

JULY 2023, ISSUE 9



ARC Industrial Transformation Training Centre for Cryo-electron Microscopy of Membrane Proteins

Quarterly newsletter

INSIDE THIS ISSUE:

Prof Renae Ryan, AM

New ICHDR

EduWeek 2023

Image credit - Dr Sarah Piper
(@SarahJ_Piper, @PiperProteins)



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CCeMMP acknowledges the peoples of the Kulin, Dharawal, Yuin and Wadi Wadi Nations on whose land the Centre and its Nodes operate. We pay our respects to their Elders, past, present and emerging.

From the Director

Professor Patrick Sexton

Centre Director

Welcome to the 9th instalment of the ARC CCeMMP quarterly newsletter.

In this newsletter we welcome our latest ICHDRs, and report on the various achievements of our members and affiliates. A warm welcome to all of our new members. We are excited to see continual expansion of our membership to new organisations and researchers.

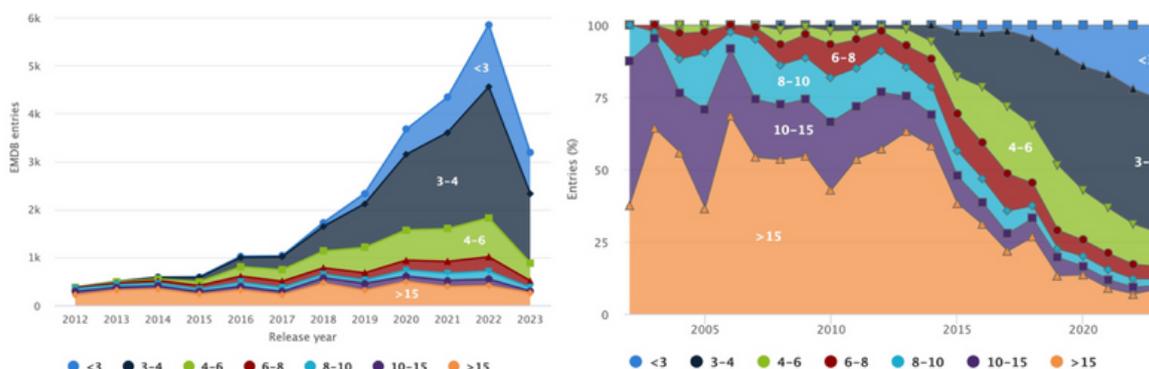
Key activity highlights for this quarter included a hands-on single particle cryo-EM workshop in June organised by ICPD Dr. Sepideh Valimehr via the University of Melbourne, Bio21 Node. This workshop was sponsored by our Partner Organisation, Thermo Fisher Scientific. June/July was also the time for our annual EduWeek that included delivery of multiple vocational workshops and advanced training for our ICHDRs. We also took this opportunity to run additional workshops in the following week for the broader Centre membership on cryo-EM, BASH scripting and data visualisation using Blender. We are grateful to all of the external and internal workshop leaders and the numerous Centre members who helped to make these activities a great success.



Professor Patrick Sexton
Centre Director

Did you know?....

It's been 10 years since the "resolution revolution" in cryo-EM of membrane proteins. In 2013, the first high resolution (3.4 Å) structure of the TRPV1 channel was reported [Liao et al., Nature 504 (7478): 107-112, 2013]. Using newly developed electron detectors and image processing algorithms, they not only broke the side chain resolution barrier, they were able to "showcase single-particle cryo-EM as a powerful and transformative advance in the structural analysis of membrane proteins". This was a major leap forward in the field as evidenced by the subsequent rise in 3 - 4 Å cryo-EM structures deposited to EMDB. We look forward to seeing your structures in the <3 - 4 Å resolution shells and in our 'structure gallery'!



Data from EMDB database: Number of EMDB entries in resolution (Å) shells by year.

On the cover: From the Glukhova lab at our WEHI node, "Shining a light on PORCN". In this ribbon diagram, the structure of Porcupine (PORCN), the membrane bound O-acyltransferase is shown with its potent inhibitor, C59, highlighted in the binding pocket. Image credit Dr Sarah Piper

Centre updates

ARC Annual Report

We are pleased to note that the ARC has formally approved the Centre's annual report. Thanks again to all those who helped us with compiling the document.

Dimerix Project Agreement

We are pleased to announce that we have finalised our project agreement with Dimerix Ptd Ltd, one of our original Partner Organisations. Dimerix is a partner with the Monash Node of the Centre and is conducting collaborative research on GPCR dimers.

ICHDR Update

We welcomed ICHDR Vignesh Kamath in early July. He has joined Associate Professor Mike Griffin at UoM/Bio21, more about Vignesh in the node updates.

The last week of June saw a gathering of our centre ICHDRs for EduWeek 2023. It was wonderful to see them all together in one place rather than a name and/or a face in a box on the zoom seminar screen. We had a full week of activities; our ICHDRs participated in all the workshops but they were also well attended by other members and affiliates of the Centre. In the middle of an intensive EduWeek, the students were able to enjoy a long lunch (a little way) off campus in their new CCEMMP hoodies; a big thank you to Prof Patrick Sexton and Dr Elva Zhao for organising and sourcing these. Many of the ICHDRs also attended the second week of 'EduWeek optional extras', learning how to write their own BASH scripts, understanding the theory behind 2D image formation and creating their own Blender3D renders.



