课程大纲
COURSE SYLLABUS

1.	**课程代码/名称** **Course Code/Title**	BIO5007/蛋白质结构与功能 Protein Structure and Function
2.	**课程性质** **Compulsory/Elective**	专业选修课
3.	**课程学分/学时** **Course Credit/Hours**	3/64 （30 hours for lectures, 6 hours for tutorials and 28 hours for experiments）
4.	**授课语言** **Teaching Language**	中英文 Chinese/English
5.	**授课教师** **Instructor(s)**	曾福星
6.	**是否面向本科生开放** **Open to undergraduates or not**	否
7.	**先修要求** **Pre-requisites**	（如面向本科生开放，请注明区分内容。 If the course is open to undergraduates, please indicate the difference.） 无

8. **教学目标**
Course Objectives

蛋白质是生命体中最具多样性的大分子，在几乎所有的生命进程中都扮演着必不可少的角色。蛋白质的天然结构是其功能发挥的基础，不同的结构决定了不同的功能。本课程的目标是通过介绍蛋白质的结构基础、结构解析手段及其结构与功能之间关系，帮助学生了解蛋白质如何行使其功能。同时，本课程也强调结构与功能研究的实验基础和技能。通过该课程的学习，学生能够对蛋白质有更深入的认识，系统的对蛋白质的结构与功能进行描述，进一步通过对结构的分析针对蛋白质和药物进行结构设计，而且能够利用所学到的理论知识和实验技能解决生物学研究和医学研究中的相关问题。本课程的教学中将采用理论结合实验的方式，有效地促进学生对于课程内容的理解，并锻炼他们的动手能力，为培养高层次创新人才奠定基础。

Proteins are the most versatile macromolecules in living systems and serve crucial functions in essentially all biological processes. Our aim is to teach the structure bases, method to determine structures and the basic principles governing protein structure-function relationship. With this course, students will have a fundamental understanding of the structure and function of proteins, an atomic overview of our living system, as well as knowledge and skills to solve problems in biological and medical research.

9. **教学方法**
Teaching Methods

本课程的教学由理论和实验两部分组成，相辅相成，互相促进，提高教学效果。实际教学中包括多项创新型教学方式，包括：

1、 应用多种基于电脑的教学游戏和程序，激发学生的学习兴趣和热情；

2、 创造性地结合实验来辅助教学，帮助学生了解各种实验手段和技术是如何被用于研究蛋白质结构与功能的关系的；

3、 教学内容紧密联系实际，给学生展示如何将学到的知识应用于科学研究和医学中；

4、 结合线上和线下的教学模式，通过提高优质的线上教学资料，有效地提高学生的学习深度和广度。

The course teaching consists of theory learning part and experimental part. The teaching combines traditional and innovative methods, including:

1. Apply computer games and programs to stimulate learning interest;
2. Creatively combine the well-designed experiments with theory for students to know why and how different experimental approaches can be applied in understanding protein structure-function relationship;
3. Tightly link the research and medicine application to the teaching;
4. Effectively combine online and offline teaching by providing related online material for student to expand their leaning scope.

10. 教学内容
Course Contents

Section 1	**From Sequence to Structure (6hrs)** 1-1.1 Peptide Bond 1-1.2 Interactions that Stabilize Structures 1-1.3 Secondary Structures Related Experiment: Proteins for structural study I: sequence alignment and secondary structure analysis 1-2.1 Protein Motifs 1-2.2 Protein Domains 1-2.3 Tertiary structures Related Experiment: Proteins for structural study II: domain analysis and structure prediction 1-3.1 Protein Family 1-3.2 Protein Folding and Stability 1-3.3 Quaternary Structure Related Experiment: Proteins for structural study III: Protein databases and structure comparison
Section 2	**Structure Determination (10hrs)** 3-1.1 Structure Determination Methods 3-1.2 X-Ray Crystallography: Basics of crystallography 3-1.3 Points of designing experiments for structural studies Related Experiment: Proteins for structural study III: Protein databases and structure comparison 3-2.1 X-Ray Crystallography: Space lattice 3-2.2 X-Ray Crystallography: Diffraction 3-2.3 Case study for good and bad diffractions Related Experiment: Data processing with iMosflm 3-3.1 X-Ray Crystallography: Phase problem 3-3.2 X-Ray Crystallography: Model building Related Experiment: Structure determination with Phenix and COOT

