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Abstract for an Invited Paper for the MAR13 Meeting of the American Physical Society

New technology for 2D IR spectroscopy and its application to protein aggregation and drug binding MARTIN ZANNI, University of Wisconsin-Madison

We are using 2D IR spectroscopy to study the aggregation and drug inhibition of proteins involved in common human diseases. It is extremely difficult to obtain precise structural information about drug inhibition of amyloid fibrillization, because it is very difficult to apply NMR spectroscopy and x-ray crystallography to these systems. As a result, there are very few molecular level details known about even the simplest inhibitors. We have studied a peptide inhibitor whose sequence was used to design an FDA approved drug, partially because this peptide has never before been observed to aggregate on its own. According to the sequence, we would expect that the C-terminal is responsible for inhibition, but in fact we found that the N-terminal was instead. In fact, we also observed that the complex formed between the inhibitor and amylin caused the inhibitor itself to form amyloid fibers. These surprising results were not previously observed, in part because the prior methods used to study inhibition was not sensitive to the specific structural fold of the fibers.