ICHDR "welcome lunch" for new students. Nice hoodies!!

This quarter will be training intensive for our first year CCEMMP PhD students. The Biochemistry rotation will be completed at their respective nodes soon after their arrival. Then August and September will see them going through rotations 2 (CryoEM training) and 3 (Data processing and analysis). Then they can use all their newly acquired skills and knowledge to accelerate their projects!

Expanding CCEMMP Membership

The Centre continues to reach out to scientists, outside of the founding academic institutions, who are involved in cryo-EM and membrane protein research to provide opportunities for them to become members or affiliates of the Centre. Of course, we continue to actively seek inclusion of new staff and students from *within* our existing Nodes, as part of the Centre.

Some of our new members will be familiar faces/names who have presented in our CCEMMP seminar series, others are new to CryoEM having just completed Dr Sepideh Valimehr's workshop. We offer a warm welcome to all our new affiliates. New members from within our nodes appear in the respective node updates.

New affiliate members from around the country joining this quarter

Dr. Mai Vu (UoM/Doherty), James Lingford (Monash, BDI), Associate Professor Michael Landsberg (UQ), Dr. Evelyne Deplazes (UQ), Professor Brett Collins (IMB, UQ), Dr. Kevin Chen (IMB, UQ), Dr. Shan Zheng (IMB, UQ), Dr. Matthew Doyle (University of Sydney), Dr. Biswa Mishra (Griffith University).

Node Updates

Monash Node

Professor Denise Wootten

Node Leader, Monash University

Dr Sarah Piper Awarded Travel Grant

Dr Sarah Piper was awarded a Monash Early Career Network Travel Grant (\$2,900). Sarah will take the opportunity to travel later in the year to visit her collaborators.

Felix Bennetts awarded Early Career Research Prize, WCP Glasgow.

Congratulations to Felix Bennetts on being awarded the Early Career Research prize at the World Congress of Pharmacology (WCP2023), Glasgow. Felix's talk was entitled "Using Cryo-EM to solve the P2X1 receptor structure - a target for male contraception."

Associate Professor Karen Gregory was awarded Fellowship of the Higher Education Academy

July 20, 2023, Associate Professor Karen Gregory was awarded Fellowship of the Higher Education Academy (via Advance HE). Advance HE are experts in higher education; their major focus is on teaching and learning, leadership development and equality, and diversity and inclusion. The Fellowship acknowledges Karen's role and commitment to professionalism in higher education teaching and learning.



Congratulations Dr Jessica Lu

Student affiliate, Jessica Lu's PhD thesis was passed. Thesis title: "Structural and Pharmacological Characterisation of Splice Isoforms of the Pituitary Adenylate Cyclase- Activating Peptide Type 1 (PAC1) Receptor."

University of Melbourne (Bio21) Node

Associate Professor Isabelle Rouiller

Node Leader and Deputy Director, University of Melbourne

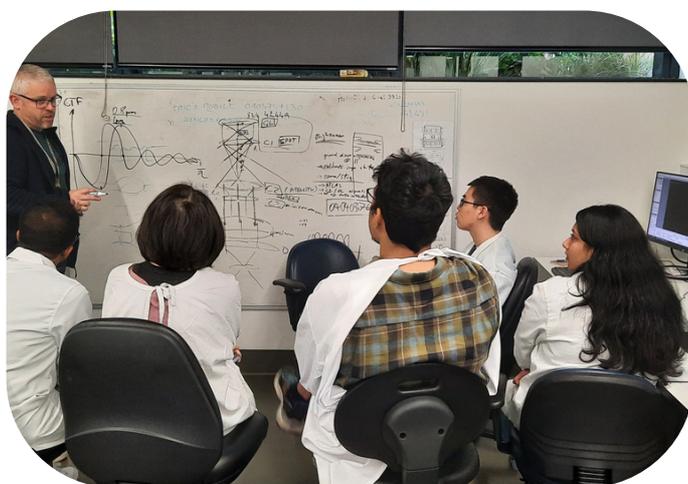
Meet ICHDR Vignesh Kamath

Welcome to our new ICHDR, Vignesh Kamath. Vignesh will be undertaking his doctoral studies in Associate Professor Michael Griffin's lab at Bio21 institute, The University of Melbourne node. His PhD will involve understanding structure and signalling of the IL6 family cytokines, developing inhibitors, and exploring their therapeutic modality. When Vignesh clocks out of work, he loves to watch movies. He is a bike enthusiast who loves to ride in nature, and he loves to have biryani for breakfast, lunch and dinner.

Supervisors: A/Prof. Mike Griffin, Dr. Tracy Putoczki.



Single Particle Cryo-EM Workshop - June 21-23 - sponsored by ThermoFisher Scientific



The workshop was sponsored by our Industry Partner Organisation, Thermo Fisher Scientific.

June 21-23, Dr Sepideh Valimehr ran her annual SPA workshop at the Ian Holmes Imaging Centre (IHIC) at Bio21 Institute, with the help of Dr Hamish Brown (IHIC), Dr Matthew Belousoff (MIPS) and Dr Josh Hardy (WEHI). This was a hands-on Cryo EM workshop with 10 attendees from various regions across Australia, including Griffith University, Charles Sturt University, Monash University, Royal Melbourne Hospital, University of New South Wales, and Peter Doherty Institute. Participants really enjoyed the hands-on aspect of this workshop and some would have liked the course to run longer, to enable a couple of days dedicated to data processing alone.

