-tagged CD63 to study EV internalization between dopamine neurons and astrocytes has been developed and successfully expressed in iPSC-derived cells. The goal of this experiment is to study internalisation of EVs from one cell type to the other by treating the recipient cells with EV-enriched media from mScarlet-tagged CD63 containing donor cells."

by Dr Hannah Britt (Chemistry) and Akansha Mehta (Physiology, Anatomy and Genetics)

WELCOME AND DEPARTURES



Professor Nynke Dekker joined Kavli Oxford on 1st January 2024 as Professor of Biophysics in the Department of Physics and Fellow of St Peter's College. An awardee of the Dutch Spinoza Prize, Nynke is a leading figure in single-molecule biophysics. Her research focuses on DNA and RNA replication, using cutting-edge techniques to explore fundamental biological processes linked to disease development. Previously at the Kavli Institute of Nanoscience, TU Delft, Nynke's innovative work has advanced the understanding of eukaryotic DNA replication. Her appointment is celebrated as a major boost to both Kavli Oxford and the broader British biophysics community.



Associate Professor Angela Minassian joins the Kavli Oxford team. Angela is an honorary consultant as an infectious disease physician and leads a clinical malaria vaccine programme at the University of Oxford. Angela is also a member of Kavli Professor Simon Draper's Group and the OptiVivax Consortium. Angela brings strong links to clinical medicine and a passion for empowering research teams where malaria is endemic.



Professor Andrew Turberfield will be retiring and we wish him well in this new chapter and express our gratitude for his support and participation in events at Kavli Oxford since we opened our doors in April 2021.



Dr Charmaine Lang has been awarded the Oxford-GSK Institute of Molecular & Computational Medicine (IMCM) Fellowship, which she will take up in Autumn 2024. While we are delighted for Charmaine and proud of her achievement, we will miss seeing her in Kavli Oxford. We wish her all the best as she continues her career at the Nuffield Department of Medicine. Congratulations, Charmaine!

INAUGURAL MEETING OF KAVLI OXFORD SCIENTIFIC ADVISORY BOARD



On 21 November 2023, Kavli Oxford, Oxford held its first Scientific Advisory Board (SAB) meeting, chaired by Professor Wolfgang Baumeister Director of the Max Planck Institute of Biochemistry, Martinsried. Kavli Oxford Director Professor Dame Carol Robinson introduced the institute, followed by scientific sessions featuring Philipp Kukura on Mass Photometry, Lindsay Baker on her Kavli Fellowship, Richard Wade-Martins on neurodegenerative diseases and updates from our K.A.R.D Awardees. The event included a poster session from 22 early career researchers (ECRs), 3-minute research presentations from five ECRs and further research presentations from Dominika Gruzska, Molly Stevens, Simon Newstead, and Esther Becker. The meeting, attended by board members and Kavli Oxford researchers, was a key milestone for our research progress. In their report, the SAB members 'applauded the leadership team for setting a high standard for an open and inclusive environment'

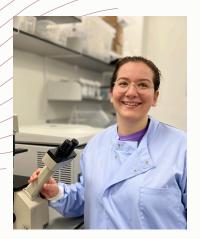
SUSTAINABILITY L.E.A.F AWARDS

* Laboratory Efficiency Assessment Framework

As testament to their commitment to progressing sustainability practices across our shared building, in the past year additional Kavli Oxford labs have secured or progressed their <u>sustainability awards</u>.

LAB NAME/S	LEAF AWARD
Biochemistry: Newstead Chemistry: Baldwin, Benesch, Kukura, Robinson DPAG: Wade-Martins	Gold
Biochemistry: Draper, Higgins NDCN: Tofaris, Becker OCDEM (RDM): David Ray	Silver
Biochemistry: Seiradake, Zitzmann Psychiatry: Buckley	Bronze

CAREER MOBILITY WITHIN KAVLI OXFORD



Dr Maya Miller

"Throughout my academic career I've been studying cancerous process with the goal of developing new drugs for cancer treatment. In my DPhil research I designed and characterized Titanium based drugs which exhibit significantly higher efficiency and biocompatibility, relative to the commonly used Platinum based treatments. I found a specific family of structures that was efficient and safe in cell culture experiments as well as in mouse models. This led me to investigate the cellular mechanism of

action of these drugs using bioinformatics tools and genomic research. Understanding the nature of cancer evolution, I was fascinated by the challenges the scientific community faces due to the cellular drug resistance mechanisms, while some living creatures are resilient to cancer development. The understanding of these properties and processes is fundamental for development of efficient, targeted and nontoxic new drugs. Such investigation required novel non-destructive method to examine cell process int their native environment. I found such a method in Professor Carol Robinson's laboratory, where the mass-spectrometry tool was adopted to examine proteins in their native cellular environment. This led me to use this method to study core proteins responsible for drug resistance mechanisms and elucidate their interplay with biomolecules such as lipids. Reaching further to dive into the interplay of membrane proteins and their environment. Now as a Marie Curie Fellow, I'm currently pursuing a deeper understanding of the extracellular matrix composition and tissue characterization in Professor Molly Stevens group."



