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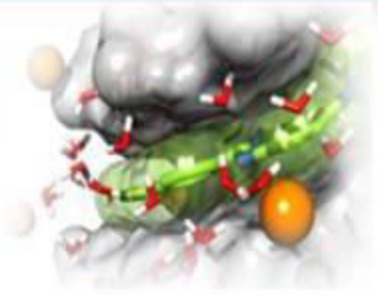

STRUCTURE AND FUNCTION OF PROTEINS AND PEPTIDES

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Ph.D. in Biophysics

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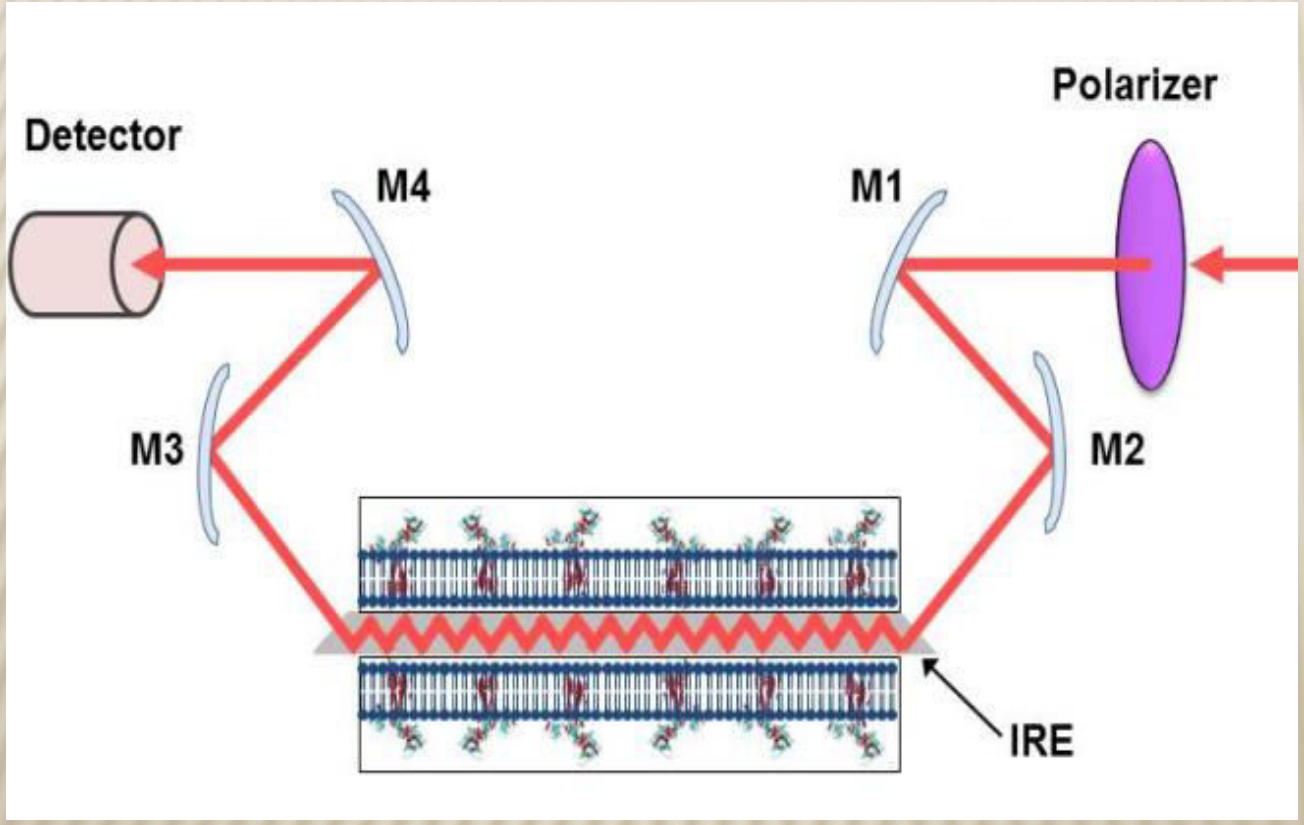
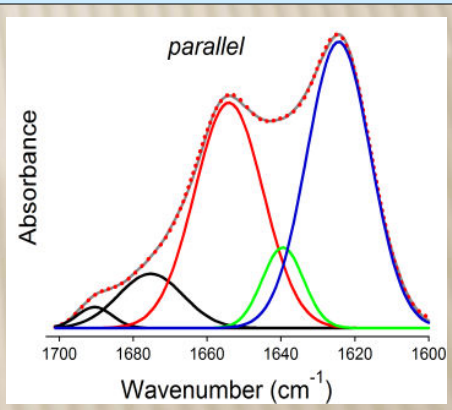
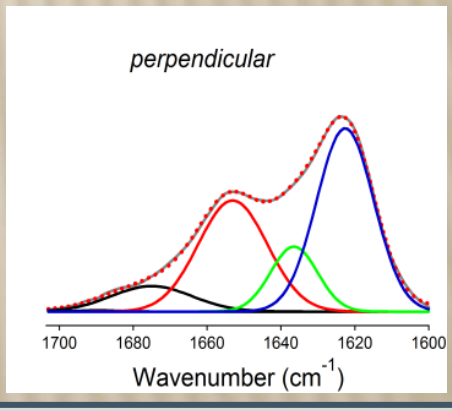
POLARIZED TOTAL INTERNAL REFLECTION INFRARED SPECTROSCOPY

