In silico Catalyst Design: Using Backbone Diversity

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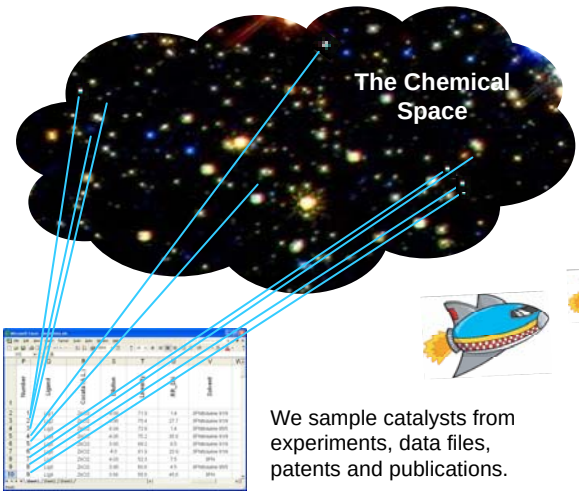
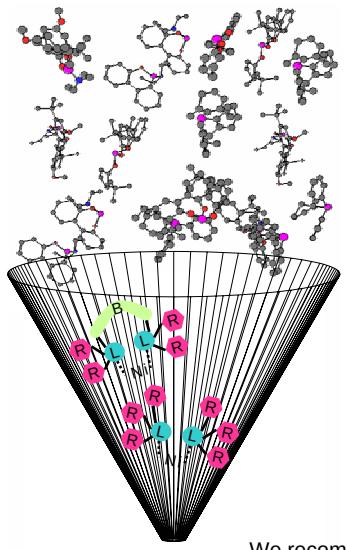
The huge diversity of the multi-dimensional ligand space in homogeneous catalysis can be addressed by isolating the main building block motifs creating a representative set of structures of manageable proportions.[1] This set is then modeled using low-cost 2D and 3D descriptors.[2] Subsets for synthesis are then chosen by maximizing their respective distance in the **descriptor space** using weighted D-optimal design. The D-optimal subset is more diverse than a random sampling.[3] This method can be applied to any metal-ligand catalytic system.



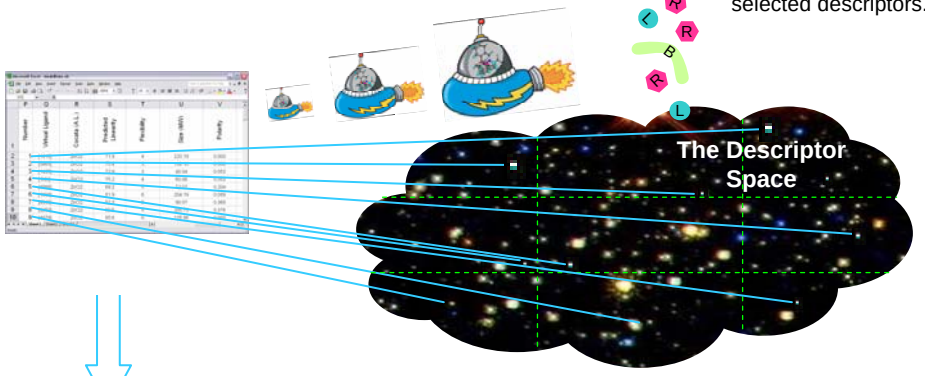
We sample catalysts from experiments, data files, patents and publications.



The catalysts are simplified as 'building blocks' models (residues, metals, backbones, ligands). They must retain the chemical features such as: polarity, size and flexibility.

We recombine these building blocks *in silico*, creating new catalyst libraries, with emphasis on selected descriptors.

Sets of catalysts are then selected using diversity analysis and weighted D-optimal design in the descriptor space.



The new group of catalysts is **better distributed** over the space. They cover a bigger range of the **desired properties** and figures of merit, and displays **structural richness**.

This implies more **diversity**. More chances to get something **new**. But within some limits, defined in the model since the beginning. We think this is the gate to **tailored catalysts design**

1 E. Burello, P. Marion, J.-C. Galland, A. Chamard, G. Rothenberg, *Adv. Synth. Catal.* **2005**, *347*, 803.
2 G. Rothenberg, *Catalysis Today*, **2008**, *137*, 2.
3 A. G. Maldonado, J. A. Hageman, S. Mastroianni and G. Rothenberg, **2008** *Submitted.*

Here we show the application of virtual screening to effectively select diverse catalysts within a tailored descriptor space. Descriptor calculation, *in silico* combinatorial chemistry and weighted D-optimal design are the techniques used to achieve our goal. Currently, we are using these techniques to find better catalysts for the Ni-catalyzed hydrocyanation of butadiene to adiponitrile, a key part of the Nylon 6.6 industrial process.