Dr Emily Carroll

"In my current research, I am seeking to identify new gene therapy approaches for Parkinson's disease using high-capacity DNA viral vector expression systems to deliver wild-type versions of familial Parkinson's disease genes to patient iPSC-derived dopamine neurons. Using a variety of different cellular and molecular biology techniques, I will then investigate whether delivery of these genes can rescue dysfunctional phenotypes in dopamine neurons. In September 2023, I was awarded a prefellowship from the Motor Neuron Diseases (MND)

Association. Prior to joining Professor Richard Wade-Martin's group, I completed my DPhil with Professor Kevin Talbot, where I utilised cellular assays and microscopy to phenotypically characterise a mouse stem cell-derived motor neuron (mESC-MN) model of amyotrophic lateral sclerosis (ALS). I then explored the value of this model as a platform for phenotypic drug discovery. In my current role, I will develop new skills in the development of DNA plasmid vectors for gene therapy whilst using previous experience in cellular biology and assay development for the later stages of the project."

PUBLIC ENGAGEMENT AND OUTREACH

In September 2024, Kavli Oxford's Co-Deputy Director Achillefs Kapanidis hosted a visit by World50, a networking and idea sharing organisation for the leaders of top global companies. The group attended practical demonstrations related to our antimicrobial resistance and AI-based rapid AMR detection efforts.

The Kapanidis Group's efforts on <u>Infection Inspection</u> is now published in Scientific Reports: "Using the power of citizen science to help with image-based prediction of antibiotic resistance in Escherichai coli" doi: https://pubmed.ncbi.nlm.nih.gov/39174600/

Weston Struwe is a member of Science Together, African Families in the UK. This is a University of Oxford initiative to promote STEM education to children in Blackbird Leys in Oxford and expose students to science beyond the classroom. With other University of Oxford researchers, they help young, underrepresented students pursue their passion in science through regular workshops, including "BioArt", that employs histology images of tissues in health and disease, as well as site visits to the Diamond Light Source and the History of Science Museum. This initiative won the 2024 Vice-Chancellor's award (University of Oxford) in the category 'Community Partnership', African Families in the UK.

A video <u>'Malaria Challenge Studies: Why and How?'</u> with Andrew Duncan and Jo Salked from Kavli Oxford's <u>Simon Draper's group</u> was produced in December 2023 explaining the challenge of investigating malaria vaccines for the public understanding of science.

TRANSLATIONAL ACTIVITIES AND INDUSTRY COLLABORATIONS

Plasmodium vivax threatens 2.5 billion people worldwide. The OptiVivax consortium, coordinated by Kavli Oxford Professor Simon Draper and Associate Professor Angela Minassian, aims to develop next-generation vaccines over the next five years. The project kicked off on 19 September 2023 at Kavli Oxford, with nine partners from the EU, Ethiopia, Switzerland, and the UK.

Oxford's Medical Science Division showcased two Kavli Oxford Professors in the 'Collaboration in Action Series' – read about <u>Simon Newstead</u> and <u>Noel Buckley's</u> first-hand experience of collaborating, or supporting collaboration, with industry partners.

TRANSLATIONAL ACTIVITIES AND INDUSTRY COLLABORATIONS

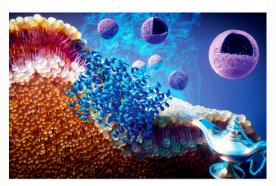


Dr Giacomo Gorini, funded by the Oxford Science Enterprises (OSE), joined Kavli Oxford in July 2024. Returning to Kavli Oxford's Professor Simon Draper's lab where he was a former Post Doctoral Researcher, Giacomo is now working to develop an in vitro technology aimed at the rapid generation of therapeutic antibodies against G Protein-Coupled Receptors (GPCRs). GPCRs represent one of the largest gene families in our genome, with over 800 members. These receptors are involved in several physiological functions and diseases – mainly of chronic, metabolic, and oncologic nature. It is well-established that it is very difficult to generate

drugs against these receptors, given their small size and structural frailty. Giacomo is working to overcome these hurdles by generating an in vitro antibody technology that can be rapidly adapted to the requirements of each GPCRs. The OSE 'Uncover Fund' was conceived to support early-stage research with entrepreneurial potential within the University of Oxford.

SELECTED AWARDS AND INDICATORS OF ESTEEM





Mootaz Salman's image featured on the front cover of <u>Biochimica et Biophysica Acta (BBA) - Biomembranes</u>, April 2024

'Cell membranes aren't just an intricate composite of multiple sets of protein and lipid species, but it is more like a screen door, because they keep things out (toxic substances), while letting air in (nutrients). In this cover, Mootaz Salman illustrates that the cell membrane, its composition and dynamism, is the source of all the "magic" that happened inside cells and governs what happens outside.'

