Bio. 3374. Physical Biochemistry. Spring semester, 2018
3 credit hours. 12:30 AM – 1:50 PM Tu, Th. Bio-Life Room 342
Prerequisites: Biology 2112, Calculus II, General Physics I, General Chemistry II.

This course covers the physical properties of macromolecules. Protein structure, cryo-EM, protein folding, protein folding in disease, interaction of light with proteins and includes optogenetics and phytochromes, the light reaction of photosynthesis, redox chemistry, nitrogen fixation, absorption, emission, and NMR spectroscopy in biological systems. X-ray crystallography, natural and artificial membranes, and membrane transport phenomena will be covered.

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Office hours: I will be in Room 352 BLS on Tuesdays, and Thursdays from 2 to 3 PM during the semester. Please e-mail me if you wish to come by at another time.

Textbook: No textbook is required. J. Lakowicz, Principles of Fluorescence, 3rd edition, Springer; is online at TU library.

Required Readings: Please note that five required readings and videos are posted on the syllabus. These articles will be posted on Blackboard as pdf files. These readings are preceded by a capital letter and an open parenthesis in the syllabus. Please make sure that you read these posted articles for each exam. Questions from these readings will be on each exam.

Lecture Attendance. Attendance at the lecture is strongly recommended during the semester.

Grading: Two in class exams and a final exam will be given during the spring semester. Exams will be multiple-choice, short answer/discussion questions, and problems. The final exam will not be cumulative. The scheduled time for the final exam is Thursday, May 4th from 10:30 AM to 12:30 PM.

Homework and quizzes. All homework assignments will be posted on Blackboard. Several [but not all] of the posted homework assignments will be collected and graded. Finally, several announced quizzes will be given during the semester. The homework and quizzes will represent 5% of your final grade.

| Exam 1 | 31% |
| Exam 2 | 31% |
| Final Exam | 33% - Please note that final exam starts at 10:30 AM. |
| Homework Assts. and quizzes | 5% - All quizzes and in-class assignments will be announced. |

Grading Scale for Final Grade. Plus-minus grading is used for final grade. No incomplete grades (I) will be given.

88% - 100%: A
78% - 87.9%: B
55% - 77.9%: C
50% - 54.9%: D
<50%: F

Withdrawals: Monday, January 29th is the last day to withdraw from a course (without a W grade).
Wednesday, March 21st is the last day to withdraw from graduate and undergraduate courses (with a W grade).

The last lecture is Thursday, April 27th. All classes end Monday, April 30th. Tuesday, May 1st, and Wednesday, May 2nd are study days. Final exams start on May 3rd. Final exam for Physical Biochemistry is Thursday, May 3rd.

12:30 -1:50 T R Thursday 5/4 10:30 AM -12:30 PM

Incompletes. Incompletes are not normally given. If you request an incomplete due to medical reasons, you will need to contact your academic advisor. I will need a note from your academic advisor in order to issue an incomplete. Please note that >50% of the coursework must be completed in order to issue an incomplete.

Makeup exams: If an hourly exam is missed due to a medical or legal reason, you MUST schedule a time to take the exam as soon as possible. No more than one lecture exam can be made up during the semester. In order to schedule a make-up exam, written documentation will be required. Written documentation includes medical, dental, and legal excuses from your physician, dentist, podiatrist, or lawyer. Notes from PAs, chiropractors, auto repair technicians, being a contestant on American Idol, public transit problems, and chiropractors are generally not accepted.

I will need a copy of the documentation for my files. If a medical, dental, or legal excuse is not presented by the student, then each missed exam will result in a grade of zero percent.

Makeup Quizzes: If a valid excuse is presented for missing an in-class quiz, the missing quiz grade will be prorated.
Lecture Topics (Five required readings are listed A through E):

I. Protein structure and protein folding
   Brief introduction to protein structure and thermodynamics
   - Amino acids and peptide bonds
   - Primary, secondary, tertiary, and quaternary structures of proteins
   - Three-dimensional structure of proteins
   - Ramachandran diagram and allowed conformations of polypeptides
   - Role of glycine and proline in determining protein structure
   - Alpha helix, beta-sheet, beta-barrel secondary structures
   - Coil-helix transitions in proteins
   - Identification of post-translational modifications of proteins
   - Predicting protein secondary structure – hydropathy plots

   Protein folding
   - The hydrophobic effect
   - Chemical crosslinks
   - Protein denaturation and renaturation – RNase A and lysozyme
   - Protein folding pathways, molten globule state
   - Hydrophobic packing model, HD lattice model of protein folding

   Two state model and downhill model of protein folding
   - Molecular chaperones and protein folding

   Protein structure and cryo-electron microscopy
   - Imaging with a transmission electron microscope
     - Single-particle cryo-electron microscopy
     - Three-Dimensional EM of Macromolecular Assemblies
     - Examples of cryo-EM - structure of membrane proteins

   The Dark Side of Proteins
   - Protein misfolding and protein disorder
   - Order-promoting and disorder-promoting sequences
   - Protein disorder and aggregation, Parallel in-register beta sheets
   - Intrinsic disorder in proteins associated with neurodegenerative disease
     - Amyloid beta protein and AD
     - Tau protein in AD and chronic traumatic encephalopathy (CTE)
   - Protein folding, protein hyperphosphorylation and axonal degeneration
   - Prions and prion-related diseases
     - Structure of native and modified prion protein
     - BSE, C-J disease, scrapie

