Novel Computational Study on π-Stacking to Understand Mechanistic Interactions of Tryptanthrin Analogues with DNA. Raymond J. Terryn III, Helen German, Theresa M. Kummerer, Richard R. Sinden, J. Clayton Baum, and Mark J. Novak. Department of Chemistry, Florida Institute of Technology, 150 W. Univ. Blvd., Melbourne, FL 32901.

Interactions based on π-stacking influence the properties of many inter- and intramolecular arrangements that occur in biological systems. Density functional theory (DFT) can provide an accurate and efficient tool for describing these types of interactions though it is strongly dependent on the density functional applied. The local density approximation (LDA), unlike many popular density and hybrid-density functionals, accounts for attractive dispersion forces, a key component in π-stacking. We have developed a method that employs the LDA functional and electrostatic potential mapping to probe the π-π stacked intercalation energies of tryptanthrin analogs onto G-C and A-T DNA base pairs. This method is being used to probe which tryptanthrins show the most favorable stacking energy and whether or not each analog shows a preference for intercalating into an A-T rich or G-C rich region of the DNA strand. The methodology and progress of this endeavor will be discussed along with future extension.