SYNTHESIS OF PEPTIDE-AMPHIPHILES FOR BINDING INORGANIC MOLECULES

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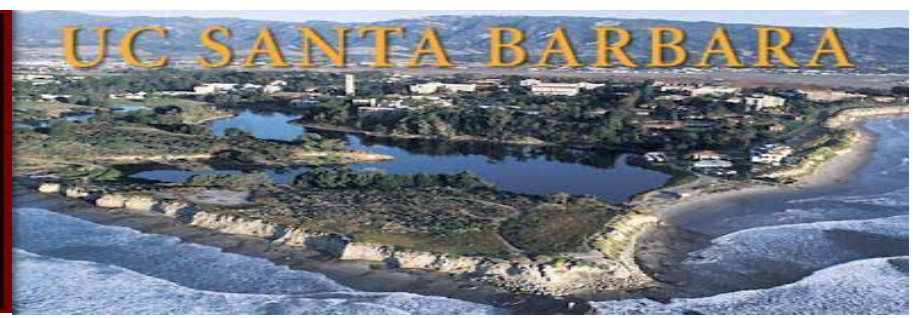


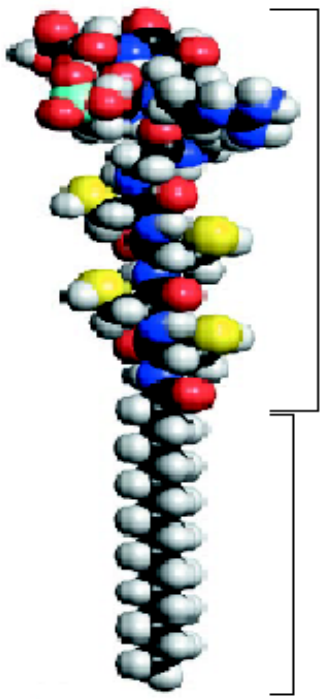
ABSTRACT

Constructing biomaterials capable of mimicking reactions and processes specific to certain proteins is a challenging endeavor of interest to many researchers. The development of peptide-amphiphiles that combine amphiphilic properties with specific bioactivity has made it possible to synthesize molecules that self-assemble to mimic protein function. This research involves synthesizing peptide-amphiphiles with a peptide head group capable of folding into the native structure of a protein involved in the condensation of bone, attached to a monoalkyl tail. The peptide-amphiphiles created were then characterized and examined to see how they self-assembled in solution and whether they displayed any specific bioactivity related to their head group molecular architecture. Analyzing the peptide-amphiphiles' structures was done by observing circular dichroism spectras, while collecting and characterizing the peptide-amphiphiles was done using HPLC (high performance liquid chromatography), MALDI-TOF MS (matrix-assisted laser desorption ionization time-of-flight mass spectrometry) and NMR (nuclear magnetic resonance). This research has far-reaching applications in synthesizing inorganic materials found in the body such as bone and helping to treat diseases where inorganic materials are involved.

WHAT IS A PEPTIDE-AMPHIPHILE?

A PEPTIDE-AMPHIPHILE IS A MOLECULE COMPOSED OF A HYDROPHILIC PEPTIDE HEAD GROUP ATTACHED TO A HYDROPHOBIC TAIL GROUP.

MOLECULAR MODEL

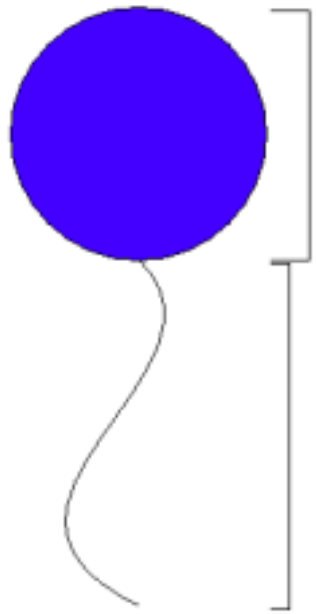


- Head Group
- Hydrophilic
  - Water-loving

- Tail Group
- Hydrophobic
  - Water-hating

⇒

SIMPLE MODEL



- Head Group
- Hydrophilic
  - Water-loving

- Tail Group
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  - Water-hating