Allows determination of the structure and orientation of membrane proteins







Publications:

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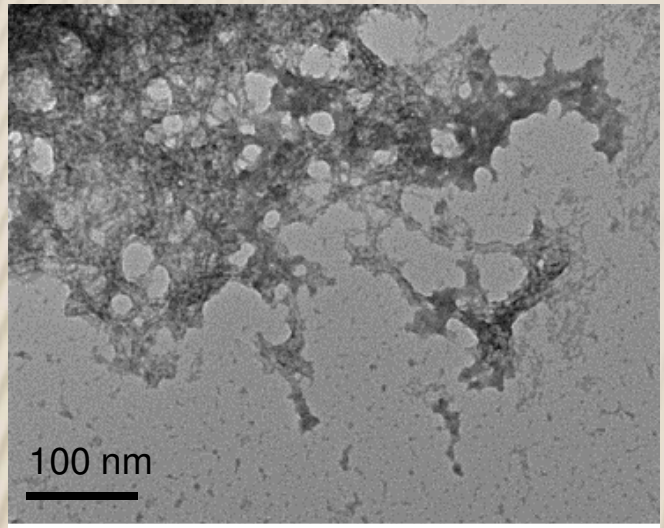
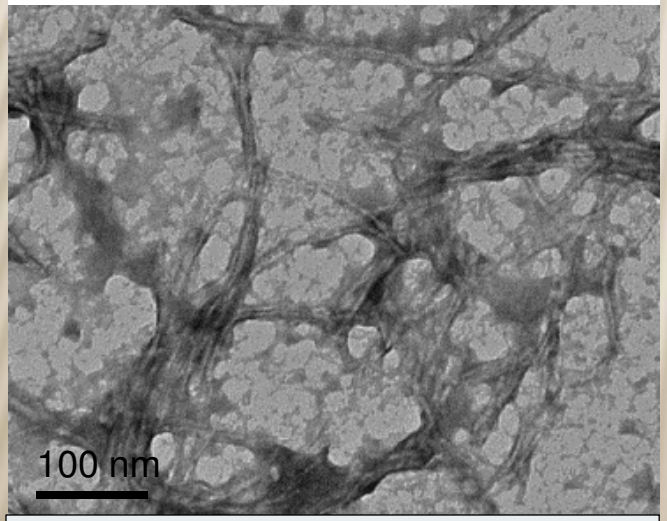
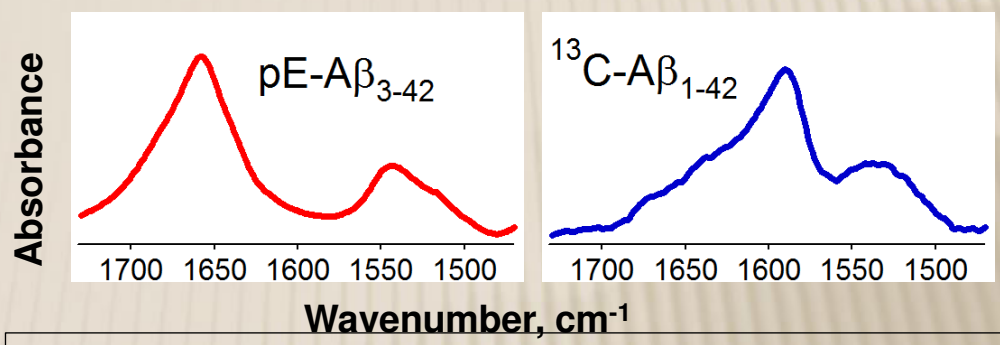
- Tatulian SA (2010) Structural analysis of proteins by isotope-edited FTIR spectroscopy. *Spectroscopy* 24:37-43.
- Tatulian SA (2003) Attenuated total reflection Fourier transform infrared spectroscopy: A method of choice for studying membrane proteins and lipids. *Biochemistry* 42:11898-907.