SELECTED AWARDS AND INDICATORS OF ESTEEM

/	NAME	AWARD & RECOGNITION
_	Lindsay Baker	British Crystallographic Association Early Career Award, 2024
_	Simon Draper	Appointed to the role of Director of the Basel-Oxford Centre for Translational Immune Engineering from 1 October 2024
	Philipp Kukura	Moore Distinguished Scholar, California Institute of Technology
	Angela Minassian	Awarded title of Associate Professor
	Stuart Peirson	Gave evidence at House of Lords Science and Technology Select Committee (Westminster) entitled 'The neglected pollutants: the effects of artificial light and noise on human health.'
	David Ray	Appointed as Head of the Oxford Centre for Diabetes, Endocrinology and Metabolism, Radcliffe Department of Medicine, Oxford
	Carol Robinson	Lifetime Achievement Award, European Patent Office, Europe
	Molly Stevens	Dame Commander of the British Empire (DBE) for services to Medicine, Novo Nordisk Prize, and Armourers and Brasiers Company Prize, Royal Society
	Weston Struwe	Associate Professor of Cellular and Molecular Biochemistry, Tutorial Fellow at Worcester College
	Vladyslav Vyazovskiy	Member of the International Consortium to Classify Ageing-Related Pathology and Member of BBSRC Pool of Experts (Committees A, C)
	Becky Carlyle Alzheimer's Research UK Senior Research Fellow	New Funding: GSK Oxford Institute of Computational & Molecular Medicine funding - Joint Project Team Leader for 'Discovery and development of predictive clinical biomarkers for stratifying different Alzheimer's disease phenotypes'.
		Presentation: 'Peptidomics and snRNAseq point towards interneurons as a key cell-type for cognitive resilience to Alzheimer's Disease',19 March 2024 / ARUK National Conference. U.K
	Hugo Fernandes Alzheimer's Society Dementia Research Leader Fellow	New Funding: Hugo joins Kavli Oxford Becky Carlyle's project team as co-investigator on the project 'Discovery and development of predictive clinical biomarkers for stratifying different Alzheimer's disease phenotypes'

SELECTED AWARDS AND INDICATORS OF ESTEEM

NAME	AWARD & RECOGNITION
Dominika Gruszka Royal Society and Wellcome Trust Sir Henry Dale Fellow	Award: 2023 Vallee Scholar Award. New Funding: Wellcome Trust Discovery Award - 'Single-molecule studies of CENP-A dynamics during DNA replication' with Professor Lars Jansen (Department of Biochemistry, University of Oxford)
Charmaine Lang Parkinson's UK and Rosetrees Trust Senior Research Fellow	New Funding: Oxford-GSK Institute of Molecular & Computational Medicine (IMCM) Fellowship, commencing in October 2024
Brent Ryan Group Leader	New Funding: Medical Research Council: Multi-level mapping of mitochondrial quality control pathways in Parkinson's dopaminergic neurons
Mootaz Salman MRC Career Development Fellow	Awards: The Inaugural ALBA-Roche Research Prize for Excellence in Neuroscience 2024 by the Federation of European Neuroscience Societies (FENS). The David Hague Early Career Investigator of the Year Award 2024 by Alzheimer's Research UK. The Society for Experimental Biology 2024 President's Medal for the Cell Biology Section, January 2024. New Funding: BBSRC Pioneer Award (with Professor Roslyn Bill, Aston University) to explore the mechanisms of brain waste clearance using organ-on-chip technology.
Valeria Calvaresi	Wellcome Early Career Fellowship
Ruxandra Dafinca	Brain Science Postdoctoral Fellow
Nick Gatford	Medical Research Foundations' Festive Science Image Competition (2nd Place)
Mohamed Ibrahim	Masao Ito Prize from the Society for Research on the Cerebellum and Ataxias
Carla Kirschbaum	Leopoldina Fellowship for Innovative Lipid-Protein Research
Emma Sylvester	Wellcome Early Career Fellowship
Jan Cristoph Thiele	Eric and Wendy Schmidt Al in Sciences Postdoctoral Fellow

Faculty

Group Leaders / Early Career Fellows

Postdoctoral Researchers

INTERDISCIPLINARY DOCTORAL CANDIDATE RESEARCH HIGHLIGHTS

As our institute has matured, we now have our second cohort of interdisciplinary DPhil* students progressing through the institute. Here they share their experiences of working across boundaries.
*Doctor of Philosophy is used by the University of Oxford and is the equivalent of a PhD.



Sigurbjörn Markusson

Provisional title: Structural basis for neuronal polyamine transport and its link to pain sensation.