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New Members

We welcome new members/affiliates Dr. Shadi Maghool, Dr. Manasi Arcot Anil Kumar, Dr. Matthew Johnson, Dr. Naveen Vankadari, Mr. Zubair Jashim and Dr. Hamish Brown.

University of Wollongong Node

Associate Professor Gökhan Tolun
Node Leader, University of Wollongong



Lisanne Spenklink Promoted to Level C

Lisanne now has a continuing position, Level C at the UoW node. Her lab is interested in the development and use of single-molecule techniques to study the dynamic behaviour of proteins in complex biological systems, with a focus on DNA replication. Lisanne currently holds a NHMRC emerging leadership grant to develop a novel single-molecule directed-evolution method. In 2021, she received a Prioritising Emerging Research Leaders (PERL) Fellowship and the Dame Bridget Ogilvie Award (career advancement award) as recognition for her contribution to health and medical research in Wollongong.

WEHI Node

Associate Professor Isabelle Lucet
Node Leader, WEHI

Dr. Winnie Tan, Finalist for the 2022 Premier's Awards for Health & Medical Research.

In May 2023, Dr. Winnie Tan was selected as one of 14 finalists for the 2022 Premier's Awards for Health and Medical Research. The award, established in 1995 by the Victorian Government and the Australian Society for Medical Research, recognises the noteworthy contributions of early- and mid-career researchers. Finalists receive \$5,000. The award has five categories: Basic Science Researcher, Clinical Researcher, Health Services Researcher, Public Health Researcher, and Aboriginal Researcher. Congratulations Winnie, your research is being recognised as being able to improve the lives of people in Victoria and around the world.



Dr. Wessel Burger Awarded Mollie Holman Medal

Dr. Wessel Burger was awarded the Mollie Holman Medal for best Doctoral Thesis (2022), Faculty of Pharmacy and Pharmaceutical Sciences, Monash University. This is one of the highest academic honours Monash University bestows on doctoral students, with a maximum of 10 awarded per year (one per faculty). The medal recognises the awardee as a researcher of the highest order.

External Affiliates Update

Professor Renae Ryan Awarded Order of Australia and a Finalist for the Eureka Prize

Professor Renae Ryan (University of Sydney) was appointed as a Member of the Order of Australia (AM) on the King's Birthday Honours list, June 12, 2023 for her contributions to biomedical science and diversity and inclusion. She is also a finalist for one of Australia's prestigious science awards, The Australian Museum Eureka Prizes. This annual award honours excellence and celebrates achievement across science in Australia, from environmental to innovative technologies, citizen science, leadership and mentoring. Professor Ryan (AM) is a finalist in the Eureka Prize for Outstanding Mentor of Young Researchers (19 July, 2023). The Eureka Prize will be awarded August 23, 2023. Congratulations Renae on your AM and all your efforts being recognised.



Dr Alice (Jeeun) Shin Awarded Travel Grant

Dr Alice Shin (ANU) was awarded a Vice-Chancellor's HDR Travel Grant (\$1,500) to attend an international conference.

Upcoming Events



Seminar Series

Our seminar series continues on the second Tuesday of the month, 10:00 AM - 11:00 AM. This quarter we will hear from the lab of Dr Alisa Glukhova, WEHI (August 8th; her PORCPN structure is this month's newsletter cover image), Dr. Max Clabbers, UCLA (September 12th) and Associate Professor Steve Reichow, Oregon Health & Science University (October 10th).

This quarter we have two additional “special” seminars. Professor Jose Maria Carazo, who is in Melbourne for the International Union of Crystallography meeting, will deliver his presentation to the Centre at the Bio21 Institute of the University of Melbourne Node (zoom enabled for those who can't attend in person), August 29 10:30-11:30 AM. There will be a networking session after the seminar and the Centre ICHDR students will also have dedicated time with him. We will also have a special seminar from Assistant Professor Tian Hua (Shanghai Tech University) October 17, 4:00 PM - 5:00 PM. Mark your calendars!

“Rotation 2”: Theoretical and Practical Aspects of Cryo-Electron Microscopy; Lecture Series, August 14-28, 2023

This year we have opened (via zoom) the lecture series associated with rotation 2, to Centre members and affiliates. So far there has been great interest from both our members/affiliates and investigators from our partner organisations (Dimerix and Pfizer) in attending these lectures. The Lecture series will be presented by Centre members (Associate Prof Isabelle Roullier, Dr. Debnath Ghosal, Dr Alisa Glukhova, Dr James Bouwer, Dr Matthew Belousoff) and our partner organisation (Dr Lingbo Yu, Thermo Fisher Scientific) and is directed towards PhD students and Postdocs who wish to improve their cryo-EM knowledge, but all members are welcome. Lectures will cover: Introduction to transmission electron microscopy (TEM); Negative stain and its application; Sample preparation & vitrification for SPA of membrane proteins; Introduction to image formation (TEM); General considerations for microscope set up (SPA); Electron detector technology. This is open to CCeMMP members and affiliates only.

“Rotation 3”: Data Processing and Analysis , September 11-22, 2023

As part of their formal training, our CCeMMP ICHDRs undertake hands-on training in data processing of cryo-EM data. This year we offered, by application, places for 6 student affiliates to participate in the training. We will progressively expand access to this training program, and expect that more places will be available to Centre members/affiliates in subsequent years.

