

**S E M I N A R**  
**Wednesday 27/3/19, 11:00 am**  
**Building 211, seminar room**

**SPEAKER:**

**Dr. Anat Milo**  
Department of Chemistry, Ben-Gurion University

**TOPIC:**

**Unravelling mechanistic features  
of an organocatalyst  
modified at the secondary sphere**

Inspired by the fundamental effect of secondary-sphere interactions on enzymatic catalysis, metal-mediated processes and transition-metal chemistry, our group seeks to offer an approach for the facile in situ modification and mechanistic interrogation of secondary-sphere interactions in organocatalysis. As a proof-of-concept, we modified the secondary-sphere of N-heterocyclic carbenes (NHCs) using boronic acids (BAs) under reaction conditions and tested their reactivity and selectivity in the benzoin reaction. This in situ modification afforded unprecedented Furthermore, the enantioselectivity is highly reproducible in the presence of BAs in contrast to enantioselectivity for challenging electron-withdrawing substrates. the reaction with the catalyst alone. We used machine learning techniques to uncover the structural origin of enantioselectivity[1], system. This strategy allowed us to propose two different methods for improving selectivity. suggesting two possible reasons for its erosion in this Our mechanistic studies unraveled the dual role of BA in determining enantioselectivity and mitigating the racemization of the benzoin product. [2]

## References

- [1] a) A. Milo, E. N. Bess, M. S. Sigman, *Nature* 2014, 507, 210-214; b) A. Milo, A. J. Neel, F. D. Toste, M. S. Sigman, *Science* 2015, 347, 737-743; c) A. J. Neel, A. Milo, M. S. Sigman, F. D. Toste, *J. Am. Chem. Soc.* 2016, 138, 3863-3875; d) C. B. Santiago, A. Milo, M. S. Sigman, *J. Am. Chem. Soc.* 2016, 138, 13424-13430; e) M. S. Sigman, K. C. Harper, E. N. Bess, A. Milo, *Acc. Chem. Res.* 2016, 49, 1292-1301.V.
- [2] Dhayalan, S. C. Gadekar, Z. Alassad, A. Milo, *Nat. Chem.* 2019. (accepted)

## Short Bio

Anat Milo received her B.S./B.A. in chemistry and humanities from the Hebrew University (Jerusalem) in 2001, her M.S. from UPMC (Paris) with Bernold Hasenknopf in 2004, and her Ph.D. from the Weizmann Institute (Rehovot) with Ronny Neumann in 2011. Her postdoctoral studies with Matthew Sigman at the University of Utah focused on developing physical organic descriptors and data analysis approaches for chemical reactions. In October 2015, she joined the faculty at Ben-Gurion University, where her research group investigates strategies for identifying molecular design principles. The Milo research group synergistically integrates experimental, computational, and statistical methods to design and construct modular catalyst libraries and provide a powerful strategy for discovering and optimizing selective catalytic reactions. To this end, transient directing groups are introduced to diversify known organocatalysts in-situ under reaction conditions by forming orthogonal bonds. These directing groups serve to control and tune the catalysts' secondary-sphere interactions. Modifying a catalyst structure in-situ is challenging due to the required orthogonality between the binding mode and catalytic activity. Nonetheless, this approach is appealing as it can uncover general molecular design principles for the facile introduction of highly modular selectivity- and reactivity-controlling handles into a variety of catalytic systems. To further streamline catalyst discovery, the Milo group employs an innovative physical-organic analysis method for exposing the structure-activity and structure-selectivity relationships within the proposed reaction manifold.