II. Interaction of proteins with light
   - Properties of light
   - Absorption of Light
     - Franck-Condon Principle
   - Review of Molecular Orbitals

Exam I. Tuesday, February 20, 2018

III. Optogenetics and opsin-based triggers of cellular activity
   - Microbial opsins
   - Optogenetic tools
     - Channelrhodopsins (ChR1, ChR2)
     - Crystal structure of channelrhodopsin
     - Halorhodopsin
     - OptoXR
   - Cre-dependent optogenetic targeting
     - Overview of excitable membrane depolarization and hyperpolarization
       - Optogenetic tools for neuronal excitation
       - Optogenetic tools for neuronal inhibition
       - Optogenetics in behavioral studies
     - Brainbow neuroimaging with fluorescent proteins


   https://www.youtube.com/watch?v=BJKkC0W-6Qk
IV. Phytochromes and cryptochromes (as time permits)
   Discovery of phytochromes
   Plant and bacterial phytochromes
   Biochemical properties of phytochromes

V. Photosynthesis, Redox chemistry, and Nitrogen Fixation
   Light-dependent reaction of photosynthesis
   Chloroplast Structure - Function, Photosynthetic Membranes of Cyanobacteria
   Absorption of Light
   Red Drop and Emerson Effect
   Photosynthetic Units and Photosynthetic Reaction Centers
   Introduction to redox chemistry, Standard redox potentials
   Nernst equation and bioenergetics
   Z Scheme of light reaction of Photosynthesis
   Photosynthetic Electron Transport and Chloroplast Membrane Structure
   ESR measurements in photosynthetic electron transport
   Photosystem II Structure and Function, including Water Oxidation
   Manganese cluster and Photosynthetic Water Oxidation
   Dangling manganese of OEC and ammonia
   Photosystem I Structure and Function
   Cyclic and Non-cyclic Photophosphorylation
   Bacterial Photosynthesis, Bacterial reaction centers

   Biochemistry of Nitrogen Fixation
   Haber process
   Biochemistry of nitrogen fixation – cyanobacteria and leguminous plants
   Leghemoglobin
   Structure and function of Nitrogenase enzyme
   Energetics of nitrogen fixation.

VI. Spectroscopy in Biological Systems
   Absorption Spectroscopy – UV/VIS spectroscopy
   Biological chromophores
   Theory of absorption of light by molecules
   Beer-Lambert Law
   Polarity effects, pH effects, orientation effects on absorption properties of chromophores
   Applications of absorption spectroscopy
   Nanodrop spectrophotometry

   Emission Spectroscopy
   Nature of emission processes - Fluorescence; Phosphorescence, Triboluminescence. Lakowicz, Ch. 1
   Electronic Transitions – Jablonski Diagram
   Quantum Yields and fluorescence lifetimes
   Solvent Effects on fluorescence emission
   Fluorescence quenching – Static and Collisional Lakowicz, Ch. 8
   Stern-Volmer plots, Modified Stern-Volmer plots and chromophore accessibility.
   Fluorescence Anisotropy measurements in biological systems Lakowicz, Ch. 10
   Time-Correlated Anisotropies and the Perrin Equation Lakowicz, Ch. 11
   Resonance (Forster) Energy Transfer, Bioluminescence resonance energy transfer
   Applications of RET and BRET
   Real time PCR
   Molecular Beacons – Identifying SNPs and Gene Haplotypes
   Fluorescence indicators of membrane potential, cytosolic calcium, etc.
   Fluorescence Microscopy – immunofluorescence, double labeling of cells and stem cells
   Fluorescence and Next-Generation DNA sequencing

MALDI-TOF Spectrometry
   Theory of MALDI-TOF
   Protein Identification by MALDI-TOF
   Other biological applications of MALDI-TOF

Nuclear Magnetic Resonance
Theory of NMR, NOESY
Biological applications – protein structure, membrane structure
Protein & nucleic acid structure determination by NMR
Functional MRI

VII. Natural and Artificial Membranes
Physical structure of biological membranes
Natural and artificial membrane bilayers – MLV, SUV, etc.
Plasma membranes in Archae
Lipid bilayers and membrane order
Role of cholesterol in phospholipid bilayers
Hexagonal II (HII) phase lipids and membrane fusion

Lipid Rafts and cell signaling
Detection of lipid rafts
Membrane proteins and lipid-protein interactions
Membrane techniques – Calorimetry, fluorescence anisotropy, NMR.

VIII. Transport Phenomena and Biological Membranes
Diffusion, random walks
Fick’s Law of diffusion
Transport across membranes
Facilitated transport
Signal transduction
ER and PM calcium transport

Final Exam (closed book and closed notes. Not comprehensive).
12:30-1:50 PM Lecture T R Thursday, May 3. 10:30 AM - 12:30 PM

Spring 2018 Academic Calendar
Tuesday, January 16 Spring Term Courses begin
Monday, January 29 Last day to add or drop a Full Term 16-week course
Monday, March 5-11 Spring Break (no classes held)
Wednesday, March 21 Last day to withdraw from Spring 2018 semester course
Monday, April 30 Classes end for Spring 2018 semester (our last class is 4/26)
Tue May 1 - Wed May 2 Study Days
Thursday, May 3-May 9 Final Exam week

Background Reading
Online book information:
   http://mhhe.com/biosci/genbio/raven6b/graphics/raven06b/other/raven06b_10.pdf
2. Plant Physiology online. http://5e.plantphys.net Chapters 7 and 8 on photosynthesis