CCeMMP Retreat

The date is set – December 4th and 5th – for the Centre retreat. Two days of scientific presentations from our ICHDRs and members and strategic planning for the future. The retreat will be held in Parkville, Melbourne. Mark your calendars!

Outreach Activities

In the Media

The Cryo-Talk podcast (June 14, episode 10) from Thermo Fisher Scientific and Bitesize Bio interviewed Associate Professor Gökhan Tolun, our node leader from the University of Wollongong. The interview is available as an audio podcast (<https://cryo-talk.bitesizebio.com/>) and YouTube video (<https://bit.ly/cryotalk10-gt>).

Dr David Thal May 30, 2023 (images prepared by Dr Sarah Piper)

<https://www.monash.edu/pharm/about/news/news-listing/latest/world-first-monash-led-study-unlocks-key-new-information-on-major-drug-target-for-psychiatric-and-cognitive-disorders-including-schizophrenia>

Dr David Thal elife magazine insight Drug Discovery: Decoding the mechanisms of allostery

<https://elifesciences.org/articles/88749>

Outreach - Training

Many thanks to our many Centre members who organised and/or assisted in delivery of both our internal and externally facing workshops. The volunteer contributions of our members are critical to the success of all Centre activities.



Dr Matthew Belousoff



Dr Jason Cao



Dr Brian Cary



Dr Josh Hardy

Dr Matthew Belousoff,

- June 21-23 (Bio21) Single Particle cryoEM workshop
- June 26-30 and July 3-5, EduWeek 2023 workshops
 - Succinct and Clear Oral Presentation Workshop
 - Consistent and Interpretable Visual Design Language for Scientific Communication
 - Introduction to BASH scripting
 - Theoretical Basis for Image Formation in a Transmission Electron Microscope
 - How to Set Up Imaging Conditions for SPA Cryo EM

Dr Jason Cao July 6-7, EduWeek 2023 workshops, Two-day Blender3D Workshop

Dr Brian Cary: July 6-7, EduWeek 2023 workshops, Two-day Blender3D Workshop

Dr Josh Hardy,

- June 21-23 (Bio21) Single Particle cryo-EM workshop
- July 3-5, EduWeek 2023 workshops
 - Introduction to BASH scripting
 - Two-day Blender3D Workshops

Dr Jesse Mobbs July 6-7, EduWeek 2023 workshops, Two-day Blender3D Workshop

Dr. Sarah Piper, June 26-30, July 6-7, EduWeek 2023 workshops

- Consistent and Interpretable Visual Design Language for Scientific Communication
- Two day Blender3D Workshop

Dr Winnie Tan Training users on using REFYN mass photometer at WEHI (on going)

Dr Sepideh Valimehr

- June 21-23 (Bio21) Single Particle cryoEM workshop
- July 6-7, EduWeek 2023 workshops, Two-day Blender3D Workshop



Dr Jesse Mobbs



Dr Sarah Piper

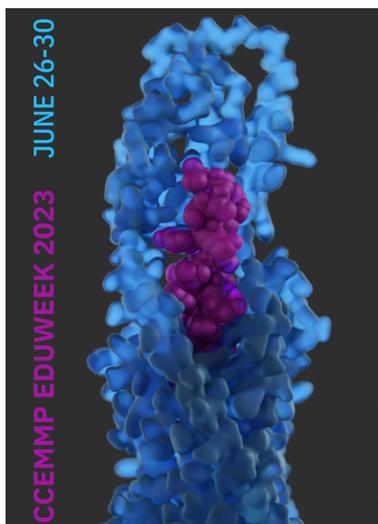


Dr Winnie Tan



Dr Sepideh Valimehr

Recent Centre Activities and Achievements



EduWeek 2023

EduWeek returned for 2023, June 26-30, inclusive. We had a full week of professional development workshops designed to provide further skills and complement where the students are in the PhD program. EduWeek was compulsory for the ICHDRs and open to all Centre members/affiliates. The workshops were very well attended with participation from all four nodes and by new affiliates from outside our nodes.

2023 workshops covered a range of different topics:-

- Research and Industry Engagement (Dr Cathy Drinkwater, Biocurate)
- Mastering Research and Industry Engagement: Business Development (Dr Cameron McDonald, Monash University)
- Safe Conversations in Research Candidate Student Supervisor Relationships - PhD Student Workshop (Andrew Carnegie, Carnegie Consulting Group)
- Safe Conversations in Research Candidate Student Supervisor Relationships - Supervisor Workshop (Andrew Carnegie, Carnegie Consulting Group)
- Consistent and Interpretable Visual Design Language for Scientific Communication (Dr Matthew Belousoff and Dr Sarah Piper, Monash University)
- Mindfulness (Prof Craig Hassed, Monash University)
- Scientific Writing: Literature Reviews (Student Academic Success, Monash University)
- Scientific Writing: Clarity and Impact (Student Academic Success, Monash University)
- Succinct and Clear Oral Presentation Workshop (Dr Matthew Belousoff, Monash University)



Scientific Writing: Literature Reviews



Mindfulness with Professor Craig Hassed. A joint activity with the Centre for Fragment Based Design



