

BIOGRAPHICAL SKETCH

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NAME: White, Simon

eRA COMMONS USER NAME (credential, e.g., agency login): SIMONWHITE

POSITION TITLE: Assistant Professor

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	END DATE MM/YYYY	FIELD OF STUDY
University of Hertfordshire, Hatfield, Hertfordshire	BS	07/2005	Applied Biology
University of Leeds, Leeds, West Yorkshire	MS	07/2006	Biosciences
University of Leeds, Leeds, West Yorkshire	PHD	01/2011	Bionanotechnology

A. Personal Statement

I am well placed to pursue the work laid out in this application for cryo-EM time. I have the experience with cryo-electron microscopy needed for success and have three structures deposited in the electron microscopy databank, and I am currently collaborating with others at the University of Connecticut on cryo-electron microscopy data. I am building my collaboration with Chen Xu at the University of Massachusetts facility and have collected data using their microscopes for other projects.

As senior postdoc in the Stockley lab for five years I have the experience of lab, project and budget management to successfully carry out the work described in this proposal. During that time I supervised 8 students. Of the 8 undergraduate students I mentored, all graduated successfully and six of them have continued on to pursue a Ph.D. Obviously I was part of a team that guides these students, but for many of them, the time spent in the lab is their only experience of lab based science and so for all of them to continue on to a Ph.D. highlights my mentorship and supervising abilities. Currently in my lab at UConn I have two graduate students as well as 4 masters students and 4 undergraduates. We have monthly lab meetings where they present their work in a friendly and supportive environment. These lab meetings are an important tool for trouble shooting problems they may have and developing new avenues of research. They are an excellent team and we are well placed to take our preliminary data, as highlighted in this application, and complete the stated aims.

1. Patel N, White SJ, Thompson RF, Bingham R, Weiß EU, Maskell DP, Zlotnick A, Dykeman E, Tuma R, Twarock R, Ranson NA, Stockley PG. HBV RNA pre-genome encodes specific motifs that mediate interactions with the viral core protein that promote nucleocapsid assembly. Nat Microbiol. 2017 Jun 19;2:17098. PubMed PMID: [28628133](#); PubMed Central PMCID: [PMC5495169](#).
2. Shakeel S, Dykeman EC, White SJ, Ora A, Cockburn JJB, Butcher SJ, Stockley PG, Twarock R. Genomic RNA folding mediates assembly of human parechovirus. Nat Commun. 2017 Feb 23;8(1):5. PubMed PMID: [28232749](#); PubMed Central PMCID: [PMC5431903](#).

B. Positions and Honors**Positions and Employment**

2010 - 2017 Post doctoral research assistant, UNIVERSITY OF LEEDS
2017 - Assistant Professor, UNIVERSITY OF CONNECTICUT

Other Experience and Professional Memberships

2018 - Member, American Society for Virology

Honors

2005	Award for Best Result in Year Group, University of Hertfordshire
2006	Award for Best Result in Year Group, University of Leeds
2015	Award for Outstanding Contribution (Oral Presentation) at the XXIV Biennial Conference on Phage/Virus Assembly, Phage and Virus Assembly
2016	Best Poster Award at FASEB: Virus Structure and Assembly, FASEB
2016	Best Poster Award at the Astbury Conversation Symposium, University of Leeds
2016	The Dean's Vacation Research Scholarship, University of Leeds

C. Contribution to Science

1. I was a PDRA at Leeds University for 5 years, working with Professor Peter Stockley, investigating the assembly mechanisms of positive sense-single stranded RNA viruses. My PDRA work has been instrumental in the discovery, characterisation and validation of a completely unsuspected aspect of the assembly mechanisms in this class of RNA viruses. It appears that they all use an evolutionarily conserved mechanism to ensure survival of the virion in the challenging environment of the infected cell. Our recent discovery of this mechanism in a picornavirus forces a re-examination of decades of research that showed that they did not exist in this family of viruses. These discoveries lead naturally to potential real world applications, including the development of novel antiviral therapies and the creation of artificial and completely safe viral vaccines.

