FINAL PUBLISHABLE SUMMARY REPORT

The project is focused on four main objectives; all of them involve the interactions between metal ions and specific peptide mimics called peptoids, which are N-substituted glycine oligomers. In short, the four objectives include: (1) to demonstrate that we can induce folding in peptoids by metal coordination; (2) to design and synthesize higher order conformations of metallopeptoids namely architectures that exceed the secondary structure and represent bundles, tubes and other tertiary structures; (3) to utilize the ease of peptoid synthesis and its backbone versatility in order to control the coordination geometry of metal complexes towards the creation of chiral switches, and (4) to attach organic catalysts to metallopeptoids and use them as intramolecular cooperative catalysts and asymmetric catalysts. Objectives 1, 2 and 4 were completed, however, working towards objective 2 led to some exciting and unexpected results that we are now further developing. Thus, we have worked to achieve some goals that were not defined in the initial proposal rather than focusing on completing objective 3 and therefore objective 3 was not completed.

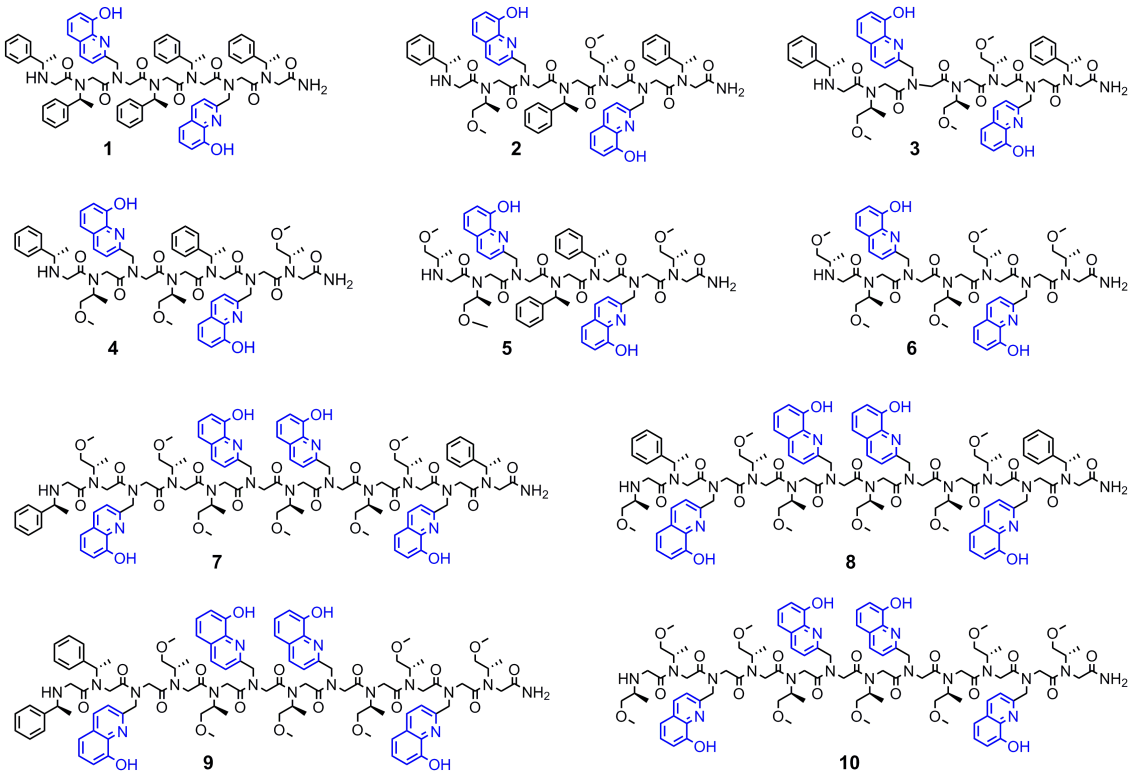

Figure 1. Representation of peptoid sequences designed for folding upon metal coordination.

