

Nicholas J. Fowler

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Education

- PhD Biophysics**, University of Manchester 2014–2018
Thesis: Investigating the role of electrostatic interactions in modulating protein function
Supervisors: Jim Warwicker, Sam de Visser and Chris Blanford
- MSc Physics**, University of Manchester 2012–2014
Thesis: Experimental confirmation of a Kibble-Zurek scaling law in a nematic liquid crystal
Supervisors: Ingo Dierking and Tobias Galla
- PGCE Physics Secondary**, University of Manchester 2011–2012
Dissertation: Teaching strategies enabling pupils with moderate learning difficulties to learn more effectively
- BSc Physics**, University of Manchester 2007–2010
Dissertation: The physics of traffic jams

Research Experience

- Research Associate**, Molecular Biology and Biotechnology, University of Sheffield 2018–2021
My current research involves developing computational methods to validate protein structures solved using NMR. NMR protein structures are important because they represent proteins in solution and include a high proportion of small proteins with under-represented folds. However, there is no reliable way to determine the accuracy of NMR protein structures deposited into the Protein Data Bank (PDB). This means that many researchers simply do not use them e.g. for structure-based drug discovery. I developed a method, Accuracy of NMR Structures Using Rigidity and RCI (ANSURR), to address this need. It works by comparing protein flexibility obtained from chemical shifts, with that predicted from the structure, using the mathematical theory of rigidity. A noteworthy conclusion was that the most common measure of structural similarity, backbone RMSD, misses many important differences relating to side chain position and hydrogen bond geometry - which my method is sensitive to. ANSURR can therefore guide NMR spectroscopists to improve this crucial aspect of their structures. The method is freely available here: github.com/nickjf/ANSURR, and validation scores for structures deposited in PDB can be found on my webserver ansurr.com. I am now working on incorporating machine learning algorithms to improve the ANSURR's scoring function and how ANSURR can be used to identify and fix errors in protein structures predicted by the latest AI-based methods.
- PhD Biophysics**, School of Chemistry, University of Manchester 2014–2018
I applied different computational methods (QM/DFT, molecular dynamics and continuum electrostatics) to model metalloproteins with potential biotechnological applications. I developed a method to predict the reduction potential of copper protein mutants and experimentally tested these predictions using techniques in molecular biology and electrochemistry. In collaboration with EPR spectroscopists at Aix-Marseille University, I performed molecular dynamics simulations in a combined experimental/computational study looking for the hypothesised closed conformation of a fruit-ripening enzyme. My simulations revealed that we had not observed a closed conformation and instead found multiple different open conformations.
- MSc Physics**, School of Physics, University of Manchester 2012–2014
I used nematic liquid crystals to validate a scaling relation for topological defect formation in symmetry-breaking phase transitions.

Publications

NJ Fowler, A Sljoka, MP Williamson. The accuracy of NMR protein structures in the Protein Data Bank. *Structure - accepted* (2021) 10.1016/j.str.2021.07.001

NJ Fowler, A Sljoka, MP Williamson. A method for validating the accuracy of NMR protein structures. *Nature Communications* 11, 6321 (2020). (**Featured in Editors' Highlights**)

N Iwakawa, NJ Baxter, DCC Wai, **NJ Fowler**, RAV Morales, K Sugase, RS Norton, MP Williamson. Conformational exchange in the potassium channel blocker ShK. *Scientific Reports* 9(1), 1-8 (2019).

E Fournier, S Tachon, **NJ Fowler**, G Gerbaud, P Mansuelle, P Dorlet, SP de Visser, V Belle, AJ Simaan, M Martinho. The Hunt for the Closed Conformation of the Fruit-Ripening Enzyme 1-Aminocyclopropane-1-carboxylic Oxidase: A Combined Electron Paramagnetic Resonance and Molecular Dynamics Study, *Chemistry–A European Journal* 25(60), 13766-13776 (2019). (**A 'Hot Paper' as chosen by editors**)

A Timmins, **NJ Fowler**, J Warwicker, GD Straganz, SP de Visser. Does substrate positioning affect the selectivity and reactivity in the hectochlorin biosynthesis halogenase? *Frontiers in chemistry* 6, 513 (2018).

NJ Fowler, CF Blanford, SP de Visser, J Warwicker. Features of reactive cysteines discovered through computation: from kinase inhibition to enrichment around protein degrons. *Scientific Reports* 7(1), 1-12 (2017).