STRUCTURAL BASIS FOR CYTOTOXICITY OF ALZHEIMER'S AMYLOID β PEPTIDE

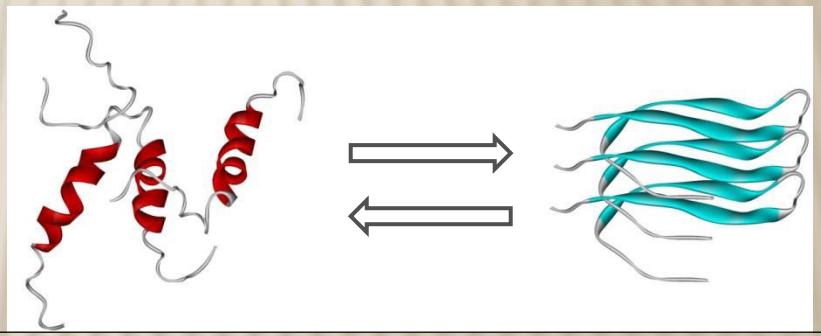




Transmission electron micrographs of amyloid β peptide $A\beta_{1-42}$ (above) and the pyroglutamylated $A\beta_{pE3-42}$ (below).



FTIR spectra of pyroglutamylated $A\beta_{pE3-42}$ (left) and uniformly ^{13}C-labeled $A\beta_{1-42}$ (right) peptides identify an augmented α-helical propensity of the former.