"My D.Phil primarily focuses on SLC45A4, a solute carrier transport protein recently identified by our collaborators as a risk locus associated with chronic pain. The function of SLC45A4 was unknown at the start of the project. We have

since identified it as a plasma membrane polyamine (PA) transporter in dorsal root ganglion (DRG) neurons. PAs, such as spermidine and putrescine, are ubiquitous polycationic alkylamines vital to several cellular processes, such as regulating gene expression, apoptosis and ion channel activity. However, how polyamines were transported between cells and within the brain remained unclear. Therefore, our identification of SLC45A4 as a plasma membrane PA transporter fills a significant gap in understanding how polyamines regulate cellular homeostasis. Using cryo-electron microscopy, we solved the structure of SLC45A4 in a novel auto-inhibited state. In conjunction with a spermidine transport assay established in neuronal cells, we have further characterised this novel PA transport system. We are further characterising the molecular mechanisms involved in PA transport by SLC45A4, its regulation, and how this function relates to pain signalling using a combination of a KO mouse model, physiological pain assays and electrophysiology"

Perspective on interdisciplinarity:

"Our discoveries so far have been achieved through various interdisciplinary methods. I predominantly use biophysical, biochemical and structural biology techniques to characterise PA transport by SLC45A4. Interdisciplinary collaborations, however, have been the key to success in this project, as the gene was initially identified in GWAS screens, its role in pain signalling was further explored using a KO mouse model, electrophysiology on excised DRG neurons, and the substrate initially identified using gene expression and metabolomic datasets."

Doctoral Training Programme: Cellular Structural Biology – Medical Science Doctoral Training Centre
Supervisors: Professors Simon Newstead (Biochemistry) and David Bennet (Nuffield Department of Clinical Neurosciences)

INTERDISCIPLINARY DOCTORAL CANDIDATE RESEARCH HIGHLIGHTS



Francesca Naughton-Allen
Provisional title: Refining Affinity-Based Mass
Photometry

Broad aim: "Developing and refining experimental and analytical workflows for affinity-based mass photometry, to detect and measure the mass of target proteins and their interaction complexes directly from cell lysates and tissue homogenates."

Methods: Mass Photometry, Native Mass Spectrometry

Perspective on interdisciplinarity:

"To me, interdisciplinarity in science means combining scientific perspectives from different disciplines to encourage collaboration and innovation, allowing us to address complex questions more effectively. As a chemist by training, I regularly collaborate with biochemists, microbiologists, molecular biologists and biophysicists in the Kavli Institute to gain a more holistic understanding of the fields related to my work, and I strongly believe that this helps me develop as a scientist."

Doctoral Training Programme: Oxford Interdisciplinary Bioscience Doctorial Training Programme (BBSRC) Supervisors: Professors Justin Benesch & Philipp Kukura (Chemistry)



Jacob Wright

Provisional title: The structure and function of transcriptional clusters in bacteria

Broad aim: "In fast-growing bacteria, we see remarkable organisation of DNA, RNA and proteins into clusters, which are thought to maximise transcription of certain genes. I'm aiming to resolve which components are present,

how clusters form, and what their function is. My project uses superresolution microscopy to track single protein molecules and localise them in 3D to within tens of nanometres. We want to discover how bacteria respond to respond to different conditions and whether clusters form via phase separation, like oil droplets in water."

Perspective on interdisciplinarity:

"Even though all science is interconnected, we often divide it into different disciplines for teaching. For me, interdisciplinarity means using knowledge from various fields to answer a single question. In my project,

INTERDISCIPLINARY DOCTORAL CANDIDATE RESEARCH HIGHLIGHTS

I use the physics of microscopy to explore the chemistry of phase separation, relating results to biological function in bacteria. These were all separate in my studies that have now converged in my DPhil."

Doctoral Training Programme: Oxford Interdisciplinary Bioscience Doctorial Training Programme (BBSRC) **Supervisors:** Professors Achillefs Kapanidis (Physics) & Stephan Uphoff

(Biochemistry)



Emma Lalande

Provisional title: Developing single-molecule RNA tagging in live Escherichia coli – in vivo single-molecule FISH

Broad aim: "The goal of my DPhil has been to progress the development of a single-molecule application of the long-established fluorescent in situ hybridisation (FISH) method, in live E. coli

cells, with the aim of tagging single RNAs of interest in the cell milieu and observing their spatial and temporal characteristics. In addition to utilising fluorescent techniques and superresolution microscopy in parallel with more classical FISH methodologies, this primary project entails bacterial cloning and engineering for producing RNA targets of interest, as well as some in vitro characterisation."

Perspective on interdisciplinarity:

"Interdisciplinarity - at its core, for me, represents the bringing together of different disciplines, backgrounds and perspectives to find new connections in what things could be and the ways things are done. The beauty of this, is that it can be applied to spheres much broader than just research, and form such strong, innovative and cohesive communities - that's part of my mission!

