

This is a repository copy of *The Biophysics of Infection*.

White Rose Research Online URL for this paper:

<https://eprints.whiterose.ac.uk/id/eprint/100137/>

Version: Accepted Version

Article:

Leake, Mark Christian orcid.org/0000-0002-1715-1249 (2016) The Biophysics of Infection. Advances in experimental medicine and biology. ISSN: 0065-2598

https://doi.org/10.1007/978-3-319-32189-9_1

Reuse

Other licence.

Takedown

If you consider content in White Rose Research Online to be in breach of UK law, please notify us by emailing eprints@whiterose.ac.uk including the URL of the record and the reason for the withdrawal request.

The biophysics of infection.

*Mark C. Leake*¹

¹ Biological Physical Sciences Institute (BPSI)

University of York

York

YO10 5DD

United Kingdom

¹ Corresponding author

e-mail: mark.leake@york.ac.uk

Tel: +44 (0)1904 322697

Abstract

Our understanding of the processes involved in infection has grown enormously in the past decade due in part to emerging methods of biophysics. This new insight has been enabled through advances in interdisciplinary experimental technologies and theoretical methods at the cutting-edge interface of the life and physical sciences. For example, this has involved several state-of-the-art biophysical tools used in conjunction with molecular and cell biology approaches which enable investigation of infection in living cells. There are also new, emerging interfacial science tools which enable significant improvements to the resolution of quantitative measurements both in space and time. These include single-molecule biophysics methods and super-resolution microscopy approaches. These new technological tools in particular have underpinned much new understanding of dynamic processes of infection at a molecular length scale. Also, there are many valuable advances made recently in theoretical approaches of biophysics which enable advances in predictive modelling to generate new understanding of infection. Here, I discuss these advances, and take stock on our knowledge of the biophysics of infection and discuss where future advances may lead.

Key words: Single-molecule biophysics, super-resolution

1. Introduction

This volume in the Advances in Experimental Medicine and Biology series consists of a collection of truly cutting-edge research studies, laboratory protocols, experimental and theoretical biophysical techniques and applications in use today by some of the leading international experts in the field of infection research. A key difference in emphasis with this volume compared with other earlier themed collections of infection research is on the emphasis on the utility of *interfacial methods* which increase the underlying physiological

relevance of infection investigation. These developments are manifest through applying methods such as *single-molecule cellular biophysics* which strive to maintain the native physiological context through investigation of living cells (1), especially experimental methods using emerging tools of optical microscopy (2), as well as methods which combine *in vivo*, *in vitro* and computational approaches to probe biological process such as the interaction of proteins with DNA (3), such as the use of fluorescence microscopy methods to probe functional, living cells, especially so using microbial systems as model organisms (4-14). The length scale of precision of experimental protocols in this area has improved dramatically over recent years and many cutting-edge methods now utilize state-of-the-art single-molecule approaches, to enable imaging of biomolecule structure to a precision better the standard optical resolution limit (15), as well as emerging biophysics tools which use single-molecule force spectroscopy (16-20). This volume also includes more complex representative methods to investigate infection through the use of advanced mathematical analysis and computation.

It is clear is that combining pioneering molecular biology, biochemistry, structural biology and genetics methods with emerging, exciting tools from the *younger* areas of biophysics, bioengineering, computer science and biomathematics, that our understanding of the processes of infection are being transformed. Improvements in all of these fields are likely to add yet more insight over the next years in the near future into the complex interactions between multiple key molecular players involved in infection.

Acknowledgments

MCL was assisted by a Royal Society URF and research funds from the Biological Physical Sciences Institute (BPSI) of the University of York, UK.