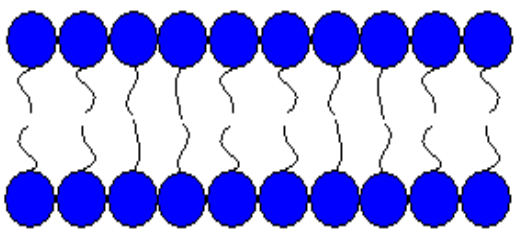
http://pubweb.northwestern.edu/~jha463/pdf/science.pdf

SELF-ASSEMBLY IN SOLUTION

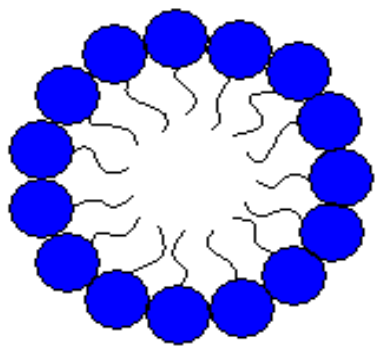
THE HYDROPHOBIC AND HYDROPHILIC REGIONS OF PEPTIDE-AMPHIPHILES ALLOW THE MOLECULES TO SELF-ASSEMBLE IN SUCH A WAY WHERE THE HYDROPHOBIC REGIONS ARE DIRECTED AWAY FROM WATER. THE FORMATIONS THAT OCCUR DEPEND UPON THE MOLECULAR STRUCTURE OF THE PEPTIDE-AMPHIPHILES.

IN REALITY, THREE-DIMENSIONAL STRUCTURES ARE FORMED RATHER THAN THE TWO-DIMENSIONAL DEPICTIONS SHOWN BELOW.

