



1. Title of Case Study:

DFT calculations in applications of NMR crystallography to organic molecules of importance to the pharmaceutical industry and in supramolecular self assembly

2. Grant Reference Number or Facility Name:

EP/J010510/1 and EP/M022501/1: Collaborative Computational Project in NMR Crystallography

EP/K003674/1 Switchable & Biomimetic Self-Assembly of Guanosines: Characterising the Interplay of Structure-Directing Non-Covalent Interactions by Solid-State NMR

3. One sentence summary:

Nuclear Magnetic Resonance (NMR) parameters, notably chemical shift, are calculated for periodic solids using the DFT-based GIPAW method, such that, by linking to solid-state NMR experiment as well as complementary diffraction experiments, new insight is obtained the solid-state structures adopted by pharmaceutical molecules.

4. One paragraph Summary

Nuclear Magnetic Resonance (NMR) is a powerful probe of the local environment of an atomic nucleus, with high-resolution solid-state NMR experiments revealing, via the chemical shift and the through-bond and through-space coupling of the nuclear magnetic moments, for example, the role of intermolecular interactions such as hydrogen bonding and aromatic pi interactions in driving the adoption of a particular crystal packing. This complements diffraction which relies on long-range periodic (i.e., repeating) order. Moreover, solid-state NMR experiment can be combined with first-principles calculations of NMR parameters, notably chemical shielding calculations using the gauge-including projector-augmented wave (GIPAW) that is applicable to periodic solids, in the emerging novel NMR crystallography concept (in 2014 recognised as a new sub area by the International Union for Crystallography and by 5 years renewal funding from EPSRC for the national collaborative computational program for NMR crystallography, www.ccpnc.ac.uk). Brown and his collaborators in industry and academia are at the forefront of showing how the solid-state characterisation of pharmaceuticals can be enhanced by such an NMR crystallography approach.

5. Key outputs in bullet points:

Use of NMR crystallography within the pharmaceutical industry (AstraZeneca, GlaxoSmithKline)

Publications showing complementarity of NMR crystallography to X-ray diffraction

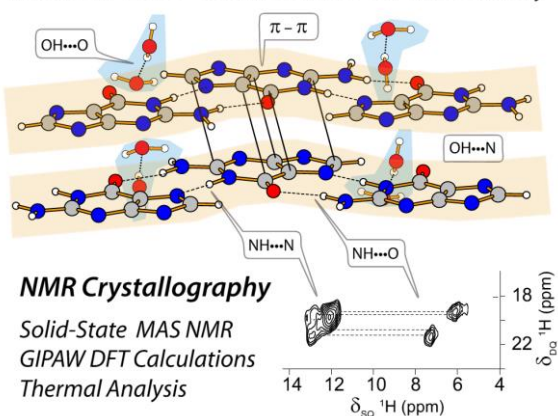
Publications showing use of NMR crystallography to understand the role of intermolecular interactions, e.g., hydrogen bonding and aromatic CH-pi and pi-pi, in directing the specific packing of organic molecules in the solid state

6. Main body text

"Interplay of Noncovalent Interactions in Ribbon-like Guanosine Self-Assembly: An NMR Crystallography Study"

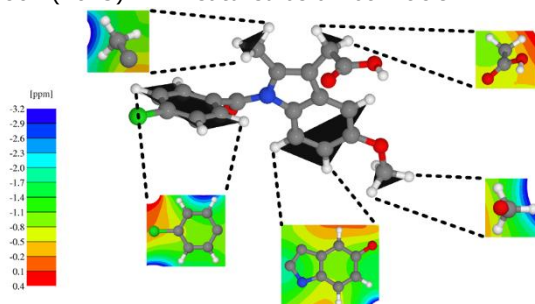
G. N. Manjunatha Reddy, Andrew Marsh, Jeffery T. Davis, Stefano Masiero, and Steven P. Brown
Crystal Growth and Design, 15, 5945–5954 (2015)

Ribbon-Like Guanosine Self-Assembly



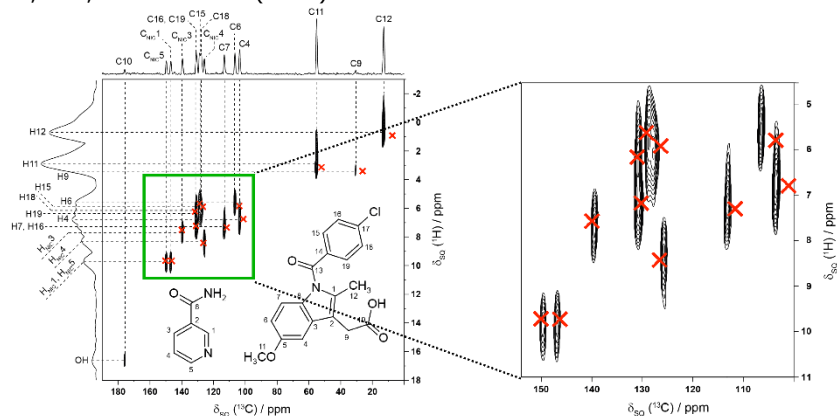
"An NMR crystallography DFT-D approach to analyse the role of intermolecular hydrogen bonding and π - π interactions in driving cocrystallisation of indomethacin and nicotinamide"

Dmytro V. Dudenko, Jonathan R. Yates, Kenneth D. M. Harris and Steven P. Brown
CrystEngComm, 15, 8797–8807 (2013) Featured as a Hot Article

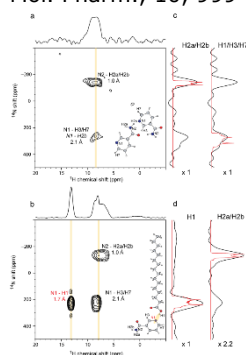


"Exploiting the Synergy of Powder X-ray Diffraction and Solid-State NMR Spectroscopy in Structure Determination of Organic Molecular Solids"

Dmytro V. Dudenko, P. Andrew Williams, Colan E. Hughes, Oleg N. Antzutkin, Sitaram P. Velaga, Steven P. Brown, and Kenneth D. M. Harris
J. Phys. Chem. C., 117, 12258–12265 (2013)



"Probing Hydrogen Bonding in Cocrystals and Amorphous Dispersions Using ^{14}N - ^1H HMQC Solid-State NMR"
Andrew S. Tatton, Tran N. Pham, Frederick G. Vogt, Dinu Iuga, Andrew J. Edwards, and Steven P. Brown
Mol. Pharm., 10, 999-1007 (2013)



7. Names of key academics and any collaborators:

Professor Steven P. Brown, Department of Physics, University of Warwick

Dr Tran N. Pham, GlaxoSmithKline

Dr Leslie P. Hughes, AstraZeneca

Professor Kenneth D. M. Harris, School of Chemistry, University of Cardiff

Professor Jonathan R. Yates, Department of Materials, University of Oxford

8. Sources of significant sponsorship (if applicable):

GlaxoSmithKline EPSRC CASE award, £32k, 36 months starting January 2014

EP/J010510/1 and EP/M022501/1: Collaborative Computational Project in NMR Crystallography

9. Who should we contact for more information?

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