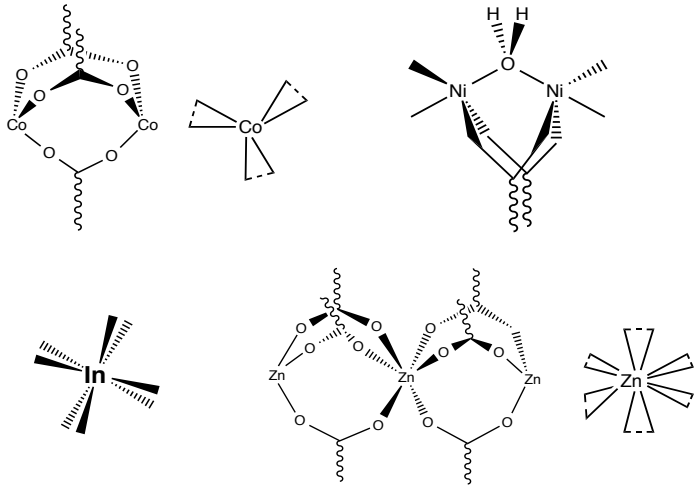
PUBLISHABLE SUMMARY OF CHIRAL MOF

The ChiralMOF project had the aim to develop rationally designed novel nanoporous materials for the separation of enantiomers. The separation of enantiomers is of great importance to industry in the domain of medicine. New treatments often rely on medication consisting of pure enantiomers. Enantiomers separation is extremely challenging as the molecules are nearly identical (shape and properties) and is achieved at great cost by relying on expensive, time consuming and complex processes. Separation through adsorption using chiral stationary phases is a viable alternative to the current technology.
It is the aim of the project to develop novel porous materials that allow for fast, efficient and inexpensive separation of enantiomers. In the past decade, a new class of porous materials was developed: metal-organic frameworks. This new class of materials can be rationally designed, exhibits highly specific properties and may be economically viable and a stable alternative to classical stationary phases. Surprisingly, very little attention has been devoted to the design of homochiral metal-organic frameworks for enantiomer separation prior to the start of the project. The chiral structure of these metal-organic frameworks favors the interaction with one specific enantiomer. The preferential interaction, adsorption, is the basis for an efficient chromatographic purification process.

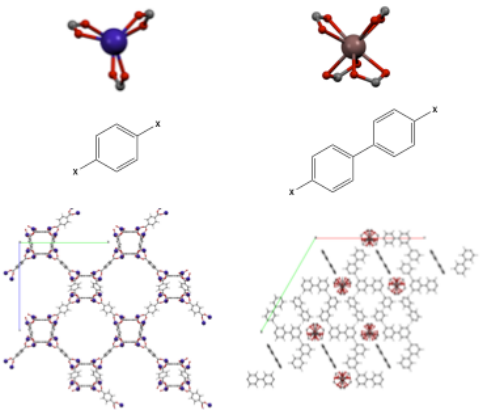
A combination of theoretical and experimental work was proposed in the research project. In order to accurately model functional group interactions, several possibilities were explored with respect to force field parameters and molecular simulation packages. Within the scope of this project, crystal structure for functionalized NU-1000 and NU-900 materials with amino acids and small chiral organic acids were defined, optimized and validated. Force fields for rigid and partially flexible (chiral ligand) are defined. In parallel the molecular adsorbate models were defined based in the OPLS force field. Initial simulation methodology was refined to quantify differences in adsorption interactions between R- and S-isomers and form the basis for screening of existing chiral MOFs (Henry constant calculations) and new hypothetical structures.

The existing literature has been reviewed and chiral MOFs within the CoReMOF database [*Chem. Mater.*, 2014, *26* (21), pp 6185–6192] identified. This effort was done in collaboration with co-workers in the Snurr research group: 73 unique structures out of 164 deposited structures with chiral topology are identified. These include MOFs with chiral linkers but most organic linkers do no contain inherent stereo centers. Several interesting metal nodes (Zn/Cu, Cd, Ni, Co, In) were identified with inherent asymmetry. Some examples are given below.



These metal nodes potentially result in chiral MOFs, even in combination with small and rigid achiral linkers. It was also found that three-connecting linkers with high symmetry are present in most materials with a helix structure. Not surprisingly, in many cases the chirality is the results from non-symmetric N/O-coordination on the metal node by multidentate linkers or ligands. The latter forces the metal node out of its preferred coordination symmetry. While this is an interesting observation, the first two observations are of more interest to the rational design of novel frameworks. The identified metal node and linkers from literature are currently implemented in the Tobacco code [*Chem. Mater.*, 2014, *26* (19), pp 5632–5639] to generate new hypothetical MOFs. A number of homochiral MOF structures was identified without chiral space group or metal node but with one or more chiral linkers. It is interesting to note that very few structures based on a single chiral linker were found. Most homochiral MOF structure are mixed ligand MOFs where the second linker acts as a spacer.

In line with the objectives of the proposal, the de novo design new metal-organic frameworks on a rational basis, based on our findings was done. The chose was to generate a number of structures based on simple building blocks and accessible topologies. The newly generated stuctures were optimized and screened for R/S separation potential. A significant number of structures seem promising, yet not always easily accessible. For example, new topological homologues of H-KUST-1 or MOF-5 were identified but are unlikely to be synthesized given the wide spectrum of synthesis conditions for both materials.



Two examples of novel hypothetical MOFs are given on the right. The nodes itself are asymmetric and taken from examples in the CoRe MOF database (co = blue, In = brown) and known to favor the chiral srs topology. The two linkers are simple in design and widely available. The same combination as for cobalt MOF is experimentally known but with a different topology (both in chiral and non chiral form).

The decision by the fellow and supervisors to maximally benefit from expertise at Northwestern University was made at the start of the fellowship. In the meantime, significant progress was made in the synthesis of novel MOF materials based on the NU-1000 node. This material has an unsaturated metal node and both micro and mesopores. The presence of the mesopores allows for facile diffusion of guest molecules. Novel chiral metal-organic frameworks could be envisioned by incorporating chiral molecules in known MOF materials with that node. Several possible techniques such as solvent assisted ligand exchange (SALE) or incorporation (SALI) could lead to chiral analogues of NU-1000 and NU-900. This has lead to the synthesis of the chiral NU-1000 materials. Amino acids and small organic acids have been chosen as grafted moieties in the framework.

The results of the CoRe MOF database screening were valorized by selecting a number of candidate structures for lab synthesis. This provided a real challenge as not each procedure was equally detailed and some reported structures were obtained from a crystal mixture. The selected materials were based on non-chiral and chiral simple linkers in combination with seemingly more water stable metal nodes such as Co or In. In most cases, a single synthesis batch yielded 50-150mg of MOF material. This effort was only partly successful as results were not always reproducible and several low crystalline

phases were obtained. Of particular interest are cyclodextrin metal-organic structures. These versatile MOF materials are known in several topologies and some adsorption or separation results were available in literature. Several different CD-MOF materials were synthesized, characterized and studied. This work was guided in part by molecular simulations that pointed to a significant theoretical separation potential between topologies. Most of the experimental results were obtained with CD-MOF-1 that shows a clear shape selective behavior for stereo-isomers and to a limited extend for enantiomers, both in our own results and the data obtained through collaboration with the Stoddart group.