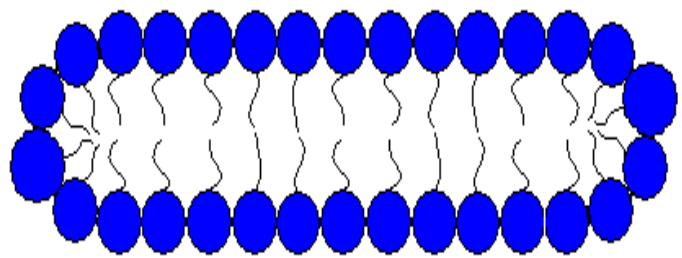
❖BILAYER



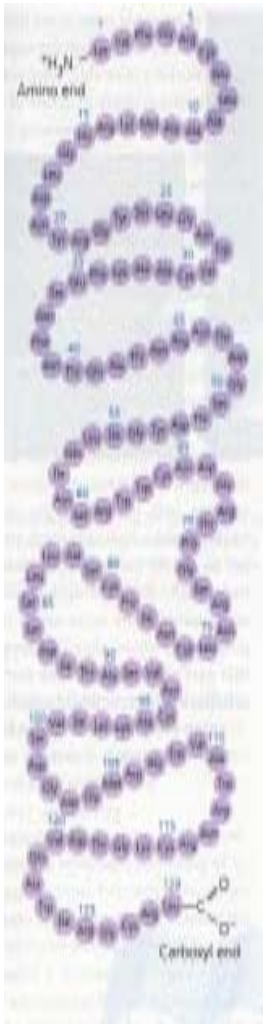
❖MICELLE



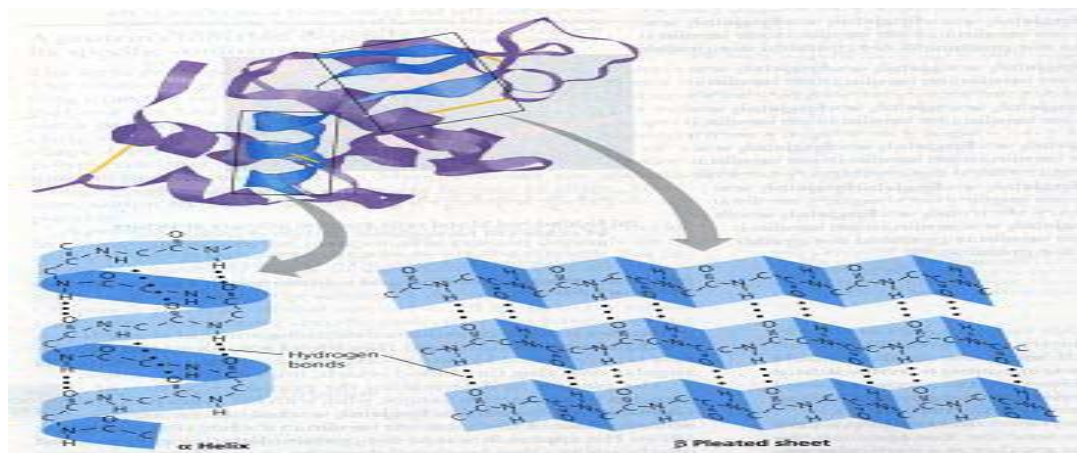
❖DISC



SELF-ASSEMBLY OF A PEPTIDE



- A PEPTIDE (SHOWN ON THE LEFT) IS A COMPOSED OF TWO OR MORE AMINO ACIDS BONDED THROUGH HYDROLYSIS.
- THE PEPTIDE HEAD GROUP OF A PEPTIDE-AMPHIPHILE CAN SELF-ASSEMBLE INTO A SPECIFIC CONFORMATION OF A PROTEIN OR PART OF A PROTEIN (EXAMPLE DEPICTED IN LOWER RIGHT).
- THE CONFORMATION OF THE PEPTIDE HEAD GROUP CAN GIVE THE PEPTIDE-AMPHIPHILE A SPECIFIC BIOACTIVITY.



From *Biology* 6th Edition by Campbell and Reece (Pearson Education, Inc.)

RESEARCH FOCUS & PURPOSE

- SYNTHESIZING A PEPTIDE-AMPHIPHILE THAT IS BIOMIMETIC OF THE PROTEIN INVOLVED IN THE CONDENSATION OF BONE
- TO UNDERSTAND BIOMINERALIZATION OF PEPTIDE-AMPHIPHILES
- TO UNDERSTAND THE BINDING OF OTHER INORGANIC MATERIALS OF BIOLOGICAL SYSTEMS
- TO UNDERSTAND HOW TO CONTROL GROWTH OF INORGANIC MATERIALS

PEPTIDE-AMPHIPHILES OF INTEREST

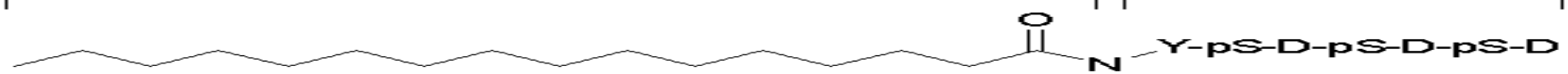
MODEL PEPTIDE(NL467) → HEAD GROUP

TAIL GROUP

FIRST PEPTIDE-AMPHIPHILE(M16-NL467) WAS CREATED BY BONDING PALMITIC ACID(TAIL GROUP) TO A MODEL PEPTIDE(HEAD GROUP). THE MODEL PEPTIDE WAS SYNTHETICALLY CREATED BY BONDING TWELVE GLUTAMIC ACIDS TOGETHER; THEORETICALLY THE MODEL PEPTIDE HAS A BETA-PLEATED SHEET CONFORMATION AND COMES OUT OF SOLUTION WITH CALCIUM.