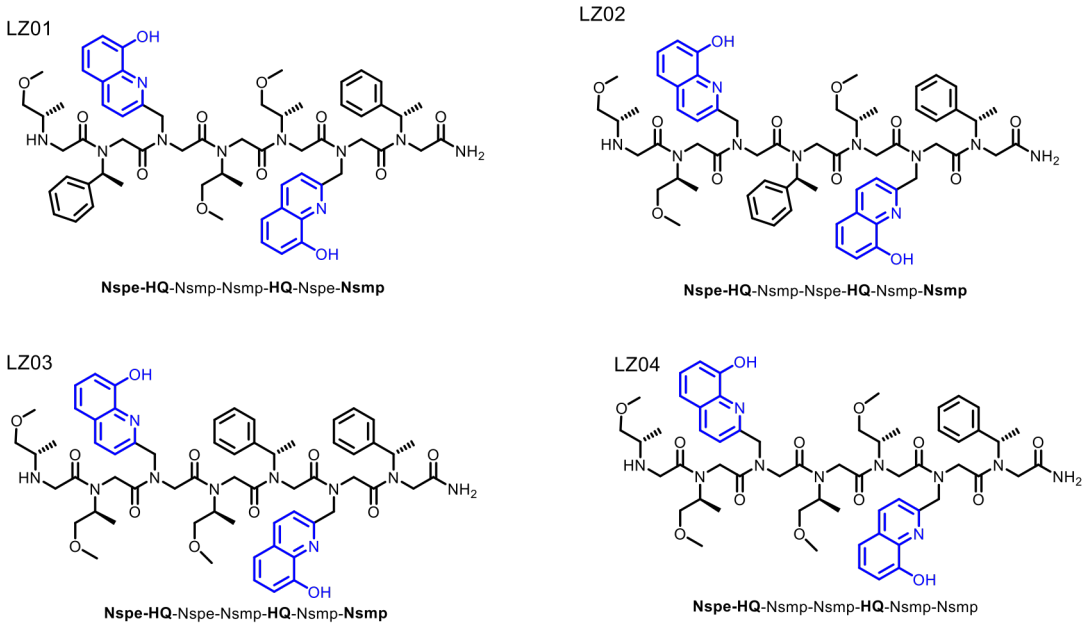

Figure 2. Peptoid sequences designed to evaluate the effect of Nspe groups positions on folding upon metal coordination.

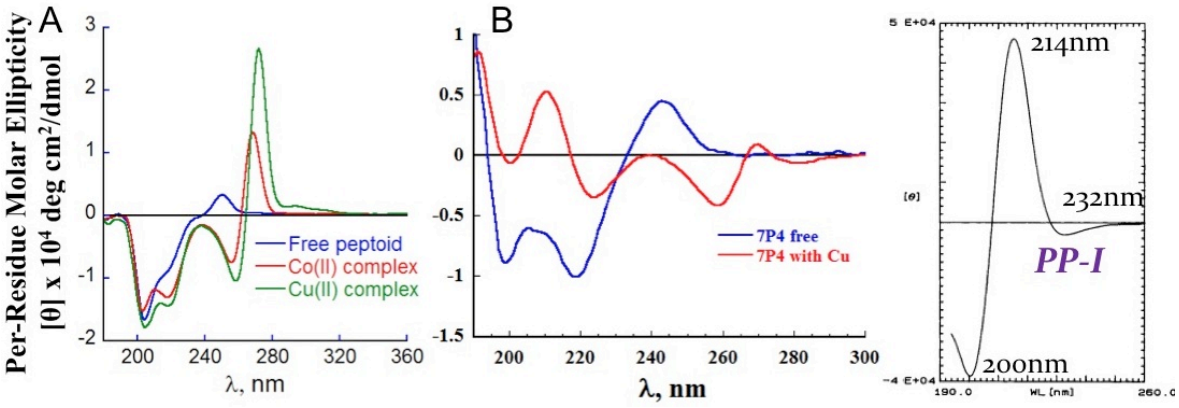

Figure 3. CD spectra of (A) Peptoid **7** and (B) Peptoid **5** (left), showing their folding upon metal binding. (B, right) CD spectrum of a typical polyproline type I helix.

Additionally, two of the peptoids12-mers were modified to include two distinct metal binding sites, one is selective to Cu(II) (Fig. 4) and demonstrated (i) that folding upon Cu(II) binding increases the binding affinity to a second metal ion (Zn(II), Co(II)) and (ii) positive allosteric cooperativity in the binding of Co(II) by folding upon Cu(II) binding. With these results we have completed our first objective: one MSc thesis and two papers about this research are now in

preparation. Moreover, these results were recently presented in an international conference and in a few chemistry departments in Israel as invited talks.

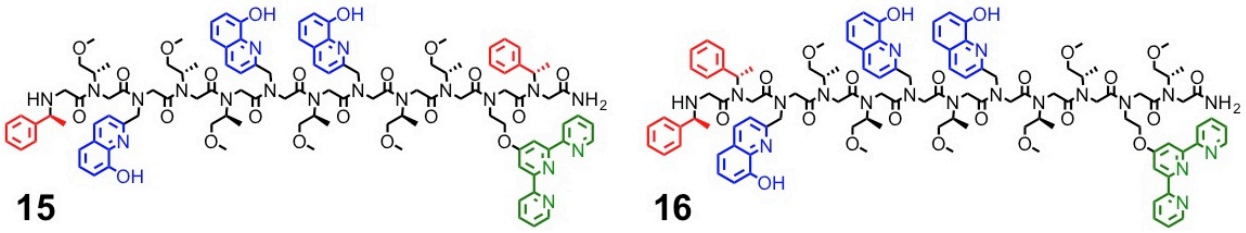

Figure 4. Peptoid sequences designed for demonstrating cooperativity by folding upon metal coordination.