Oral Presentation workshop with Dr Matthew Belousoff



Research and Industry Engagement with Dr Cathy Drinkwater



Safe Conversations (for students) with Andrew Carnegie



Safe Conversations (for supervisors) with Andrew Carnegie



Scientific Writing: Clarity and Impact



Consistent and Interpretable Visual Design Language for Scientific Communication with Dr Matthew Belousoff and Dr Sarah Piper

EduWeek 2023 July 3-July 7: Optional Activities

For the first time, we added a series of optional workshops in the week following the main EduWeek activities, July 3-7 inclusive. These included:

- Introduction to BASH scripting (Dr Matthew Belousoff, Monash University; Dr Josh Hardy, WEHI)
- Theoretical Basis for Image Formation in a Transmission Electron Microscope (Dr Matthew Belousoff, Monash University).
- How to Set Up Imaging Conditions for SPA Cryo EM (Dr Matthew Belousoff, Monash University)
- Two-day Blender3D Workshop (Brady Johnston, University of Western Australia; assisted by Dr Sarah Piper, Dr. Jesse Mobbs, Dr Brian Cary, Dr Jason Cao, Monash University; Dr Sepideh Valimehr, UoM/Bio21; Dr Josh Hardy, WEHI).

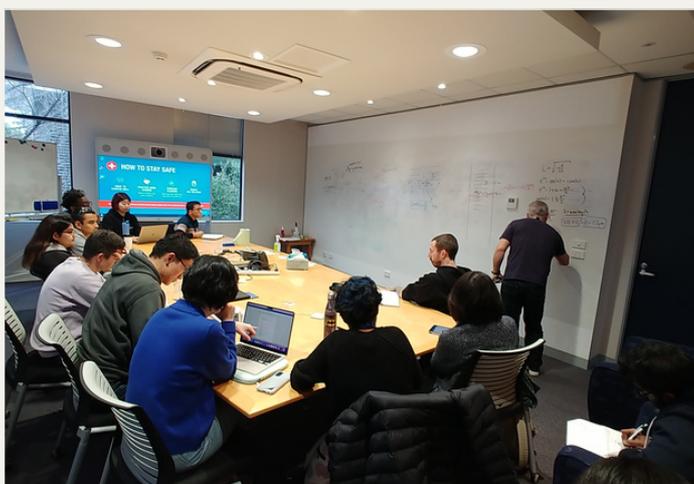


Introduction to BASH scripting with Dr Matthew Belousoff and Dr Josh Hardy

BASH and Blender workshops were both zoom-enabled to allow our UoW, U Syd, UQ and Griffith members and affiliates to participate. All workshops were well attended by our members and affiliates.

We hope all who were able to attend the workshops found them inspiring.

A huge thank you must go to our ICPDs Dr Matthew Belousoff, Dr Sarah Piper, Dr Sepideh Valimehr and PostDoc members Dr Josh Hardy, Dr Jesse Mobbs, Dr Brian Cary, Dr Jason Cao for running and/or assisting in the various workshops. Your expertise, time and passion for what you do is immensely appreciated.



Theory of 2D image formation with Dr Matthew Belousoff



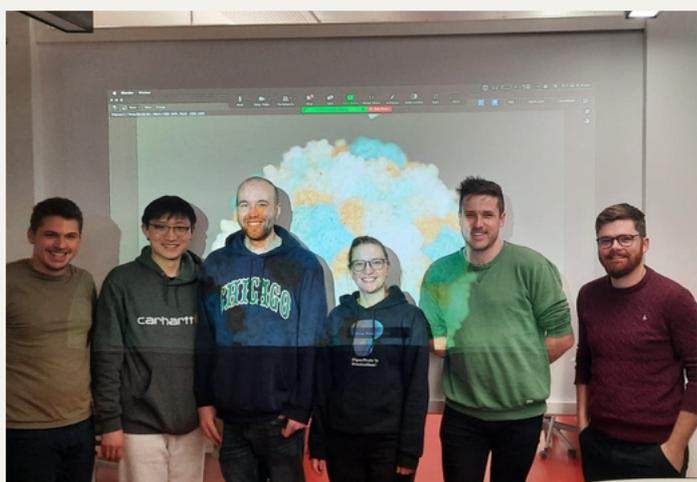
Blender day 1 with Brady Johnston

Making Atoms Visible: Blender3D Workshop with Brady Johnston

As part of the 'Optional Extras' to EduWeek 2023, Dr Sarah Piper organised a two-day Blender3D workshop led by Dr. Brady Johnston, biochemist and Blender-in-Science expert. There were 32 attendees, both in person and zoom (University of Wollongong, University of Queensland, University of Sydney and Griffith). Due to the large number of participants, we also had six able assistants (who had completed the February workshop) who helped to facilitate training across the two days; thanks for volunteering Dr Sarah Piper, Dr Josh Hardy, Dr Sepideh Valimehr, Dr Brian Cary, Dr Jesse Mobbs and Dr Jason Cao.



Working hard on their renders in the Blender workshop, day 2



Blender3D workshop (L to R): Dr Jesse Mobbs, Dr Jason Cao, Dr Brian Cary, Dr Sarah Piper, Brady Johnson, Dr Josh Hardy

Blender is a free and open-source 3D computer graphics software (<https://www.blender.org>) used for creating 3D animation movies and video games. For us, however, it is also a useful tool to create engaging scientific renders. In the workshop, Brady taught the group how to use the software interface as well as presenting his own Molecular Nodes add-on, which makes it easy to load structural data, such as PDB files, into Blender.