PEPTIDE FROM NATURE(NL569) → HEAD GROUP

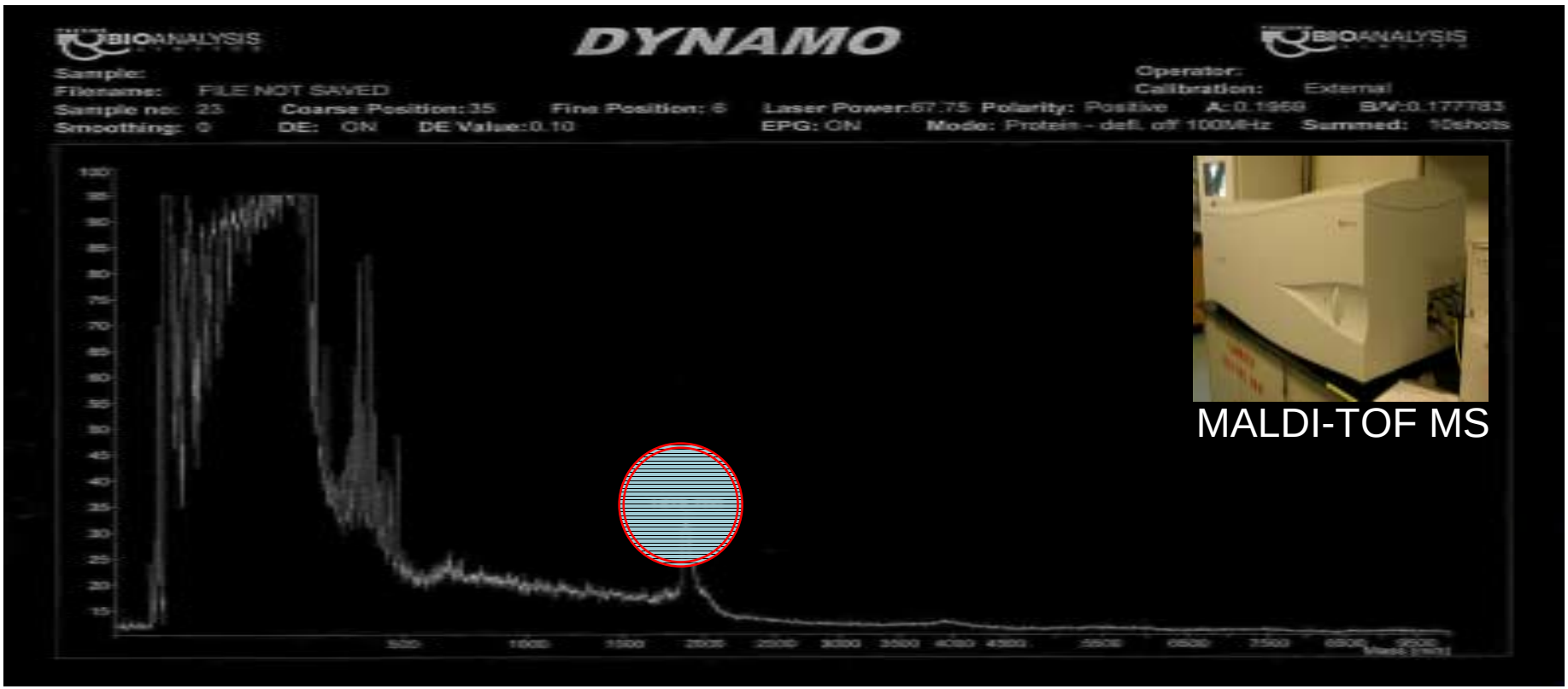
TAIL GROUP



SECOND PEPTIDE-AMPHIPHILE(M16-NL569) WAS CREATED BY BONDING PALMITIC ACID(TAIL GROUP) TO A PEPTIDE(HEAD GROUP) OBTAINED FROM THE ACTIVE SITE OF A PROTEIN INVOLVED IN THE CONDENSATION OF BONE. THE NATIVE CONFORMATION OF THE PEPTIDE IS A BETA-PLEATED SHEET.