Building on my interest in how interdisciplinary research (IDR) is conducted, what effective IDR communication looks like, and how we can mold an optimal research culture, I completed an internship in policy at The Academy of Medical Sciences (AMS) in the summer of 2024. At AMS, I worked across multiple collaborative national and international health system projects and enjoyed the opportunity to investigate research culture from an even broader aspect. I look forward to feeding my learnings back into the Oxford Kavli and further support AMS too."

Doctoral Training Programme: Oxford Interdisciplinary Bioscience Doctorial Training Programme (BBSRC)

Supervisors: Professors Achillefs Kapanidis (Biological Physics) & Stephan Uphoff (Biochemistry)

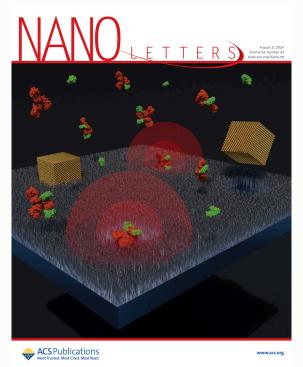
DOCTORAL CANDIDATE HIGHLIGHTS

Yohan Arman: In August 2024, Yohan was invited to present his research on novel screening technologies that can aid in identifying substandard and falsified medical products, to the Indonesian Food and Drug Authority and Indonesian National Research and Innovation Agency.

Victor (Shijun) Yan was awarded the Goodger and Schorstein scholarship, University of Oxford (2024).

Yin Chung (Vincent) Cheng was awarded a Graduate Research Fellowship from the National Ataxia Foundation (2024).

Tia Hawkins was awarded the Barber Prize for the Best Early Career Research Presentation entitled "Functional Evolution of Nipah G Protein Glycosylation" at the British Mass Spectrometry (BMSS) and British Society for Proteome Research (BSPR) Super Meeting, University of Warwick, U.K, 4-6 September 2024.

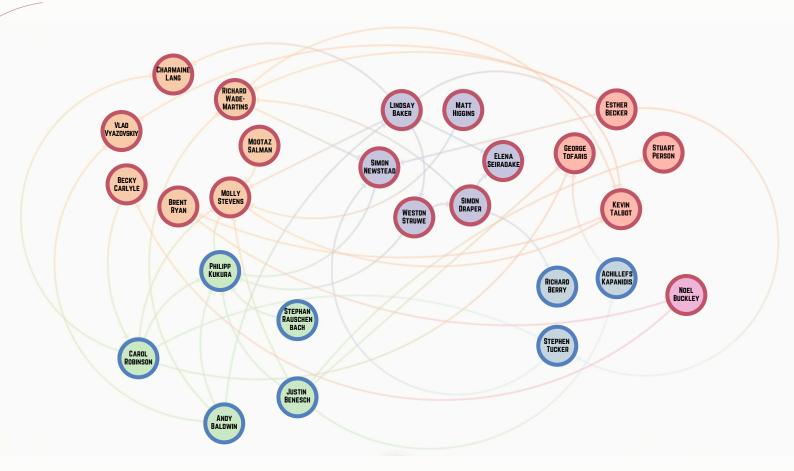


Dan Loewenthal (DPhil Candidate) along with post doctorial researcher Jiří Kratochvíl in Phillip Kukura's group created an image using Blender 3D software. The nanocube 3D model was generated using the FCC nanoparticle generator asset made by Ryo Mizuta Graphics. 3D models of antibody and Fc binding protein were generated by the Atomic Blender (PBD/XYZ) plugin using the PBD entries 111A and 11GY. The image is published on the cover of NANOLetters, 21 August 2024

"Nanopatterning of a passivation coating by nanocube lithography enables the measurement of low-affinity protein—antibody interactions. Nanoparticle deposition is followed by PEGylation and sonication, leaving empty nanoholes in the passivating layer. The nanopatterned surface results in a low biomolecular binding rate, enabling optical detection and mass measurement of single biological macromolecules at up to micromolar concentrations."

COLLABORATIONS

We are proud to share that with interdisciplinarity and collaboration at our core, 26 of our 39 Principal Investigators and Group Leaders have formed internal partnerships in addition to their external collaborations. The map below highlights the connections between different PIs, departments, and divisions.



- MEDICAL SCIENCES DIVISION
- MATHEMATICAL, PHYSICAL AND LIFE SCIENCES DIVISION
- DEPARTMENT OF BIOCHEMISTRY
- NUFFIELD DEPARTMENT OF CLINICAL NEUROSCIENCES
- DEPARTMENT OF CHEMISTRY
- DEPARTMENT OF PHYSICS
- DEPARTMENT OF PHYSIOLOGY, ANATOMY AND GENETICS
- DEPARTMENT OF PSYCHIATRY

LOCAL AND NATIONAL RECOGNITION

On 8 May 2024 Kavli Oxford and our home departments celebrated acknowledgement in four categories at the University of Oxford's <u>Vice-Chancellor's Awards</u>.

