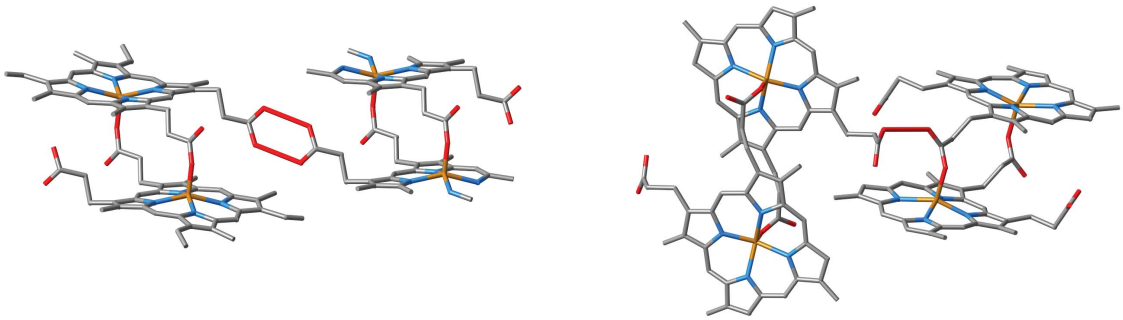
A New Malaria Pigment Structural Motif and Potential Drug Target

*Peter W. Stephens** [a], *Liliana Suárez* [b], *Erin L. Dodd* [b], *David Kuter* [b,c], *and D. Scott Bohle* [b]

[a] *Department of Physics and Astronomy, Stony Brook University, USA;*
[b] *Department of Chemistry, McGill University, Montreal H3A 0B8 CANADA;*
[c] *Dept. of Chemistry and Polymer Science, Stellenbosch University, South Africa.*
**pstephens@stonybrook.edu*

It is well established that the structure of both natural and synthetic hemozoin (malaria pigment or hematin anhydride, HA) is a chain of proprionate-linked dimers of iron(III)(protoporphyrin-IX); this is true also of solvated crystals, and of the partially soluble mesoporphyrin analog in which the vinyl groups are hydrogenated. It is widely regarded, that the quinoline family of antimalarials inhibits of the formation of hemozoin, although the mechanism is still unclear. We have recently obtained the structure of another slightly soluble analog, iron(III)(deuteroporphyrin-IX), in which the vinyl groups are replaced by hydrogen atoms. As determined from powder diffraction data, the crystal is monoclinic, with $Z = 4$.

The deuterohematin anhydride (DHA) structure also comprises proprionate-linked dimers, but the intra-dimer geometry and inter-dimer interactions are significantly different than hemozoin. Influencing precipitation in the direction of the DHA binding motif, in order to increase the solution concentration of heme, could be a new approach to seeking drug targets, complementary to currently pursued mechanisms based on binding to the facets of the growing hemozoin crystal in the parasite's digestive vacuole.



Left: Structure of hematin anhydride. Right: Structure of deuterohematin anhydride

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