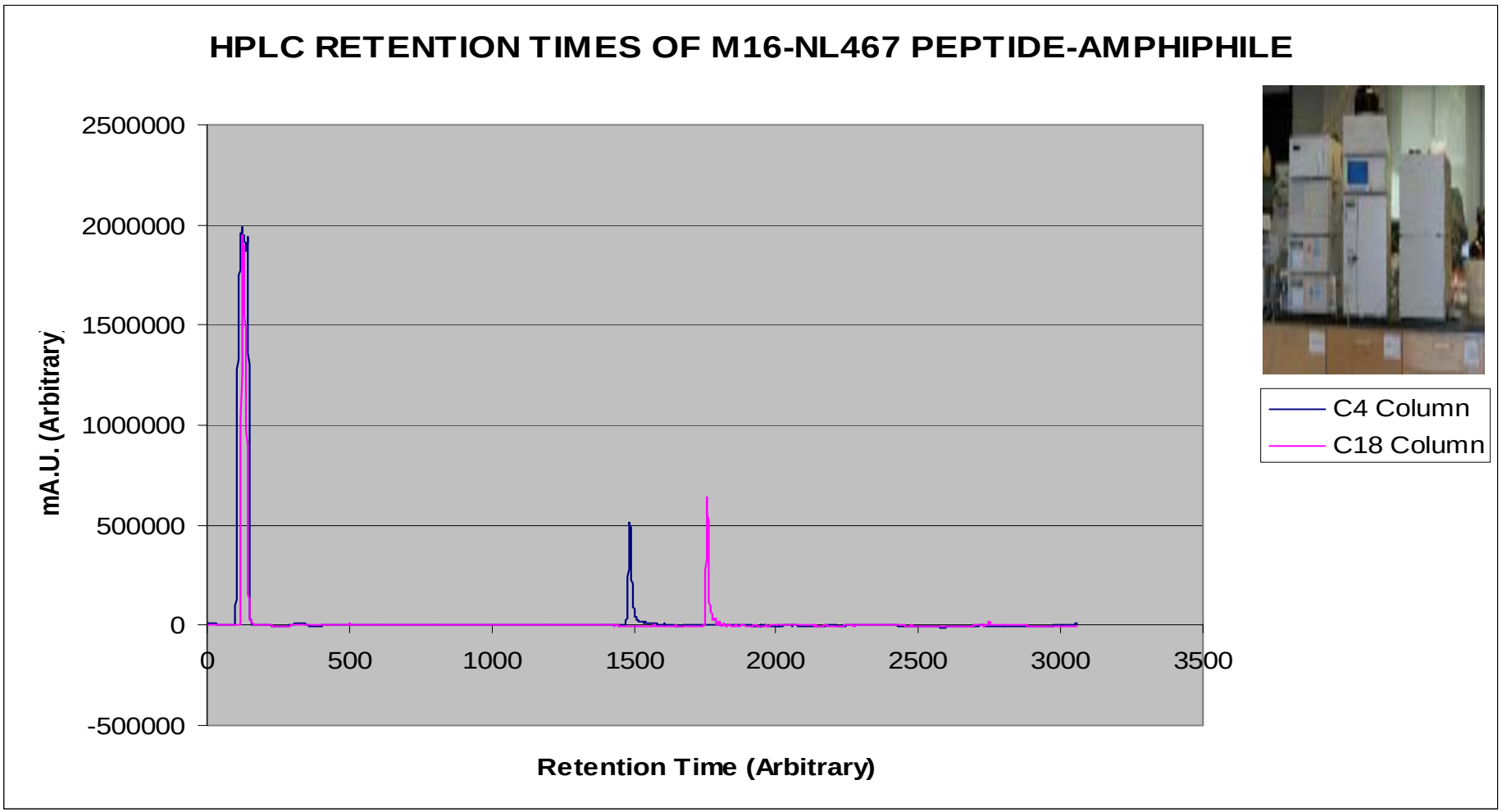
ANALYSIS AND RESULTS

MALDI-TOF MS IS USED FOR DETECTION AND CHARACTERIZATION OF BIOMOLECULES. BIOMOLECULES ARE COUPLED TO A MATRIX AND SENT THROUGH ELECTRIC FIELDS AFTER BEING HIT WITH A LASER. THEY ARE SUBSEQUENTLY SEPARATED BY MASS/CHARGE AS THEY REACH A DETECTOR AT DIFFERENT TIMES. THE GRAPH BELOW DEPICTS THE M16-NL467 PEPTIDE-AMPHIPHILE RAN THROUGH THE MALDI-TOF MS, GIVING IT A MASS OF 1878.265 g/mol WHICH IS CLOSE TO THE THEORETICALLY CALCULATED VALUE OF 1805.8 g/mol. THIS RESULT SHOWS THAT THE PEPTIDE HEAD GROUP BONDED TO THE TAIL GROUP CORRECTLY.