Winner in the Community Partnership Award including Associate Professor Weston Struwe et al

Highly Commended in the Innovation and Commercialisation Award including Professors Justin Benesch, Philipp Kukura & Weston Struwe et al

Shortlisted in the category Inclusive Teaching and Assessment Award including Professor Simon Kyle, Dr Sumathi Sekaran & Dr Rachel Sharman et al

Shortlisted in the category Research Culture Award including Kavli Oxfords' Organisational Development and Culture Lead, Désirée Tennant et al



The Research Culture Award acknowledged the work of the MRC Funded X-Net Project, a national interdisciplinary partnership between the Universities of Edinburgh, Dundee, Aberdeen and Oxford (Kavli Oxford is a contributing member). Common career and funding roadblocks and recommendations to increase the retention and impact of interdisciplinary researchers in the UK were published on 5 March 2024 in the report, Sweeping Away Barriers to Interdisciplinary Research. The report was reviewed by the UKRI (UK Research and Innovation) and further discussions with the MRC (Medical Research Council) to address challenges and potential policy implications are ongoing.

On 25 January 2024, Kavli Oxford hosted the X-Net project team during a workshop attended by The Wellcome Trust, The British Academy, University of Liverpool and Northumbria University amongst others culminating in the report <u>Lessons from equality, diversity and inclusion: How might interdisciplinary research culture evolve and be strengthened?</u> and the Wheel of Privilege.

The project has published several further outcomes, reports, interviews and a blog post for The Higher Education Policy Institute, <u>It's time to change the culture around interdisciplinary research - HEPI</u>.

Further funding has been secured from the MRC Biomedical Data Science Leadership Award by both Oxford and Edinburgh to continue the work commenced by X-Net.

"Désirée has been critical for reporting X-Net's recommendations to funders and policymakers on the obstacles faced by interdisciplinary researchers in the UK and solutions that might help overcome these barriers. Her insightful feedback was essential to delivery of these recommendations."

Professor Chris Ponting, Principal Investigator, MRC Human Genetics Unit, Institute of Genetics and Cancer, University of Edinburgh

KAVLLINSIGHTS: DIRECT FROM OUR RESEARCHERS

We are tracking and exploring our researchers experience of being in the institute.

Amena Saleh: "I believe that research cannot be walled in and people need to discuss their work more often, especially with researchers from outside your discipline. It helps in thinking outside the box and might even help you overcome hurdles that you might be facing. Joining Kavli Oxford as a post doc scientist has been a welcome change for me and I believe it will be instrumental in shaping my career trajectory."

Lindsay Baker: "For myself, being in Kavli Oxford has kept me exposed to new ideas and potential collaborations, which is scientifically invigorating and motivating. For my group, the interest from other Kavli Oxford groups in collaborative work ensures that they have opportunities to grow and develop outside of their main research project. They learn to work collaboratively and discuss science across disciplines, bettering understanding their and others' assumptions and perspectives."

Brent Ryan: "The exposure to different research disciplines that would not be as accessible e.g. chemistry and clinical colleagues in Nuffield Department of Clinical Neurosciences and Psychiatry have directly impacted projects in my research group and enabled new research questions to be asked which extend our group's existing research. Our collaboration has accelerated our optogenetics-based research and has been mutually beneficial"

We asked our researchers for their perspectives on their interdisciplinary research portfolios.

Stuart Peirson: "Much of our work is at the level of whole organism physiology and behaviour, though this raises many interesting questions relating to molecular mechanisms. My research focuses on the effects of light on physiology and behaviour, and this does include a strong background in photobiology and light signalling mechanisms – from the molecular processes to cellular physiology."

Charmaine Lang: "My entire portfolio is reliant on interdisciplinary activities. My research into neuron/astrocyte communication & extra-cellular vesicles in neurodegenerative disease benefits from interdisciplinary techniques including native proteomics (Robinson Group), Fluid wall microfluidics (Walsh Group) and Cryo-EM (Baker Group)"

Stephan Rauschenbach: "As a group that develops instrumentation, we always have to work in diverse fields: physics and engineering are key to instrumentation development, chemistry and biology are our applications."

