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## *NMR crystallography, diffraction and modeling of small organic molecules*

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Solid-state NMR (SSNMR) is a powerful atomic-level characterization technique able to study the local chemical environment of a nucleus in crystalline/amorphous solids. Toward a better understanding of how small molecules self-assemble in the solid-state and reorganizes to produce its hydrate/anhydrous forms, an experimental SSNMR, X-ray diffraction (XRD), and computational study of the supramolecular assemblies of selected small pharmaceuticals is presented. The effect of crystal packing on the 1H and 13C chemical shifts including nonconventional hydrogen bonds, pi···pi and CH···pi contacts, is studied through computer simulations. It will be shown that NMR chemical shifts are sensitive detectors of hydration/dehydration states in highly insoluble antibiotics.[1] Recently, SSNMR became an important gadget in the process of crystal structure solution in powders. This is a non-trivial task and using powder XRD methods alone may often lead to the wrong structure solution. In this talk, a new hybrid approach for structure determination of crystalline solids, will be presented, based on the combination of SSNMR, XRD and an ensemble of computational-assisted structure solution tools including a genetic algorithm based on evolution-inspired operators repeatedly applied to populations of possible crystal structure solutions that evolve to eventually produce the best new offspring candidates. Such methodologies are successfully applied to challenging cases involving multiple component crystals composed by flexible molecules such as a trihydrate β-lactamic antibiotic [2] and an azole-based co-crystal featuring an hydrogen bond network of α-helixes involving NH···N/CH···π intermolecular interactions. ACKNOLEDGEMENTS: Supported by Fundação para a Ciência e a Tecnologia (FCT), Portuguese National NMR Network (RNRMN), CICECO (PEst-C/CTM/LA0011/2013), FEDER, COMPETE, and University of Aveiro. FCT is greatly acknowledge for the consolidation grant IF/01401/2013.

***[1]*** *Mafra, L., Santos, S. M., Siegel, R., Alves, I., Paz, F. A. A., Dudenko, D., & Spiess, H. W. (2012). JACS, 134(1), 71–74.,* ***[2]*** *Santos, S. M., Rocha, J., & Mafra, L. (2013). Crystal Growth & Design, 13(6), 2390-2395.*

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