NJ Fowler, CF Blanford, J Warwicker, SP de Visser. Prediction of reduction potentials of copper proteins with continuum electrostatics and density functional theory. *Chemistry–A European Journal* 23(61), 15436-15445 (2017).

NJ Fowler, I Dierking. Kibble–Zurek scaling during defect formation in a nematic liquid crystal. *ChemPhysChem* 18(7), 812-816 (2017).

Funding, Prizes and Awards

Poster Prize , EMBO Workshop, Advances and Challenges in Biomolecular Simulations	2021
Summer Student Bursary (£2080) , Physics of Life Network 2	2019
Biomedical Vacation Scholarship (£1600) , Wellcome Trust (awarded but I declined)	2019
Travel Award , NMR in Biophysics and Molecular Biology, Uni. of Leeds	2019
Talk Prize and Travel Award , MGMS Young Modellers Forum, Uni. of Greenwich	2017
Talk Prize , School of Chemistry PhD Conference, Uni. of Manchester	2017
Talk Prize , BBSRC/MRC DTP PhD Conference, Uni. of Manchester	2017
Poster Prize , Reson8 2nd Biophysical and Biochemical Symposium, Uni. of Leeds	2017
Outstanding Contribution to Public Engagement , Better World Awards, Uni. of Manchester	2016
Talk Prize , Computational and Evolutionary Biology Symposium, Uni. of Manchester	2015
BBSRC DTP PhD Studentship	2014–2018

Invited Talks

CCPN Conference, Ambleside Title: Validating NMR proteins structures with ANSURR	Aug 2021
RPI NMR Methods Workshop, Rutgers (online) Title: Protein structure validation Assessment with ANSURR	Jun 2021
ICMRBS ECR Webinar Series Title: Is your NMR protein structure accurate? We have the ANSURR!	Apr 2021
European Bioinformatics Institute (EMBL-EBI), Cambridge Title: Validation of NMR protein structures using structural rigidity theory and random coil index	Jun 2019

Title: Validation of NMR protein structures using structural rigidity theory and random coil index

Research Activity

- Poster** presented at EMBO Advances and Challenges in Biomolecular Simulations, Online 2021
 Title: Validating NMR protein structures using structural rigidity theory and random coil index
- Talk** at ICMRBS Early Career Researcher Webinar, Online 2021
 Title: Is your NMR protein structure accurate? We have the ANSURR!
- Poster/Flash Talk** at Reson8 5th Biophysics and Biochemistry Symposium, Uni. of York 2020
 Title: Is your NMR protein structure accurate? We have the ANSURR!
- Attended/Summer student Poster** presented at Physics of Life Town meeting, The Royal Society 2019
 Title: Investigating the flexibility of protein regions containing post-translationally modified cysteines
- Poster** presented at the European Conference on Computational Biology, Uni. of Basel 2019
 Title: Validating NMR protein structures using structural rigidity theory and random coil index
- Invited Seminar** given at the European Bioinformatics Institute (EMBL-EBI), Cambridge 2019
 Title: Validation of NMR protein structures using structural rigidity theory and random coil index
- Poster** presented at NMR in biophysics and molecular biology conference, Uni. of Leeds 2019
 Title: Validation of NMR protein structures using structural rigidity theory and random coil index
- Invited Talk** given at Reson8 4th Biophysics and Biochemistry Symposium, Uni. of Sheffield 2019
 Title: Validation of NMR protein structures using structural rigidity theory and random coil index
- Attended** ICMRBS 2018, University College Dublin 2018
- Academic Visit** Kwansai Gakuin University and Osaka University, Japan 2018
 2 week visit to discuss project with collaborators and PDBj
- Poster/Flash Talk** at Reson8 3rd Biophysics and Biochemistry Symposium, Uni. of Manchester 2018
 Title: Features of reactive cysteines discovered from computation
- Talk** given at MGMS Young Modellers Forum, Uni. of Greenwich 2017
 Title: Prediction of reduction potentials of copper proteins with continuum electrostatics and density functional theory
- Poster** presented at QM/MM Methods and Applications, Uni. of Manchester 2017
 Title: Prediction of reduction potentials of copper proteins with continuum electrostatics and density functional theory
- Talk** given at BBRSC/MRC DTP PhD Conference, Uni. of Manchester 2017
 Title: Biophysical correlates of lysine acetylation
- Talk** given at School of Chemistry PhD Conference, Uni. of Manchester 2017
 Title: Prediction of reduction potentials of copper proteins with continuum electrostatics and density functional theory
- Poster** presented at Reson8 2nd Biophysics and Biochemistry Symposium, Uni. of Leeds 2017
 Title: Modulating the reduction potential of copper proteins