The work to identify packaging signals in human pathogens (human parechovirus, hepatitis B and C) had a major collaborative association with Prof. Reidun Twarock at the University of York (Department of Mathematics, Centre for Complex Systems Analysis). It features in high impact papers, which have been published in Nature Communications (Shakeel, Dykeman and White [joint first authors], et al.) and Nature Microbiology (Patel and White [joint first authors], et al.). It was an important corner-stone of a patent on a novel anti-viral strategy (jointly held by the Universities of York, Leeds and Helsinki, US20160326529), for which I am a co-inventor, and a Wellcome Trust Joint Senior Investigator Grant to Profs. Stockley and Twarock as well as a grant from the Medical Research Council for which I was named post-doc. The Nature Communications paper received widespread media coverage and resulted in 32 news articles, including articles in CNN and ABC. Likewise, the Nature Microbiology paper resulted in 7 news articles, a "Behind the paper" article in Nature Microbiology, a specific article in Nature Reviews Microbiology discussing the work (York, A. (2017). Viral Infection: Packing to Leave. Nature Reviews Microbiology. 15: 450-451) and three cryo-electron microscopy structures (in which I did the reconstructions) deposited in the electron microscopy data bank (EMDB-3714, EMD-3715 and EMD-3716).

My other work on packaging signals has focused on one of the model systems for viral assembly: the bacteriophage MS2. Working with Prof. Reidun Twarock (York University) and Prof. Cheng Kao (Indiana University), I was part of the team that identified the 60 coat protein:RNA contacts in MS2, the first time that all of the packaging signals have been identified within a virus (see Direct Evidence for Packaging Signal-Mediated Assembly of Bacteriophage in JMB). Our work was the focus of a review by Peter Prevelige (Follow the Yellow Brick Road: A paradigm Shift in Virus Assembly, 2016, Journal of Molecular Biology, 428: 416-418) which highlights the importance of my work. The entire field of (+)ssRNA viruses must now revisit existing mechanisms of assembly in the light of our work and I expect many groups to start exploring packing signals in other (+)ssRNA viruses.

- a. Patel N, White SJ, Thompson RF, Bingham R, Weiß EU, Maskell DP, Zlotnick A, Dykeman E, Tuma R, Twarock R, Ranson NA, Stockley PG. HBV RNA pre-genome encodes specific motifs that mediate interactions with the viral core protein that promote nucleocapsid assembly. Nat Microbiol. 2017 Jun 19;2:17098. PubMed PMID: [28628133](#); PubMed Central PMCID: [PMC5495169](#).