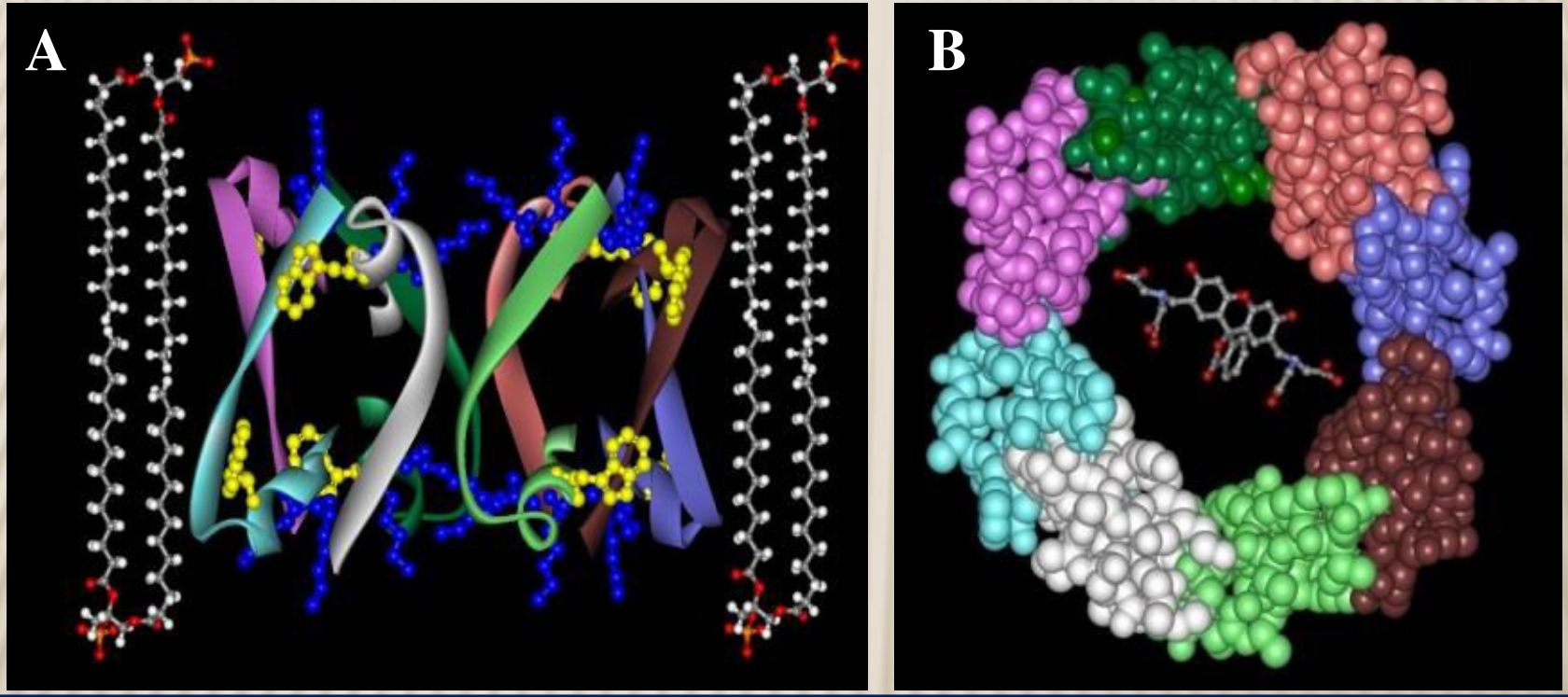


The pyroglutamylated Aβ peptide may form hypertoxic α-helical intermediates and convert the Aβ peptide into similar assemblies of increased cytotoxicity.

Publication:

Matos JO, Goldblatt G, Jeon J, Chen B, Tatulian SA (2014) Pyroglutamylated amyloid-β peptide reverses cross β-sheets by a prion-like mechanism. *J. Phys. Chem. B* 118(21):5637-43

STRUCTURE OF A MEMBRANE PORE FORMED BY EIGHT PEPTIDE MONOMERS

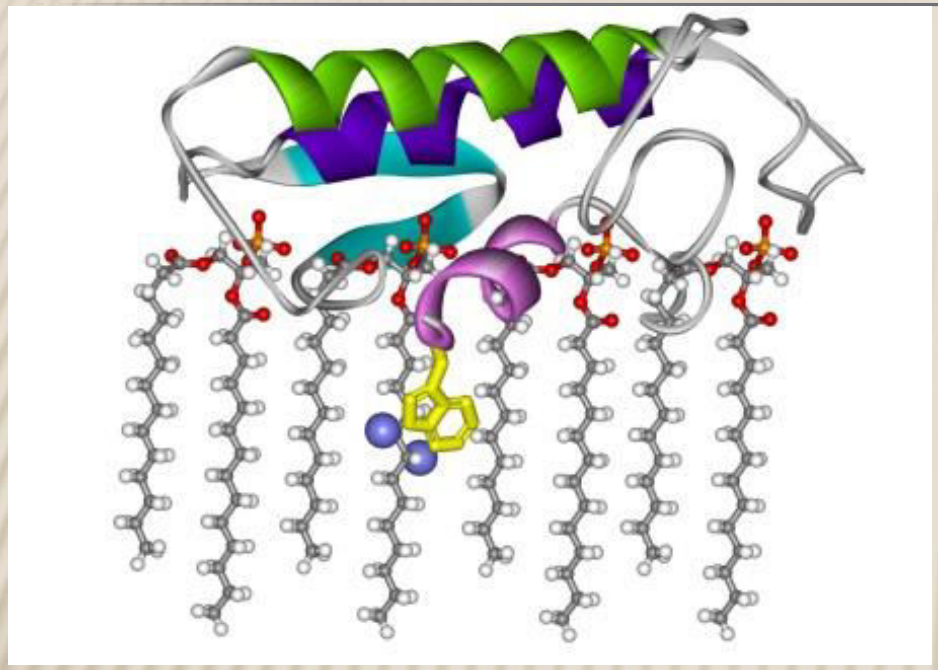


The C-terminal 20-residue peptide of Bax protein was shown to form large pores in lipid bilayer membranes. The pore was shown to assume a previously unknown structure, an α/β ring, where 8 peptide molecules, each partially α-helical and partially β-strand, form the pore.