References

1. M.C. Leake. (2013) The physics of life: one molecule at a time. *Philos Trans R Soc Lond B Biol Sci.* 368(1611):20120248.
2. A.J.M. Wollman, R. Nudd, E.G. Hedlund, et al. (2015) From Animaculum to single molecules: 300 years of the light microscope, *Open Biology.* 5, 150019–150019.
3. A.J.M. Wollman, H. Miller, Z. Zhou, et al. (2015) Probing DNA interactions with proteins using a single-molecule toolbox: inside the cell, in a test tube and in a computer, *Biochemical Society Transactions.* 43, 139–145.
4. T. Lenn, M.C. Leake, and C.W. Mullineaux (2008) Are Escherichia coli OXPHOS complexes concentrated in specialized zones within the plasma membrane?, *Biochemical Society transactions.* 36, 1032–6.
5. M. Plank, G.H. Wadhams, and M.C. Leake (2009) Millisecond timescale slimfield imaging and automated quantification of single fluorescent protein molecules for use in probing complex biological processes., *Integrative biology : quantitative biosciences from nano to macro.* 1, 602–12.
6. S.-W. Chiu and M.C. Leake (2011) Functioning nanomachines seen in real-time in living bacteria using single-molecule and super-resolution fluorescence imaging., *International journal of molecular sciences.* 12, 2518–42.
7. A. Robson, K. Burrage, and M.C. Leake (2013) Inferring diffusion in single live cells at the single-molecule level., *Philosophical transactions of the Royal Society of London. Series B, Biological sciences.* 368, 20120029.
8. S.J. Bryan, N.J. Burroughs, D. Shevela, et al. (2014) Localisation and interactions of the Vipp1 protein in cyanobacteria., *Molecular microbiology.*

9. I. Llorente-Garcia, T. Lenn, H. Erhardt, et al. (2014) Single-molecule in vivo imaging of bacterial respiratory complexes indicates delocalized oxidative phosphorylation., *Biochimica et biophysica acta*. 1837, 811–24.
10. R. Reyes-Lamothe, D.J. Sherratt, and M.C. Leake (2010) Stoichiometry and architecture of active DNA replication machinery in *Escherichia coli*., *Science*. 328, 498–501.
11. A. Badrinarayanan, R. Reyes-Lamothe, S. Uphoff, et al. (2012) In vivo architecture and action of bacterial structural maintenance of chromosome proteins., *Science*. 338, 528–31.
12. A. Wollman and M.C. Leake (2015) Single Molecule Microscopy: Millisecond single-molecule localization microscopy combined with convolution analysis and automated image segmentation to determine protein concentrations in complexly structured, functional cells, one cell at a time, *Faraday Discussions*. 184, 401-424.
13. T. Lenn and M.C. Leake (2015) Single-molecule studies of the dynamics and interactions of bacterial OXPHOS complexes. *Biochim Biophys Acta* 2015 Oct 20. pii: S0005-2728(15)00215-7. doi: 10.1016/j.bbabbio.2015.10.008.
14. Cordes T, Moerner W, Orrit M, Sekatskii S, Faez S, Borri P, Prabal Goswami H, Clark A, El-Khoury P, Mayr S, Mika J, Lyu G, Cross D, Balzarotti F, Langbein W, Sandoghdar V, Michaelis J, Chowdhury A, Meixner AJ, van Hulst N, Lounis B, Stefani F, Cichos F, Dahan M, Novotny L, Leake M, Yang Frsc H. (2015) Plasmonics, Tracking and Manipulating, and Living Cells: general discussion. *Faraday Discussions* (2015) In Press. DOI: 10.1039/C5FD90093J.

15. H. Miller, Z. Zhaokun, A.J.M. Wollman, et al. (2015) Superresolution imaging of single DNA molecules using stochastic photoblinking of minor groove and intercalating dyes, *Methods*.
16. M.C. Leake, D. Wilson, B. Bullard & R.M. Simmons. (2003) The elasticity of single kettin molecules using a two-bead laser-tweezers assay. *FEBS Lett.* 535, 55-60.
17. M.C. Leake, D. Wilson, M. Gautel & R.M. Simmons (2004) The elasticity of single titin molecules using a two-bead optical tweezers assay. *Biophys. J.* 87, 1112-1135.
18. W.A. Linke & M.C. Leake (2004) Multiple sources of passive stress relaxation in muscle fibres. *Phys. Med. Biol.* 49, 3613-3627
19. M.C. Leake, A. Grutzner, M. Kruger & W.A. Linke (2006). Mechanical properties of cardiac titin's N2B-region by single-molecule atomic force spectroscopy. *J Struct Biol.* 155, 263-72.
20. B. Bullard, V. Benes, G. Tzintzuni, M.C. Leake, W.A. Linke & A.F. Oberhauser (2006) The molecular elasticity of the insect flight muscle proteins projectin and kettin. *Proc. Natl. Acad. Sci. U S A.* 103, 4451-6.