KAVLI INSIGHTS: DIRECT FROM OUR RESEARCHERS

Dominika Gruszka: "In accordance with Kavli Oxford's mission, my research integrates approaches from several disciplines across physical, life and medical sciences to better understand the dynamic processes that are fundamental to life. My main research goal is to dissect the molecular mechanisms underpinning chromatin replication and the associated epigenetic inheritance. This field is currently dominated by classic single-discipline-led (genetic and/or cell biological) approaches that generally lack spatiotemporal resolution needed to investigate these dynamic processes. By amalgamating concepts and tools from engineering, physics, chemistry, physiology, genetics and biochemistry, I have developed a novel methodology that enables us to shine a new 'quantitative' light on chromatin replication. My laboratory at Kavli Oxford combines this unique approach with other state-of-the-art chemical, physical and cell biological methods to address longstanding questions in the field of epigenetics. Moreover, I collaborate with groups to exploit and develop some or all of these approaches in addressing other biological questions, such as DNA repair (see Belan et al), sister chromatid cohesion (see Cameron et al), centromere biology (Wellcome Trust Discovery Award with Lars Jansen, Biochemistry), chromatin compaction (joint project with Madhavi Krishnan, Chemistry) and energy transduction across the bacterial cell envelope (joint BBSRC project grant with Colin Kleanthous, Biochemistry)."

COMMUNICATIONS

"The 'See the Unseen' video series of short-form interviews with Kavli Oxford researchers has continued to grow and gain independence; with one of the founding members, Jussi Tolonen leaving the institute, we have successfully adapted the series to accommodate rotating hosts, ensuring continuity of the series. Both the interviewers and interviewees have found the experience valuable, firstly for the process of shaping and expressing their research effectively in making the videos, and secondly in finding new contacts and potential collaborators across the institute, as their research summary is picked up by people across the university.

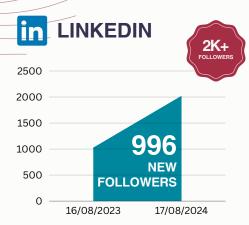
We are also using the experience from this video series as a springboard to promote and encourage science outreach across the university; Susanne Mesøy, one of the 'See the Unseen' founders, was interviewed for the Department of Chemistry to provide a departmental case study as a resource for researchers starting science outreach – be it video, audio, or any other format.



Beyond the university, Susanne also spoke at a Kavli Foundation wide online 90minute panel discussion on "Integrating Communication and Engagement into your Scientific Career", which participants described as 'insightful' and 'inspiring'."

The 'See the Unseen' video series is coproduced by Dr Isil Senol (Kalvi Oxford Marketing and Communications Lead) and Dr Susanne Mesøy (Postdoctoral Researcher)

SOCIAL MEDIA ACTIVITY



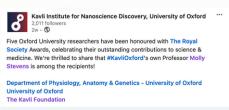
GROWTH



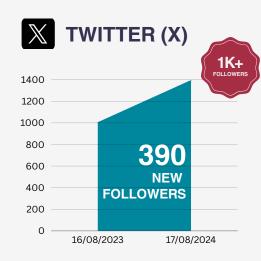
996 NEW FOLLOWERS IN 1 YEAR

15.2% 2022 35.2% 2023 49.5% 2024 **98.22% INCREASE**

TOP POST - 295 REACTIONS







GROWTH



390 NEW FOLLOWERS IN 1 YEAR

40.28% 2022 32.37% 2023 28.06% 2024 **39% INCREASE**

TOP POST - 15K IMPRESSION







40
VIDEOS



5,4K+



35,613

IMPRESSIONS

TOP CONTENT - 908 VIEWS



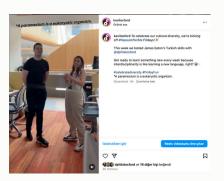
SOCIAL MEDIA ACTIVITY



TOP POST



#REPEATAFTERME



We launched our Instagram channel this year to engage with our audience in a more fun and informal way.

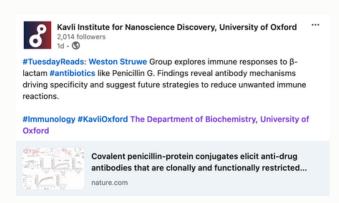
#MEETTHERESEARCHER



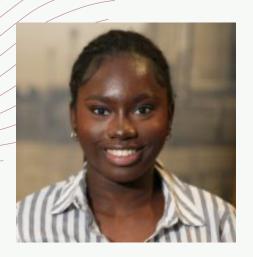
Launched on 8th November 2023, the "Meet the Researcher" campaign highlights the work and professional profiles of our early career researchers, while strengthening their connection with the institute by increasing their visibility across our channels. Posts from the campaign are shared every Wednesday on Kavli Oxford's Instagram, Twitter (X), and LinkedIn accounts.

#TUESDAYREADS

Every Tuesday, on Kavli Oxford's Twitter (X) and LinkedIn channels, we share at least two publications from our researchers that were published in the past month. This helps increase our scientists' visibility and provides up-to-date information about their research to both external and internal audiences.



