Modern chemicals that are used in medicinal chemistry are almost exclusively single stereoisomers of an organic molecule. Regulations present in this industry oblige the producers of those chemicals to provide compounds as pure enantiomers. Thus, it is crucial to develop new methods that allow their synthesis in an effective and stereoselective manner. This is why asymmetric catalysis is such a valuable and practical tool and why novel catalysts are being developed widely. The most widespread method used for asymmetric catalysis is a combination of a metal complex with an appropriate chiral ligand, which can yield the desired enantiomerically enriched product. Historically speaking, new catalysts were often discovered rather than rationally designed. Research made during those discoveries generate staggering amount of chemical data, most of which are discarded when specific reaction conditions and validation of a catalytic process are not fruitful. Although the quantity of this data can be overwhelming for a human mind, machine learning algorithms can handle it with ease. Therefore, we postulate that recent advances in chemical Artificial Intelligence (AI) could provide a thoughtful insight into the process of designing a novel metal complex - chiral ligand catalysts.

Our group has been extensively working on developing new catalytic systems for almost two decades. We were able to demonstrate numerous highly stereoselective transformations, but during the development process learned about those which show low or no enantioselectivities at all. This allowed us to accumulate large amounts of such data. We propose that this proprietary collection of results is fed to data-hungry algorithms. In fact, we have been co-developing (with prof. Grzybowski's group) a unique AI methodology to vectorize non-covalent interactions which dictate outcomes of certain catalytic transformations. We believe that our skills, knowledge and the newly developed AI tools can help us rationally design new and more efficient catalysts for organic reactions.

Moreover, our goal is to develop novel catalysts for asymmetric synthesis with the use of less expensive and more environmentally friendly metals: zinc and iron, rather than platinum-group metals that seem to be preferred by the majority of researchers. We propose to demonstrate an AI-guided design and subsequent experimental validation of novel chiral Lewis acids containing zinc and iron cations as well as their catalytic application in selected organic reactions. We base this project proposal on our previous success in applying those metals in asymmetric catalysis. The goal of our research is to overcome issues that we have encountered during prior endeavors in this field and to use a vast database of both positive and negative results that we have obtained previously.

We propose a closed-loop theory-experiment protocol in which (i) AI models trained on the current set of catalysts will be used to predict new catalyst candidates; (ii) these candidates will be synthesized in our laboratory; (iii) the experimental outcomes will be combined with the training set to develop an improved model that will (iv) predict a new candidate for experimental screening. The (i)-(iv) cycle will be repeated until the enantioselectivities are maximized, in effect realizing the AI-guided evolution of an original candidate.