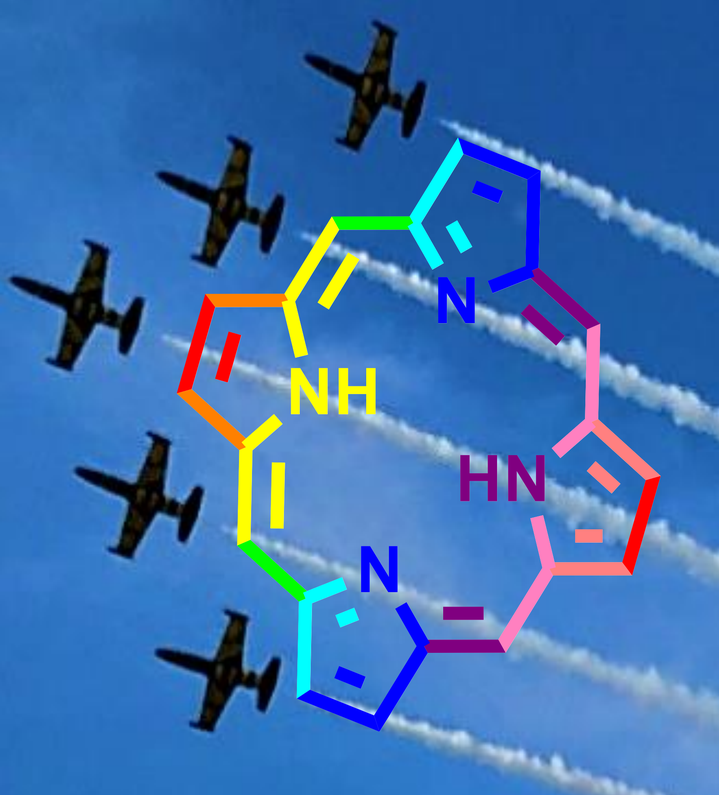
Spectroscopic Analysis of Nonplanar Porphyrin Atropisomers with Specialized Binding Cavities

Karolis Norvaiša, Mathias O. Senge*

*School of Chemistry, Trinity Biomedical Sciences Institute
152–160 Pearse Street, Trinity College Dublin, The University of Dublin, Dublin 2, Ireland