UNDERGRADUATE NEWS



In her blog post, <u>Blog – A reflection of my</u> <u>year in an Oxford Lab (nihr.ac.uk)</u>, Yasmin Bonsu discussed her experience as a 3rd year undergraduate student from University of Manchester while she spent a 'Year in Industry' as an intern in Dr Becky Carlyle's lab

NEW EQUIPMENT FUNDING SECURED FOR CELLULAR AND BIOMOLECULAR ANALYSIS



Discovering Host-Virus Interactions by Establishing the Solution-Phase Glycan Array

Funder: Royal Society/Kavli Oxford Lead investigator: Weston Struwe

"Funding was awarded to purchase an HPLC to develop a new method to screen and quantify protein-carbohydrate interactions, specifically those involved in HIV and Ebola infection. Current methods for screening protein-glycan interactions is best achieved using glycan microarrays, a well-established method that uses printed glycans on solid surfaces to detect interactions with fluorescently tagged proteins but it requires precision equipment and considerable amounts of oligosaccharide standards which often do not represent the biological system. The Solution-Phase Glycan Array (SPGA) is designed to simultaneously identify and quantify binding between glycan binding proteins and their biologically-derived oligosaccharide targets using a straightforward HPLC platform."

Written by Associate Professor Weston Struwe

NEW EQUIPMENT FUNDING SECURED FOR CELLULAR AND BIOMOLECULAR ANALYSIS

High-resolution hydrogen-deuterium exchange mass spectrometry platform

Funder MRC/Lead by Jani Bolla and Kavli Oxford Co-investigators Justin Benesch, Weston Struwe and Carol Robinson et al

"We are obtaining a Xevo MRT mass spectrometer (Waters Corp) to increase our capacity and capability to define the conformational landscape of proteins – the cells' workhorses. All protein functions, including pathogenic processes, require coordinated flexing and motion. Understanding changes in protein conformation and dynamics is therefore critical not only for learning the underlying mechanism of biological processes and the cause of various human diseases but also for drug development. Hydrogen–Deuterium Exchange Mass Spectrometry (HDX-MS) provides valuable information about solution phase protein dynamics and is highly complementary to the static snapshots provided by conventional high-resolution structural tools (e.g. cryoEM). This instrument will this be a valuable addition to the infrastructure in the Kavli Institute for Nanoscience Discovery, enabling our community to better understand the molecular mechanisms at play in protein function."

Written by Professor Justin Benesch



Rachel Heon-Roberts, Kavli Oxford DPhil candidate (Physiology, Anatomy & Genetics) successfully obtained an ARUK Thames Valley Network Equipment Grant with Dr Nate Gould (Post Doctorial Reseearcher - Psychiatry) and Raman Van Wee (DPhil candidate - Chemistry)

"This funding has purchased a sonicator system to produce high-quality and consistent alpha-synuclein aggregates. This will enable Kavli Oxford researchers to study alpha-synuclein at different scales from aggregation kinetics (Chemistry) to the effects of aggregates on neuronal biology (Physiology, Anatomy and Genetics & Neuroscience)"

By Rachel Heon-Roberts, DPhil candidate

Selected Publications Reflecting Collaboration

An exciting new combination of methods bringing together chemists and biologists to show softlanded particles from the gas phase to the EM grid.

Cryo-EM of soft-landed β-galactosidase: Gasphase and native structures are remarkably similar.

https://doi.org/10.1126% 2Fsciadv.adl4628 A meeting between Wade-Martins (DPAG) and Talbot (NDCN) in our institute led to exchange of ideas and a new collaboration was borne.

C9orf72-ALS human iPSC microglia are proinflammatory and toxic to co-cultured motor neurons via MMP9.

https://doi.org/10.1073/pn as.2208737120 Tackling yet another challenge of our time – researchers try to speed up the process of understanding antimicrobial resistance employing deep learning approaches.

Deep learning and single-cell phenotyping for rapid antimicrobial susceptibility detection in Escherichia coli.

https://doi.org/10.1038/s4 2003-023-05524-4

Eight Kavli Oxford authors, together with multiple colleagues from the wider Oxford research network, bring their expertise together to understand important aspects of binding and inhibition of the SARS-CoV-2 virus.

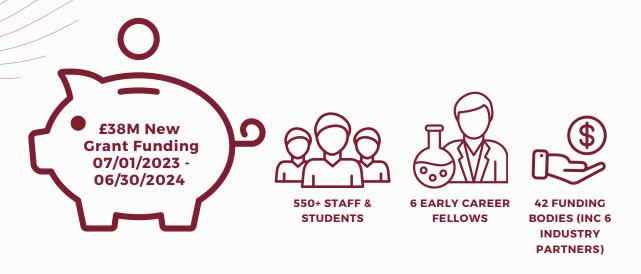
Oligomerisation-driven avidity correlates with SARS-CoV-2 cellular binding and inhibition.

https://www.pnas.org/doi/10.1073/ pnas.2403260121 An exciting Kavli Oxford collaboration (Biochemistry: Higgins and Draper) which provides fresh insight into the molecular mechanism of erythrocyte invasion- of significance for rational vaccine design.

The PfRCR complex bridges malaria parasite and erythrocyte during invasion.

https://doi.org/10.1038/s41586-023-06856-1

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