Parallel grid computing for modelling mycolic acids from *Mycobacterium tuberculosis*

Athina Meletiou[a], Gareth Shannon[b], Wilma Groenewald[c], Christof Jäger[a], Anna Croft[a]

[a]*Department of Chemical and Environmental Engineering, University of Nottingham, University Park, Nottingham, NG7 2RD, UK*

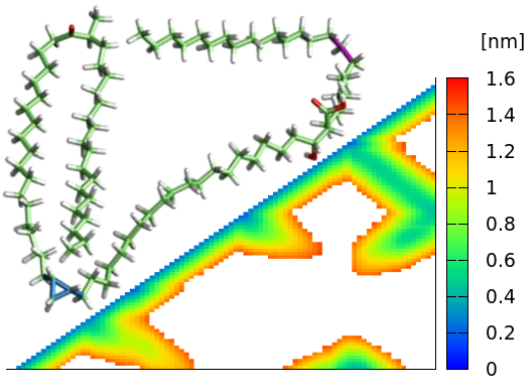
[b]*Centre for Biomolecular Sciences, University of Nottingham, University Park, Nottingham, NG7 2RD, UK*

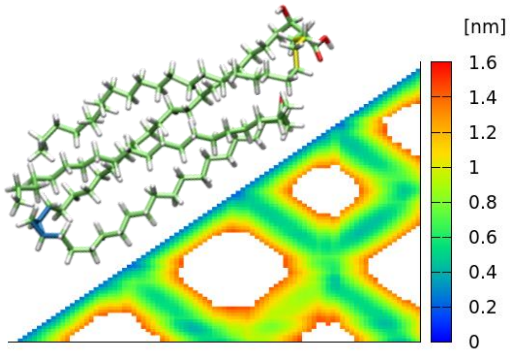
[c]*School of Chemistry, Bangor University, Bangor, Gwynedd, LL57 2UW, UK*

Mycolic acids (MAs) are significantly long fatty acids that occur as dominant constituents in the cell walls of mycobacteria. This group of bacteria includes the pathogen *Mycobacterium tuberculosis* (*M. tb*), the causative agent of the disease tuberculosis (TB). Although largely curable, TB is the world's deadliest disease with 9.6 million new cases and 1.5 million TB-related deaths reported in 2014 alone. The pathogen's defiance of medical treatment, because of its drug resistance, pathogenicity and cell wall impermeability, is largely attributed to the MA's chemical nature[1], which allows *M. tb* to establish a lethal persistent infection. MA's chemical nature primarily determines the molecules' conformational preferences and folding patterns.[2,3] MAs tend to assume different conformations, and this may impact the structure and function of the inner leaflet of the bacterium's cell wall.

Numerous studies[4-6] have focused on the structure-function relationships of MAs, however these are only beginning to be unraveled. We now want systematically to investigate differences in folding dynamics and conformations of a comprehensive set of MAs in order to retrieve insights into their complex structure-function relationships and the correlation of MA conformation and biological function. This information will further provide the basis for more complex and coarse grained simulations of the bacterial cell wall.

A grid computing approach is being used to generate a large set of long-timescale atomistic molecular dynamics (MD) simulations. These simulations provide detailed structural data, which is being collated for a representative set of 166 natural and unnatural MAs. We will present our attempts for efficient analysis of selected examples from the vast amount of simulation data we will retrieve from the grid computing approach and will focus on dihedral clustering and distance matrix analysis methods (example of a semi-folded and a fully folded MA and corresponding carbon atom distance matrix below).





[1] E. Dubnau *et al.*, *Mol Microbiol*, **2000**, *36*, 630-637.
[2] W. Groenewald *et al.*, *Chem Phys Lipids*, **2014**, *180*, 15-22.
[3] M. Villeneuve *et al.*, *Microbiology*, **2013**, *159*, 2405-2415.
[4] S. Vander Beken *et al.*, *Eur J Immunol*, **2011**, *41*, 450-460.
[5] M. Beukes, *et al.*, *Chem Phys Lipids*, **2010**, *163*, 800-808.
[6] V. Rao *et al.*, *J Clin Invest*, **2006**, *116*, 1660-1667.