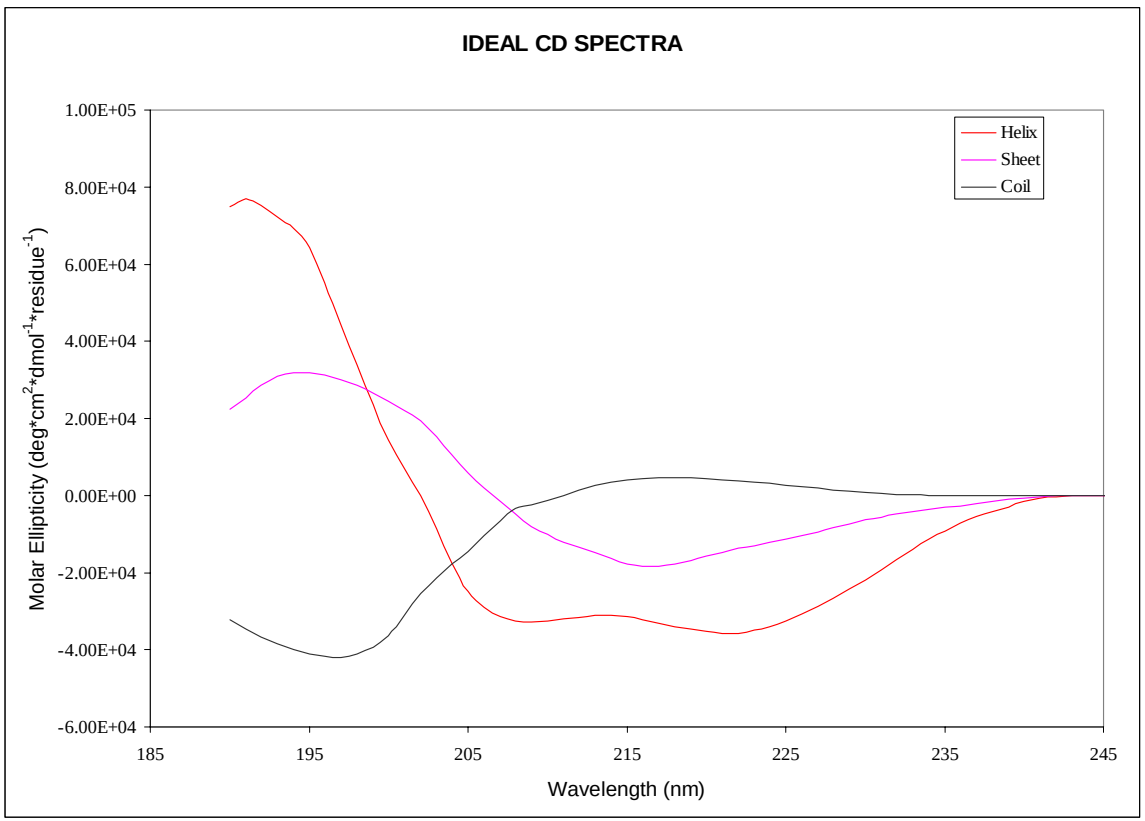
ANALYSIS AND RESULTS

SHOWN BELOW IS GRAPH TAKEN FROM A HPLC RUN. BECAUSE THE C18 PEAK IS FARTHER TO THE RIGHT THAN THE C4 PEAK, THIS TELLS US THAT THE PEPTIDE-AMPHIPHILE IS FAIRLY HYDROPHOBIC.

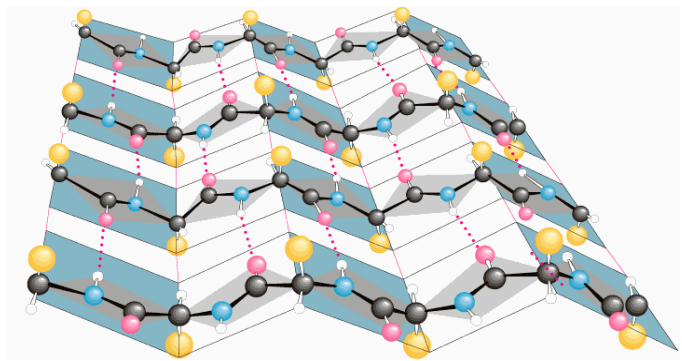


ANALYSIS AND RESULTS

THIS GRAPH SHOWS THE IDEAL CIRCULAR DICHROISM SPECTRA FOR VARIOUS FORMATIONS. THE PINK LINE DEPICTS THE IDEAL CURVE FOR A BETA-PLEATED SHEET FORMATION. BOTH THE M16-NL467 AND M16-NL569 PEPTIDE-AMPHIPHILES SHOULD PRODUCE A CURVE SIMILAR TO THE PINK LINE, BUT SO FAR THE M16-NL467 HAS ONLY BEEN RUN AND IT'S CURVE IS TOO NOISY TO BE ACCEPTABLE.



Circular Dichroism Instrument



Beta-Pleated Sheet Formation

From *Biochemistry* 2nd Ed. by Garrett and Grisham (Harcourt, Brace & Company)

WORK IN PROGRESS…

- BOTH M16-NL467 AND M16-NL569 NEED TO BE FURTHER CHARACTERIZED
- PURIFICATION OF PEPTIDE-AMPHIPHILES SO THAT THEY ARE IN SOLUTION WITH NO OTHER IMPURITIES OR SUBSTANCES
- ONCE THE PEPTIDE-AMPHIPHILES HAVE BEEN THOROUGHLY CHARACTERIZED, THEY CAN BE TESTED TO SEE IF THEY POSSESS DESIRED BIOACTIVITY.

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