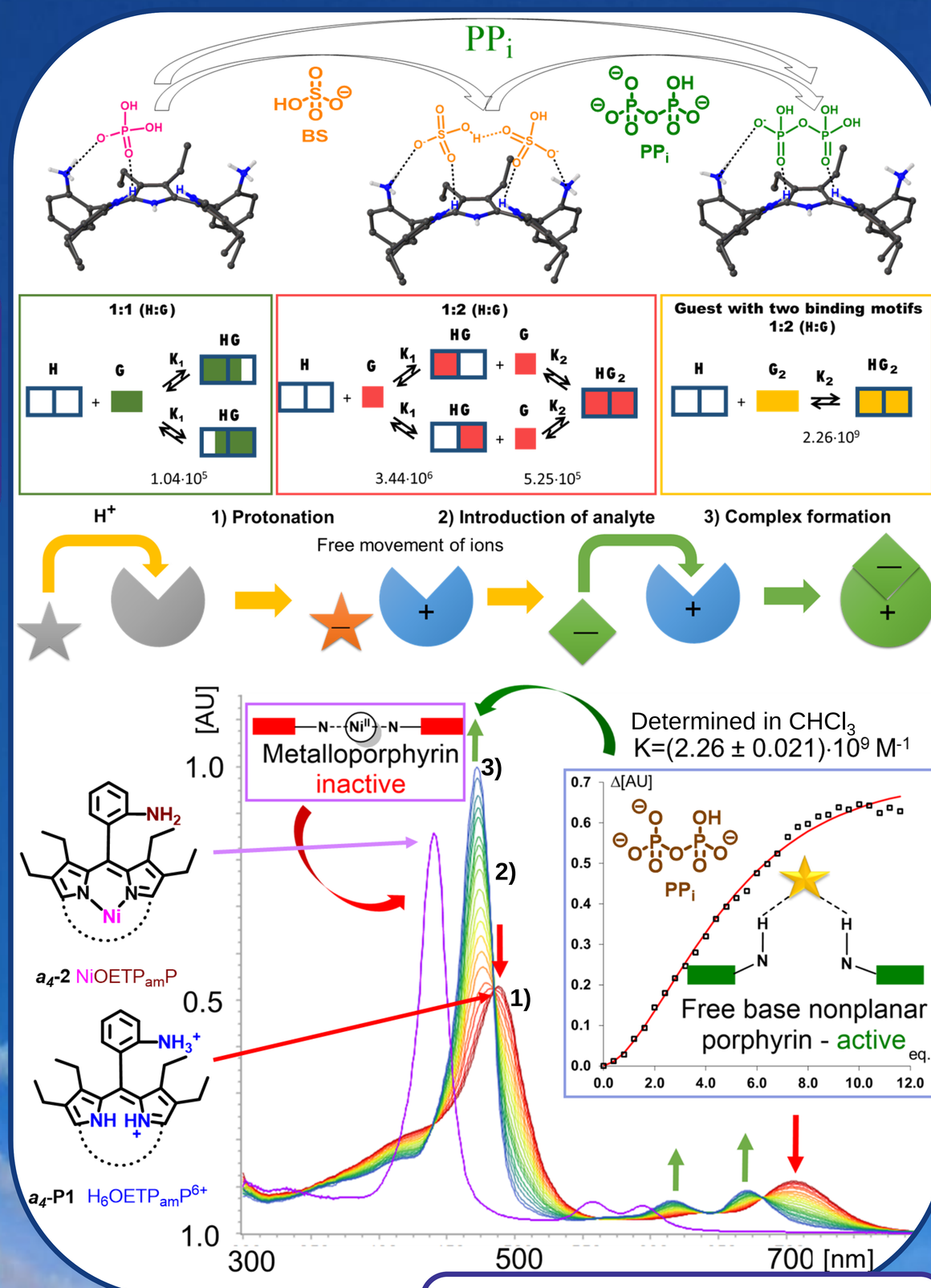
Senge Group

The selectivity and functional variability of porphyrin cofactors are typically based on substrate binding of metalloporphyrins wherein the pyrrole units only serve to chelate the metal ions. Yet, using the free base porphyrin inner core system for other functions is possible through conformational engineering.[1] Detection of these N–H···X-type[2] interactions in porphyrins were limited to X-ray crystallography as solvation and dilution drastically affect weak interactions by dispersing the binding agent to its surroundings. However, specially designing the binding pocket allowed us to develop a switchable probe for various analytes detectable using other spectroscopic methods: UV-vis and ^{1}H NMR



A: As a first step towards porphyrin 'enzyme-like' active centers, a simple colorimetric test highlighted the selectivity [α_4-2,3,7,8,12,13,17,18-octaethyl-5,10,15,20-tetrakis(2-aminophenyl)porphyrin] (α_4-1) to phosphonic and sulphonic moiety containing analytes by the strong solution color changes (brown → green), in the presence of TFA.[3]

B: UV-vis analysis of substrates binding to the inner core of a porphyrin system showed highly saddle distorted porphyrin with peripheral amino receptor groups exhibits exceptionally high affinity upon protonation to the pyrophosphate anion $(2.26 \pm 0.021)\cdot10^9$ M^{-1} and does so in preference to other anions. The inner core system plays an essential role in complex formation as indicated by the lack of UV-vis spectroscopic changes with Ni(II)$OET_{am}PP$ (α_4-2) (metalated analogue of α_4-1).[3]