The workshop results were stunning!

Thanks so much to Brady for coming all the way from Perth to teach us how to use Blender3D.

Industry Engagement

- Prof Patrick Sexton and Prof Denise Wootten: visit to Boehringer Ingelheim for collaborator meetings, 8th-9th June, 2023, Biberach, Germany.
- Prof Denise Wootten: Invited talk "Linking structure to function - GLP-1R biased agonism and allosteric modulation" Boehringer Ingelheim, 8th-9th June, 2023, Biberach, Germany.
- Dr Winnie Tan: chaired a virtual presentation of Chameleon, high speed plunger with SPT LabTech, "Delivering more routine sample optimization for cryo-EM", delivered by Dr Paul Thaw. 13th April 2023.
- Members and ICHDRs continue to have regular project meetings with their respective industry partners (Boehringer Ingelheim, Astex, Servier, Astra Zeneca, Dimerix and Pfizer).

International Conference Presentations

Felix Bennetts: Oral presentation "Using Cryo-EM to solve the P2X1 receptor structure - a target for male contraception." World Congress of Pharmacology (WCP2023), 2-7 July, 2023 Glasgow, UK.

Prof. Arthur Christopoulos: Keynote Lecture "Allosteric Drug Discovery: From Theory To Practice". World Congress of Pharmacology (WCP2023), 2-7 July, 2023 Glasgow, UK.

Prof. Chris Langmead: Oral presentation "Academic drug discovery: misnomer or master-stroke?" World Congress of Pharmacology (WCP2023), 2-7 July, 2023 Glasgow, UK.

Prof. Patrick Sexton: Keynote presentation "Advancing GPCR drug discovery using cryo-EM". 26th Swedish Conference on Macromolecular Structure & Function (SWEPROT), June 16-22, 2023, Tällberg, Sweden.

Prof. Patrick Sexton: Oral presentation "Understanding structure and activation of amylin and calcitonin receptors". World Congress of Pharmacology (WCP2023), 2-7 July, 2023 Glasgow, UK.

Dr David Thal: Invited talk "Where the allosteric modulators are". 11th Adrenoceptor Symposium, June 30-July 1, 2023 Glasgow, UK.

Dr David Thal: Oral presentation "Discovery of novel allosteric binding sites for selective allosteric modulators at the M5 mAChR". World Congress of Pharmacology (WCP2023), 2-7 July, 2023 Glasgow, UK.

Prof Denise Wootten: Invited talk "Structural approaches to deciphering the nature of Class B receptor biology." Gordon Research Conference, "Molecular Pharmacology: Progressive Technologies and Approaches Revealing Novel GPCR Biology and Drug Development Potential", Jun 11 - 16, 2023, Les Diablerets, Switzerland.

Prof Denise Wootten: Invited talk "Mechanisms of signalling and biased agonism in G protein-coupled receptors" World Congress of Pharmacology (WCP2023), 2-7 July, 2023 Glasgow, UK.

Dr Alice Shin: Poster presentation "Structural investigation of multi-drug resistance ABC transporter CalbCDR1 of *Candida albicans*". Gordon Research Conference, "Mechanisms of Membrane Transport: Structure, Dynamics and Allosteric Regulation". Jun 18 - 23, 2023, Les Diablerets, Switzerland.

Dr Elva Zhao: Poster presentation "RGS proteins, new player in the class B game?" Gordon Research Conference, "Molecular Pharmacology: Progressive Technologies and Approaches Revealing Novel GPCR Biology and Drug Development Potential", Jun 11 - 16, 2023, Les Diablerets, Switzerland.

Academic Seminar Presentations

Dr. Joe Brock, invited seminar. "The Structural basis of multi-drug transport: A story of a SynBio curious structural biologist." May 9, 2023, CCeMMP Seminar Series 2023

Dr. Sarah Piper, invited seminar. "Seeing is believing: Visualising dynamics of membrane receptors using structural biology data in 3D animations." June 16, 2023 Chemistry Society, University of Sydney, Sydney.

Dr. Sarah Piper, invited seminar. "Membranes under the lens: Using structural biology data to visualise receptor dynamics." June 22, 2023 Division of Biomedical Science and Biochemistry, ANU, Canberra.

Prof. Renae Ryan, invited seminar. "The split personality of glutamate transporter: a chloride channel and a transporter." June 13, 2023, CCeMMP Seminar Series 2023

Social Media



Publications

New Publications

Bumbak F, Bower JB, Zemmer SC, Inoue A, Pons, M, Paniagua JC, Yan F, Ford J, Wu H, Robson SA, Barthgate RAD, Scott DJ, Google PR, Ziarek JJ (2023). Stabilization of pre-existing neurotensin receptor conformational states by β -arrestin-1 and the biased allosteric modulator ML314. *Nat Commun* 14, 3328. <https://doi.org/10.1038/s41467-023-38894-8>

Jörg M, van der Westhuizen ET, Choy KHC, Shackelford DM, Khajehali E, Tobin AB, **Thal DM**, Capuano B, **Christopoulos A**, Valant C, Scammells PJ (2023). Design, synthesis and evaluation of novel 2-phenyl-3-(1H-pyrazol-4-yl)pyridine positive allosteric modulators for the M4 mAChR. *Eur. J. Med. Chem* Oct 5; 258: 115588 DOI: [10.1016/j.ejmech.2023.115588](https://doi.org/10.1016/j.ejmech.2023.115588) Epub 2023 Jul 1.