- b. Shakeel S, Dykeman EC, White SJ, Ora A, Cockburn JJB, Butcher SJ, Stockley PG, Twarock R. Genomic RNA folding mediates assembly of human parechovirus. *Nat Commun.* 2017 Feb 23;8(1):5. PubMed PMID: [28232749](#); PubMed Central PMCID: [PMC5431903](#).
 - c. Stewart H, Bingham RJ, White SJ, Dykeman EC, Zothner C, Tuplin AK, Stockley PG, Twarock R, Harris M. Identification of novel RNA secondary structures within the hepatitis C virus genome reveals a cooperative involvement in genome packaging. *Sci Rep.* 2016 Mar 14;6:22952. PubMed PMID: [26972799](#); PubMed Central PMCID: [PMC4789732](#).
 - d. Rolfsson Ó, Middleton S, Manfield IW, White SJ, Fan B, Vaughan R, Ranson NA, Dykeman E, Twarock R, Ford J, Kao CC, Stockley PG. Direct Evidence for Packaging Signal-Mediated Assembly of Bacteriophage MS2. *J Mol Biol.* 2016 Jan 29;428(2 Pt B):431-48. PubMed PMID: [26608810](#); PubMed Central PMCID: [PMC4751978](#).
2. I have made contributions to the field of bio-nanoscience, exploring bio-templated device construction in collaboration with Profs. Giles Davies and Christoph Wälti at the University of Leeds and Dr. Steve Johnson at the University of York. This utilized the M13 bacteriophage displaying coiled-coil motifs to specifically assemble the phage particle between two electrodes. This work culminated in the publication in the high impact journal of *Angewandte Chemie* studying the structure and assembly of coiled-coils on a 2-D surface. I showed that the assembly of coiled-coils on a surface results in molecular crowding and results in the properties of the coiled-coil changing, i.e. the pH at which they assemble/disassemble is radically changed when crowded onto a 2D surface, as compared to solution. This work has important implications for various 2-D surface techniques, e.g. surface plasmon resonance, and bio-nano diagnostic devices. It has been cited 9 times. The work is continuing using the B23 (circular dichroism) beamline at the diamond light source to study the control of coiled-coil interactions using voltage controlled electrodes with the aim of making a switchable surface for the capture and release of various biological molecules, e.g. specific cell types in cell sorting applications.
 - a. White SJ, Johnson SD, Sellick MA, Bronowska A, Stockley PG, Wälti C. The influence of two-dimensional organization on peptide conformation. *Angew Chem Int Ed Engl.* 2015 Jan 12;54(3):974-8. PubMed PMID: [25413024](#); PubMed Central PMCID: [PMC4506555](#).
 - b. White SJ, Johnson S, Szymonik M, Wardingley RA, Pye D, Davies AG, Wälti C, Stockley PG. Directed surface attachment of nanomaterials via coiled-coil-driven self-assembly. *Nanotechnology.* 2012 Dec 14;23(49):495304. PubMed PMID: [23154792](#); PubMed Central PMCID: [PMC4785676](#).
 - c. White SJ, Morton DW, Cheah BC, Bronowska A, Davies AG, Stockley PG, Wälti C, Johnson S. On-surface assembly of coiled-coil heterodimers. *Langmuir.* 2012 Oct 2;28(39):13877-82. PubMed PMID: [22934624](#); PubMed Central PMCID: [PMC4820041](#).
3. I have used SELEX to identify many novel RNA aptamers which have played an important role in the development of biosensors. The first set of aptamers was involved in the detection of the aminoglycoside antibiotics in collaboration with FERA (Food and Environment Research Agency) in the U.K. who wanted to develop a cheap and quick biosensor for the detection of aminoglycoside antibiotics in milk. Aptamers were discovered that could be used in an assay and detect the antibiotics in the nM range. The second set of RNA aptamers that I developed was for the differentiation between different conformations of amyloid precursors. I successfully identified aptamers that could achieve this.
 - a. Sarell CJ, Karamanos TK, White SJ, Bunka DH, Kalverda AP, Thompson GS, Barker AM, Stockley PG, Radford SE. Distinguishing closely related amyloid precursors using an RNA aptamer. *J Biol Chem.* 2014 Sep 26;289(39):26859-71. PubMed PMID: [25100729](#); PubMed Central PMCID: [PMC4175327](#).
 - b. Derbyshire N, White SJ, Bunka DH, Song L, Stead S, Tarbin J, Sharman M, Zhou D, Stockley PG. Toggled RNA aptamers against aminoglycosides allowing facile detection of antibiotics using gold nanoparticle assays. *Anal Chem.* 2012 Aug 7;84(15):6595-602. PubMed PMID: [22793869](#);

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

17-EXO17_2-0063, NASA White, Simon (PI) 04/01/18-03/31/21

Characterizing the molecular mechanisms and the limits of archaeal gene transfer using *Haloferax volcanii* as a model genetic system

Though archaea are largely unexplored for horizontal gene transfer mechanisms, the model archaeon *Haloferax volcanii* has demonstrated a cell-cell contact mediated DNA transfer mechanism involving cell fusion events that generate a 1N/2N/1N chromosome copy number cycle. This mechanism leads to the recombination of DNA, and changes their genotype and phenotype. How this mechanism functions in the genetically tractable *Haloferax volcanii* is still not understood and many of the features remain elusive. The following specific aims/objectives are proposed to delve deeper into the ambiguities! 1) Identify and characterize components required for cell-cell contact mediated gene exchange (mating) in *Haloferax volcanii*. 2) Identify and characterize components of a homoserine lactone based quorum sensing system in *Haloferax volcanii*. 3) Characterize the limits to HGT via mating in *Hfx. volcanii*.

Role: Co-Investigator

Start-up grant, University of Connecticut White, Simon (PI) 08/23/17-08/23/22

Department Start-up grant.

The purpose of this grant is to set up the PI's laboratory, as well as a facility for cryoEM sample preparation. To be used to fund preliminary studies needed to be competitive for extramural research support

Role: PI

AIMS, ATOMWISE AIMS AWARD White, Simon (PI) 05/31/18-05/31/19

EV71 2C as a drug target

The EV71 crystal structure was used to identify 72+ compounds identified with a customized small molecule virtual screen using Atomwise's AI technology. Atomwise ship these compounds to the researcher for testing in a malachite green ATPase assay.

Role: PI