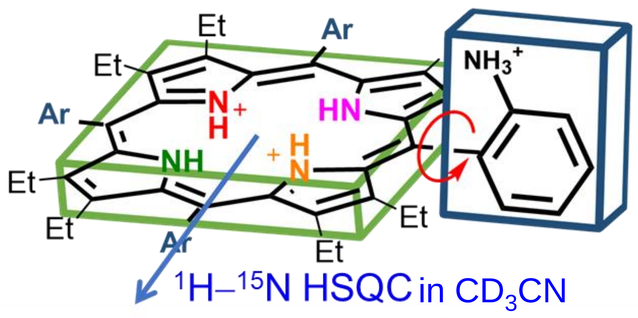
B: UV-Vis Spectroscopy

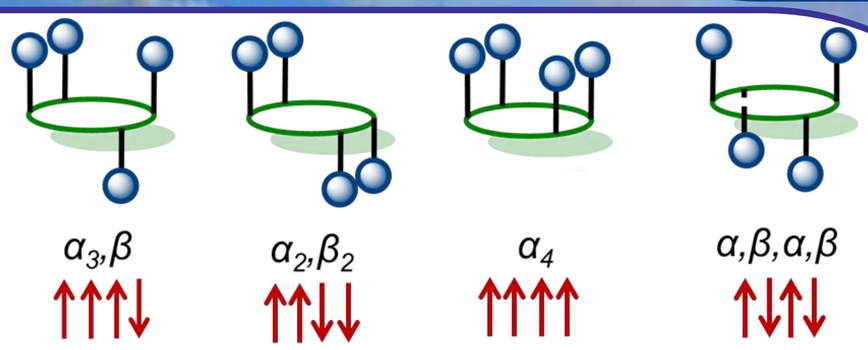
C: A counter anion (benzenesulphonic acid) locks in the anion-selective inner core system and reduces the proton exchange rate, generating static proton signals for higher resolution NMR analysis. This allowed us to report an ideal case study in which all atropisomers can stand in rotation-restricted states.[4]

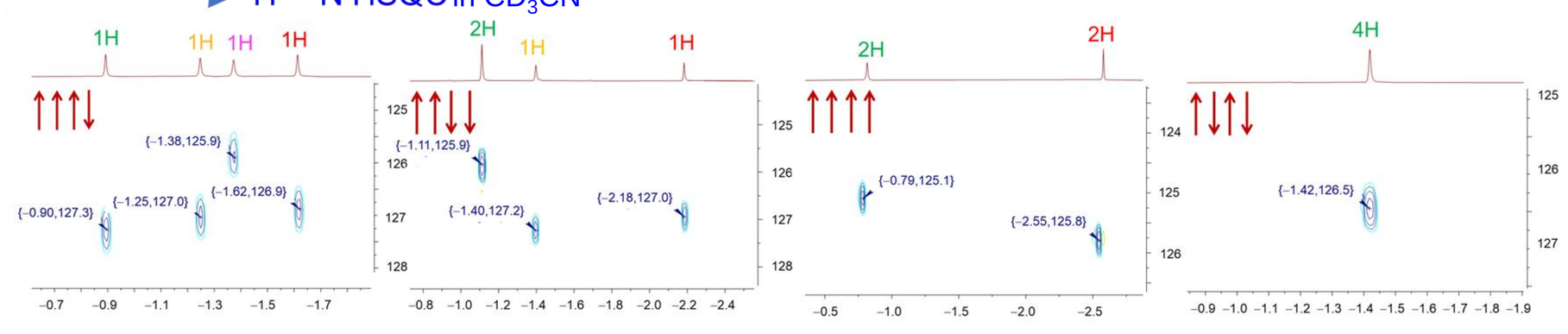
The fingerprint-like ^{1}H and ^{15}N signals were found to be specific for a given rotamer providing intrinsic porphyrin atropisomer characteristics which could be used as a fast identification method for a particular orientation.[4]