Working towards the completion of objective 2, we have recently described the facile incorporation of 2,2-bipyridine ligand (bipy) into peptoid sequences for the design and synthesis of versatile bipy modified peptoid-ruthenium complexes. These include helical bundles via intermolecular metal binding and a unique cyclic metallopeptoid complex via intramolecular metal ligation of three pedant groups. We were also able to show that a helical hexamer having two different metal binding ligands HQ and Terpy (**Helix HQT i+3**) can selectively bind two different metal ions, each at a specific metal-binding site, form a mixture containing both ions, to generate the intermolecular heteronuclear bimetallic duplexes (**Helix HQT i+3**)CuM, M = Co^{2+}, Zn^{2+}, Fe^{3+} (Fig. 5). With these results we have completed objective 2 and two papers about this research were recently published. These results were also presented in international and national conferences and in a few chemistry departments in Israel and abroad.

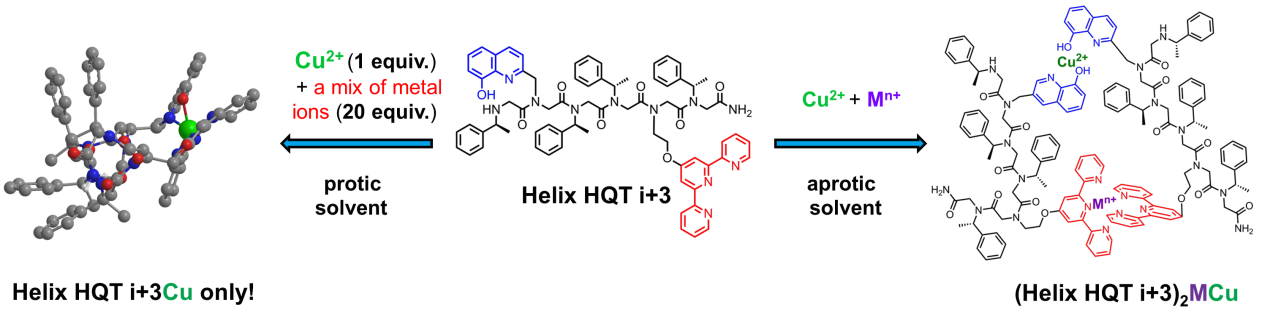

Figure 5. Peptoid helix HQT i+3 and its homo- and heteronuclear Cu(II) complexes.

To address objective 3, we have measured and detected ECCD in all of the hydroxyquinoline-based metallopeptoids and also in all of the bipy-modified metallopeptoids. In order to realize the coordination geometry of the metal centers within these metallopeptoids, we are now doing

quantum-based CD calculations varying the angle between the chromospheres (metal binding ligands). This objective was not completed mainly because the unexpected selective recognition and binding to Cu(II), which was very interesting to us, shifted this project towards the search for more selective chelators and towards making such chelators water soluble aiming for biological applications. This research is now on going in our lab and a grant proposal about this topic was recently funded by the Israel Science foundation.

Working towards the completion of objective 4, we succeeded to show biomimetic intramolecular cooperative catalysis by catalytic alcohol oxidation using achiral peptoid trimmers bearing a metal catalyst, an organocatalyst and a bulky group (Fig. 6) and the results were published (*Chem. Comm.* 2015) and presented in several international and national conferences. The second part of the project is now on going; we already synthesized five chiral and/or helical peptoids and are currently performing reactions attempting for asymmetric oxidative catalytic transformations.

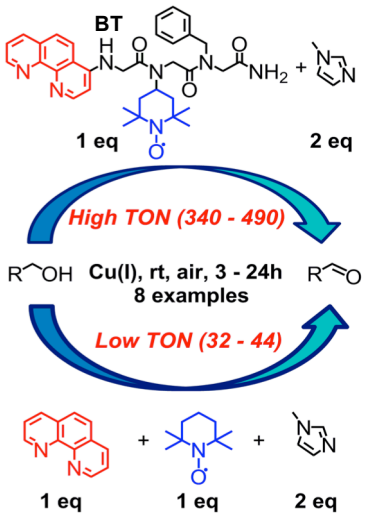

Figure 6. The cooperative peptoid **BT** as an efficient catalyst for the oxidation of primary alcohols.

Overall, this project was very successful, as evident by my personal achievements being now in my 5th year of a 6-year tenure-track, the list of publications, the list of invited talks and as reflected in the success of my students and postdocs, some have received fellowships for excellence, and who are all have either published their results and/or are in the stage of writing at least one paper based on their results. I also believe the Marie Curie Re-Integration grant that have been awarded in the beginning of 2013 had a crucial impact on the success of this project and on the high achievements of my self and my co-workers in the last 4 years.