- Poster** presented at Protein Electrostatics Berlin, Freie Universität Berlin 2016
 Title: Modulating the reduction potential of copper proteins
- Poster** presented at Dalton 2016: Inorganic Reaction Mechanisms Discussion Group, Uni. of Oxford 2016
 Title: Modulating the reduction potential of copper proteins
- Attended** Reson8 Biophysics and Biochemistry Symposium, Uni. of Liverpool 2016
- Talk** given at Computational and Evolutionary Biology Symposium, Uni. of Manchester 2015
 Title: Modulating the reduction potential of copper protein mutants
- Poster** presented at British Liquid Crystal Society Annual Conference, Durham University 2014
 Title: Experimental confirmation of the Kibble-Zurek mechanism in a nematic liquid crystal

Conference and seminar organisation

- ICMRBS Early Career Researcher Webinars** 2020–present
 – I jointly organise the monthly ICMRBS Early Career Researcher Webinars which was highlighted in an editorial in the Journal of Magnetic Resonance (10.1016/j.jmr.2020.106854).
- PhD and postdoc seminars** 2019–2020
 – I organised a monthly seminar for PhD students and postdocs for department of Molecular Biology and Biotechnology.
- Manchester Energy PhD conference** 2017
 – Organised and chaired the inaugural Manchester Energy PhD conference.
 – Secured funding from the University for printing, catering and prizes.

Peer Review

Biochemical Society Transactions, PSB Proceedings

Teaching Experience

- Level 1/level 2 tutor**, Molecular Biology and Biotechnology, Uni. of Sheffield 2018–present
 – Six six-student tutorials per year.
 – Mark essays, give feedback and facilitate discussion on how to write a scientific essay.
- Student supervision**, Uni. of Manchester and Uni. of Sheffield 2015–present
 – Devised and ran an 8 week project for an undergraduate Summer student, who used this experience to secure a PhD at the University of Oxford.
 – Day-to-day supervision of PhD, MSc and undergraduate students.
- Teaching assistant**, Uni. of Manchester 2015-2017
 – Supported the delivery of maths workshops for BBSRC PhD students.
 – Facilitated "Introduction to reaction mechanisms" tutorials for first year students.
 – Demonstrated how to run and analyse computational chemistry simulations in a workshop for final year students.
- Teacher of science**, Loreto High School, Chorlton, Manchester 2012-2014
 – Taught physics, chemistry and biology to pupils aged 11-16.
 – Graded 'Outstanding' according to Ofsted criteria.
- Academic mentor** 2012–present
 – Mentored a student during their A levels and physics degree at Oxford. They are now in their second year of their PhD at the University of Bristol.
- Private tutor** 2012-2014
 – Taught maths and physics at A level and maths, physics and chemistry at GCSE level.

Outreach and Public Engagement

- Widening participation fellow**, Uni. of Manchester 2014–2018
- Created and delivered workshops, talks and tutorials for University events, schools and science festivals aimed at children less likely to be considering higher education. Topics included astrobiology, protein synthesis, computational population dynamics, rocket building and electrochemical cells.
- Outreach events**, Uni. of Manchester 2014–2018
- Participated in numerous outreach activities outside of my role as a widening participation fellow including training and managing science busking teams, presenting my research to the public at SciBAR events and judging a national science competition at the Big Bang Fair.

Other Experience

- Maintenance of Linux cluster** 2018–present
- I maintain a cluster of 12 Linux computers used by the bioNMR group at the University of Sheffield.
- Motivational speaker**, various schools and colleges in Manchester 2017–2018
- Wrote and delivered interactive lectures talking about my experience of higher education and why students should consider going to University.
- Internship at Manchester Energy**, Uni. of Manchester 2015
- Developed a ‘Sim City’ style computer game where the player controls the National Grid while trying to meet 2050 environmental targets.