Publications:

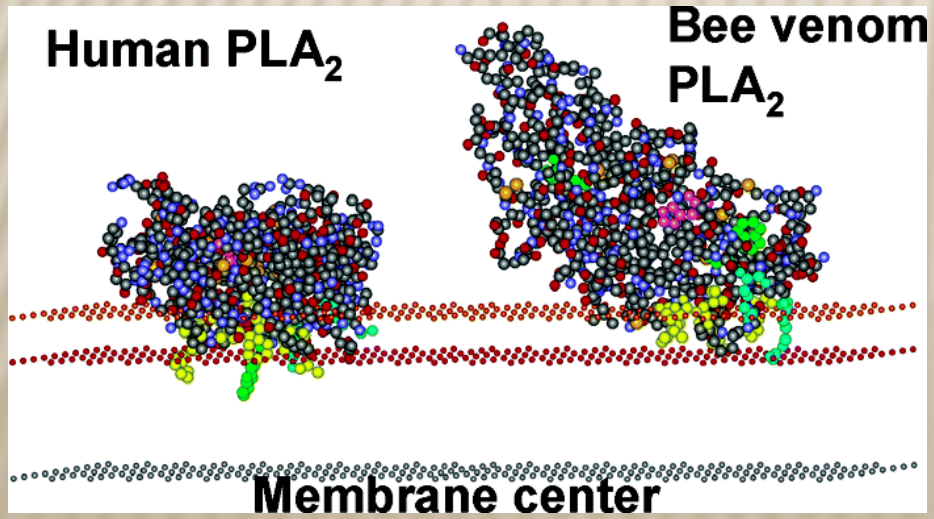
- Garg P, Nemec KN, Khaled AR, Tatulian SA (2013) Transmembrane Pore Formation by the Carboxyl Terminus of Bax Protein. *Biochim. Biophys. Acta* 1828:732-42.
- Tatulian SA, Garg G, Nemec KN, Chen B, Khaled AR (2012) Molecular Basis for Membrane Pore Formation by Bax Protein Carboxyl Terminus. *Biochemistry* 51(46):9406-9419.

PHYSICAL MECHANISMS OF INTERFACIAL ENZYMES



The depth of membrane insertion of human pancreatic phospholipase A2 (PLA2) is determined by tryptophan fluorescence quenching by bromines attached at different positions of membrane lipids.

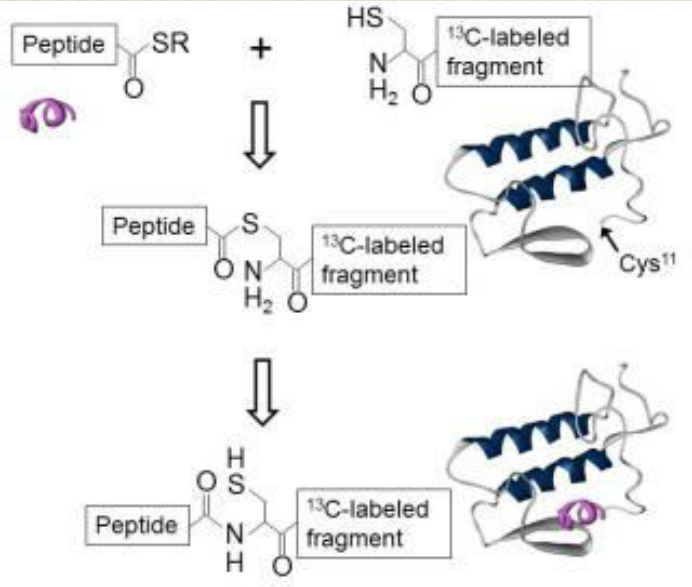
Human and bee venom PLA2s bind to membranes with distinct modes, which explains differences in their interfacial activation.

