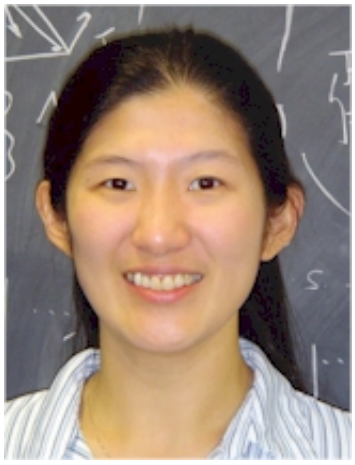
# Computational studies on cyclic peptide design

TCI SEMINAR

**Monday, April 20, 2015**
**3:00 p.m. Room 8335**

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Cyclic peptides are promising modulators of supposedly "undruggable" protein-protein interactions. They can bind large protein surfaces with high affinity and specificity and they have enhanced biostability and bioavailability compared to their linear counterparts. There are several examples of successful clinical applications of cyclic peptides as immunosuppressants, antibiotics, and antifungals, but most of these cyclic peptides are natural products and their derivatives. *Synthetic* cyclic peptides are severely underexploited in medicinal chemistry owing to the current difficulty of accurately predicting their three-dimensional structures *de novo*. This challenge has rendered the optimization of cyclic peptides for biological targets a purely empirical pursuit, requiring brute force synthesis of many variants in hopes of finding one with appropriate conformational and target-binding properties. The value of cyclic peptides as potential drugs would increase exponentially if we could accurately and rapidly predict their conformations. In this talk, we describe a novel computational method integrating bias-exchange metadynamics simulations, a Boltzmann reweighting scheme, dihedral principal component analysis and a modified density peak-based cluster analysis to provide converged structural descriptions of cyclic peptides.


**Theoretical Chemistry Institute Seminar Series**