The symmetry elements and point-group notions were applied after assigning all the ^{1}H and ^{13}C signals using a variety of 2D NMR techniques such as ^{1}H–^{1}H TOCSY, ROESY, and ^{1}H–^{13}C HSQC, HMBC. The symmetry order was found two-fold lower in comparison to the suggested planar porphyrin point-group notations. The basis for this decrease in symmetry lies in the saddle-shaped deformations of the porphyrins, making distortion a molecular engineering tool to achieve symmetry reduction in macrocycles.[4]

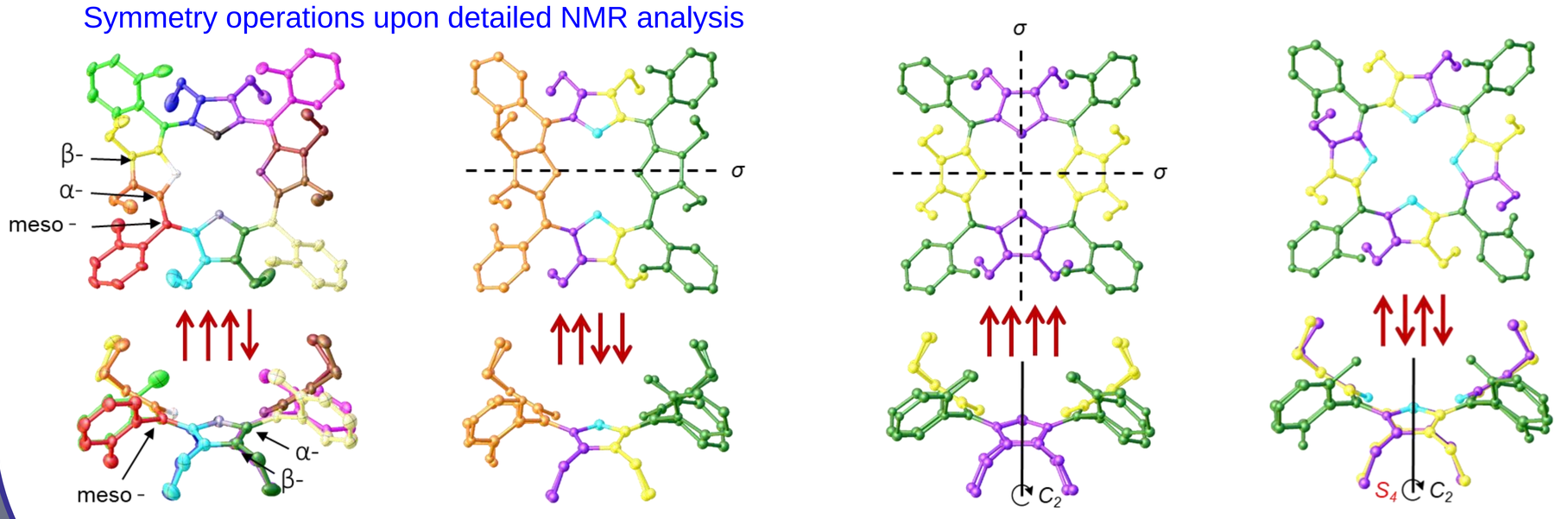
C: NMR Spectroscopy







Symmetry operations upon detailed NMR analysis



Point group {order}	C_1 {1}	C_s {2}	C_{2v} {4}	S_4 {4}
Planar*	C_s {2}	C_{2h} {4}	C_{4v} {8}	D_{2d} {8}

References:
[1] K. Norvaiša, M. Kielmann, M. O. Senge, *ChemBioChem* 2020, *21*, 1779
[2] M. Kielmann, M. O. Senge, *Angew. Chem. Int. Ed.* 2019, *58*, 418.
[3] K. Norvaiša, K. J. Flanagan, D. Gibbons, M. O. Senge, *Angew. Chem. Int. Ed.* 2019, *58*, 16553.
[4] K. Norvaiša, J. E. O'Brien, D. Gibbons, M. O. Senge, *Chem. Eur. J.* 10.1002/chem.202003414

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