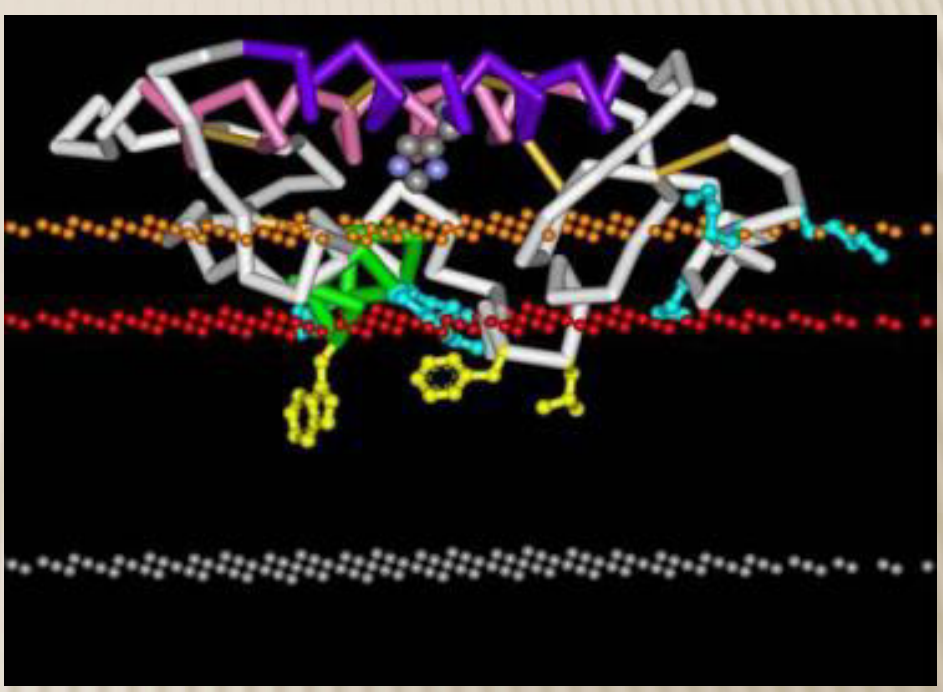


Publications:

- Ray S, Scott JL, Tatulian SA (2007) Effects of Lipid Phase Transition and Membrane Surface Charge on the Interfacial Activation of Phospholipase A_2. *Biochemistry* 46:13089-100.
- Pande AH, Qin S, Nemec KN, He X, Tatulian SA (2006) Isoform-specific membrane insertion of secretory phospholipase A_2 and functional implications. *Biochemistry* 45:12436-47.
- Pande AH, Qin S, Tatulian SA (2005) Membrane fluidity is a key modulator of membrane binding, insertion, and activity of 5-lipoxygenase *Biophys. J.* 88:4084-94.

NATIVE CHEMICAL LIGATION OF PROTEINS, SEGMENTAL ISOTOPE LABELING FOR STRUCTURAL STUDIES





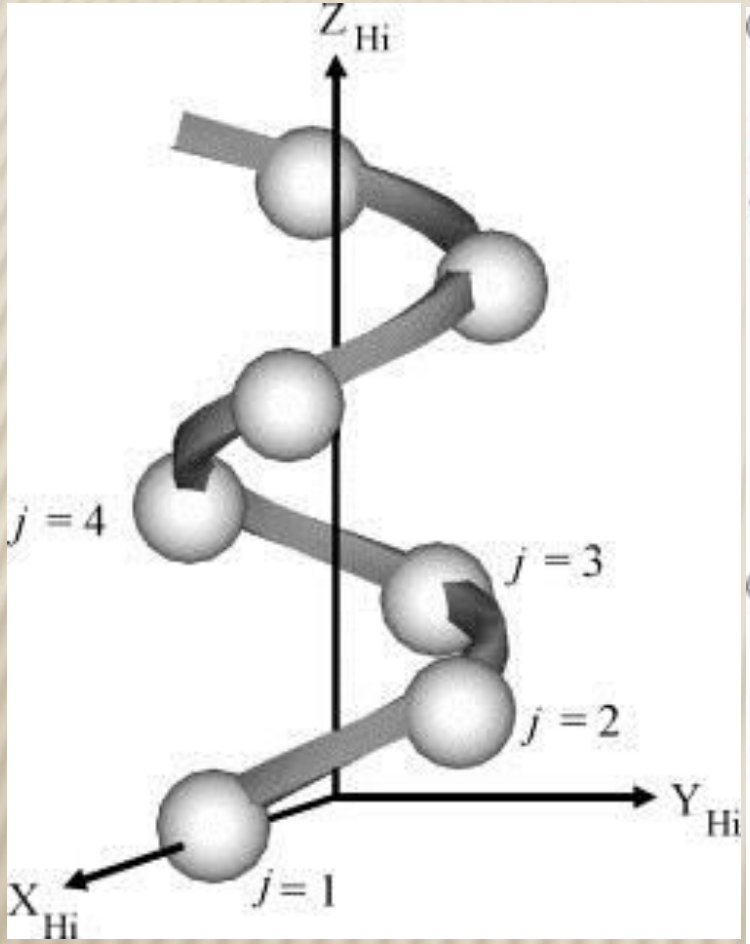
The peptide is synthesized with a thioester group at the C-terminus, which is reacted with the N-terminal cysteine of a recombinant, ^{13}C-labeled fragment to create a segmentally ^{13}C-labeled protein.