Pham V, Jansen MCCH, Thompson G, Heitman LH, **Christopoulos A**, **Thal DM**, Valant C (2023). Role of conserved tyrosine lid residues in the activation of the M2 muscarinic acetylcholine receptor. *Mol. Pharm.* June 22. DOI: [10.1124/molpharm.122.000661](https://doi.org/10.1124/molpharm.122.000661)

Tran M, Yang K, **Glukhova A**, Holinstat M, Holman T. Inhibitory investigations of acyl-CoA derivatives against human lipoxygenase isozymes. *Int J Mol Sci.* 2023 Jun 30;24(13):10941. doi: [10.3390/ijms241310941](https://doi.org/10.3390/ijms241310941).

Vuckovic Z, Wang J, Pham V, **Mobbs JI**, **Belousoff MJ**, Bhattarai A, **Burger WAC**, Thompson G, Yeasmin M, Nawaratne V, Leach K, van der Westhuizen ET, Khajehali E, Liang Y-L, **Glukhova A**, **Wootten D**, Lindsley CW, Tobin A, **Sexton P**, Danev R, Valant C, Miao Y, **Christopoulos A**, **Thal DM** (2023) Pharmacological hallmarks of allostery at the M4 muscarinic receptor elucidated through structure and dynamics. *eLife* May 30;12:e83477 doi: [10.7554/eLife.83477](https://doi.org/10.7554/eLife.83477).

Vuillemot R, **Rouiller I**, Jonić S. MDTOMO method for continuous conformational variability analysis in cryo electron subtomograms based on molecular dynamics simulations. *Sci Rep.* 2023 Jun 30;13(1):10596. doi: [10.1038/s41598-023-37037-9](https://doi.org/10.1038/s41598-023-37037-9).

Xu Z-Q, Jetgic S, Lo ATY, **Pradhan AC**, **Brown SHJ**, **Bouwer JC**, Ghodke H, Lewis PJ, **Tolun G**, Oakley AJ, **Dixon NE** (2023). Structural characterisation of the complete cycle of sliding clamp loading in *Escherichia coli* *BioRx* July 21, 2023 doi: <https://doi.org/10.1101/2023.07.20.549978>.

Yu H, Angelova A, Angelov B, Dyett B, Matthews L, Zhang Y, Mohamad ME, Cai X, **Valimehr S**, Drummond CJ, Zhai J (2023). Real-time pH-dependent self-assembly of ionisable lipids from COVID-19 vaccines and in situ nucleic acid complexation. *Angewandte Chemie International Edition*, June 30. <https://doi.org/10.1002/ange.202304977>.

Updated Publications

Kreida S, Narita A, **Johnson MD**, Tocheva EI, Das A, **Ghosal D**, Jensen GJ. Cryo-EM structure of the *Agrobacterium tumefaciens* T4SS-associated T-pilus reveals stoichiometric protein-phospholipid assembly. *Structure*. 2023 Apr 6;31(4):385-394.e4. doi: [10.1016/j.str.2023.02.005](https://doi.org/10.1016/j.str.2023.02.005).

Cary BP, Zhang X, Cao J, Johnson RM, Piper SJ, Gerrard EJ, Wootten D, Sexton PM. New insights into the structure and function of Class B1 GPCRs. *Endocr Rev*. 2023 May 8;44(3):492-517. doi: [10.1210/endrev/bnac033](https://doi.org/10.1210/endrev/bnac033).

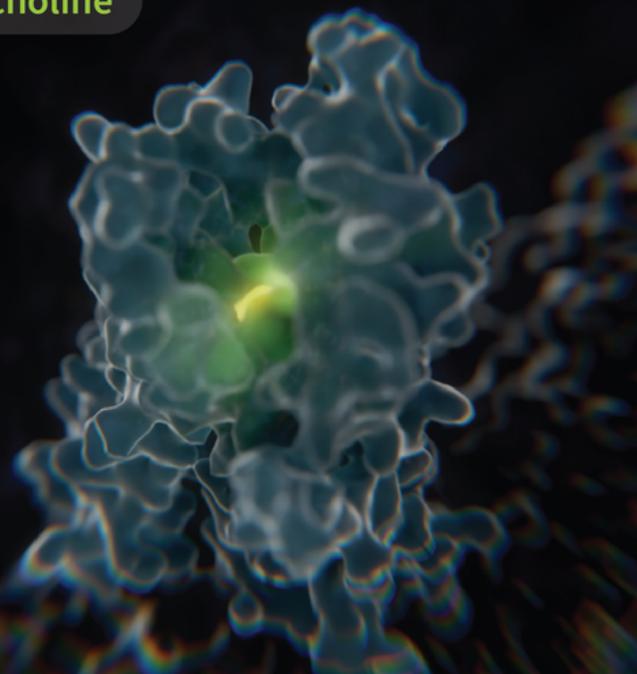
Deposited Structures

Jesse Mobbs, Matthew Belousoff, Alisa Glukhova, Patrick Sexton, David Thal
7TRS, 7TRK, 7TRP, 7TRQ