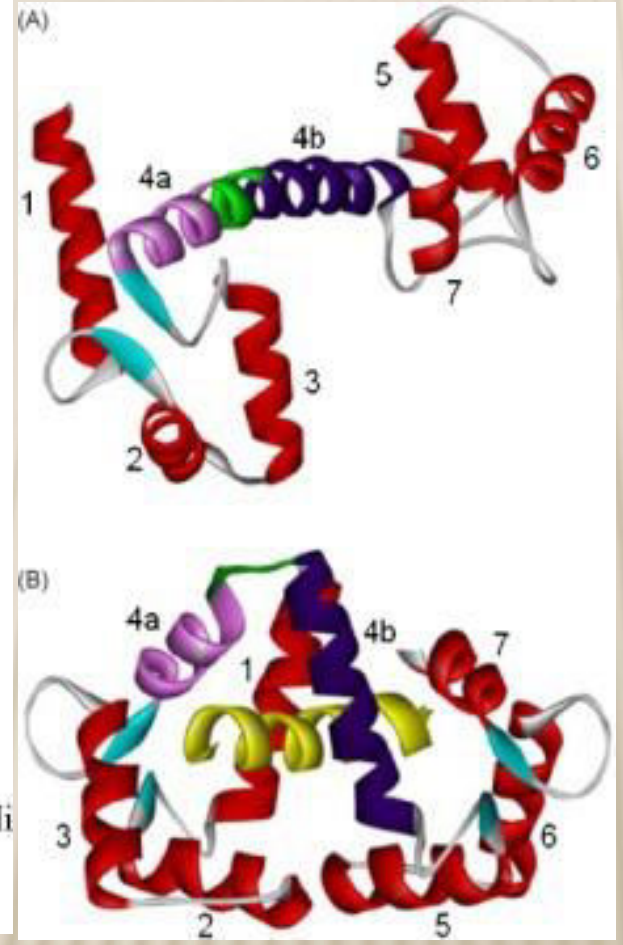
Analysis of the segmentally ^{13}C-labeled PLA2 by polarized FTIR and fluorescence quenching allows positioning of the protein in a membrane (PDB entry 1ysk).

Publications:

- Tatulian SA, Qin S, Pande AH, He X. (2005) Positioning membrane proteins by novel protein engineering and biophysical approaches. *J. Mol. Biol.* 351:939-947
- Qin S, Pande AH, Nemec K N, He X, Tatulian SA. (2005) Evidence for the regulatory role of the N-terminal helix of secretory phospholipase A_2 from studies on native and chimeric proteins. *J. Biol. Chem.* 280:36773-83.

ALGORITHMS FOR PROTEIN STRUCTURE ANALYSIS





An algorithm, named HELO (Helix Orientation), has been developed to determine the interhelical angles and helical bends or twists, using alalytical geometry operations with the protein's atom coordinates. Conformational changes in calmodulin upon binding to a target peptide were described at greater detail.

Publication:

Tatulian SA. (2008) Determination of helix orientations in proteins. *Comput. Biol. Chem.* 32:370-374.

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