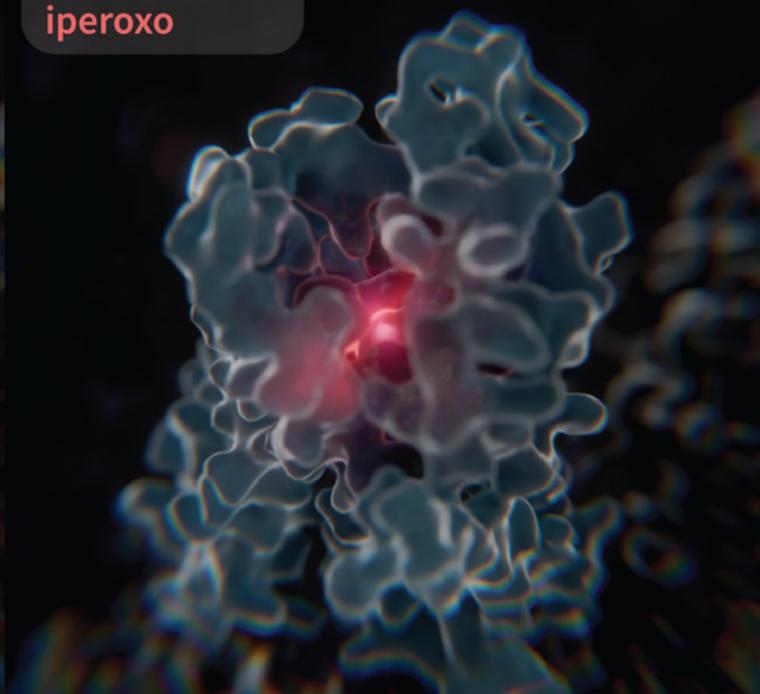
Jesse Mobbs, Matthew Belousoff, Alisa Glukhova, Patrick Sexton, David Thal
EMD-26102, EMD-26099, EMD-26100, EMD-26101

CCeMMP Cryo-EM Structure Image Gallery

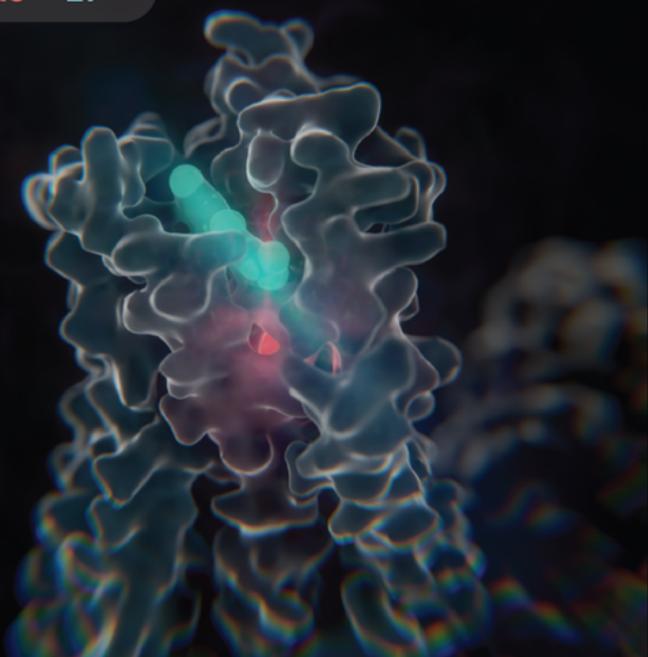
PDB: 7TRS
acetylcholine



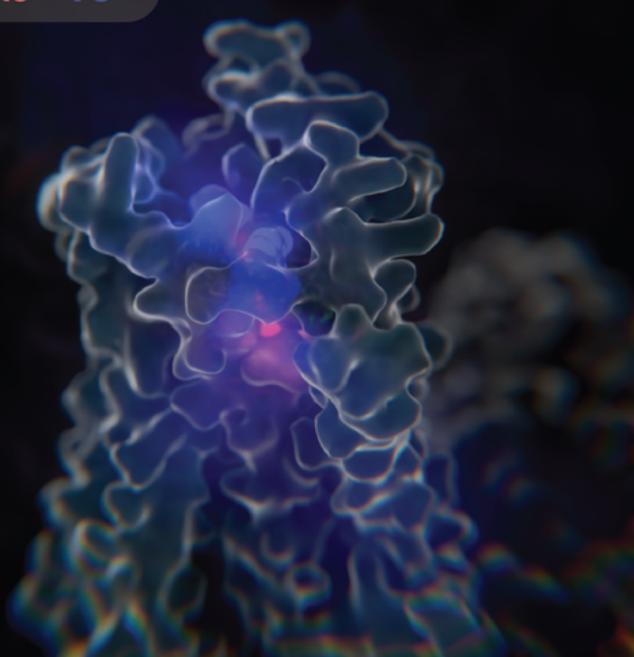
PDB: 7TRK
iperoxo



PDB: 7TRP
iperoxo + LY



PDB: 7TRQ
iperoxo + VU



The M4 muscarinic Acetylcholine Receptor in complex with endogenous agonist (acetylcholine) or high affinity agonist (Iperoxo), with and without positive allosteric modulators (LY or VU)

Image credit: Sarah Piper
(@SarahJ_Piper, @PiperProteins)