	3-4.1 CryoEM: Introduction 3-4.2 CryoEM: Single Particle technique Related Experiment: Model building with Chimera for cryoEM reconstruction 3-5.1 NMR 3-5.2 Other methods 3-5.3 Importance of resolution 3-5.4 Flexible region 3-5.5 Case study: Can we trust the conclusion in the literatures Related Experiment: Structure quality check
Section 3	**From Structure to Function (6hrs)** 3-1.1 Molecular Recognition 3-1.2 Functional Sites 3-1.3 Active Sites 3-1.4 Location and Nature of Binding Sites 3-1.5 Case study: Predict the binding sites Related Experiment: Structure analysis 3-2.1 Catalysis 3-2.2 Proximity and Ground-State Destabilization 3-2.3 Stabilization of Transition States and Exclusion of Water 3-2.4 Active-Site Geometry and Chemistry 3-2.5 Cofactors 3-2.6 Multi-Step Reactions 3-2.7 Multifunctional Enzymes Related Experiment: Identification of functional sites 3-3.1 Membrane Protein Structure and Folding 3-3.2 Membrane Protein Prediction 3-3.3 Structure and Function of GPCR and Ion Channel 3-3.4 Functional Properties of Structural Proteins Related Experiment: Membrane protein analysis
Section 4	**Control of protein function (8hrs)** 4-1.1 Flexibility and Protein Function 4-1.2 Protein Interaction Domains 4-1.3 Regulation by Location 4-1.4 Control by pH and Redox Environment 4-1.5 Case study: Control the protein expression with different environment Related Experiment: Interaction analysis I 4-2.1 Effector and Allostery 4-2.2 Competitive Binding and Cooperativity 4-2.3 Conformational Change 4-2.4 GTPase switches Related Experiment: Interaction analysis II 4-3.1 Co-translational Modification 4-3.2 Post-Translational Modification 4-3.3 Methylation and Epigenetics 4-3.4 Phosphorylation

	4-3.5 Ubiquitination and SUMOylation Related Experiment: Function prediction base on structure 4-4.1 Principle for protein design 4-4.2 Principle for drug design 4-4.3 Case study: Design the protein mutants and optimize the compound structures Related Experiment: Drug design

Week	Content	Experiment
	From sequence to structure	
1	Introduction, primary and secondary structure	
2	Protein motif, domains and tertiary structure	Proteins for structural study I: sequence alignment and secondary structure analysis
3	Protein folding and quaternary structure	Proteins for structural study II: domain analysis and structure prediction
	Structure Determination	
4	Introduction and basics of X-Ray Crystallography	Proteins for structural study III: Protein databases and structure comparison
5	Principle of X-Ray Crystallography	Data processing with iMosflm
6	X-Ray Crystallography: structure determination	Structure determination with Phenix and COOT
7	cryoEM: Single Particle technique	Model building for cryoEM reconstruction
8	NMR and other methods	Structure quality check
	From structure to Function	
9	Functional sites in protein structures	Structure analysis
10	Catalysis	Identification of functional sites
11	Membrane and structural proteins	Membrane protein analysis
	Control of protein function	
12	Environmental controls	Interaction analysis I
13	Cooperativity and allostery	Interaction analysis II
14	Modification regulations	Function prediction base on structure
15	Protein and drug design	Drug design
16	**Project presentation**	**Experimental design**

11. 课程考核
Course Assessment

（①考核形式 Form of examination；②.分数构成 grading policy；③如面向本科生开放，请注明区分内容。If the course is open to undergraduates, please indicate the difference.）

考核形式 Form of examination：分数构成 grading policy

实验/Experiments：(30%)
论文研讨及报告/Journal Club：(20%)
期末考试/Final Exam：(30%)
期末报告/Final Presentation（Presentation + Article）：(20%)

12. **教材及其它参考资料**
Textbook and Supplementary Readings

教材/Textbook

Protein Structure and Function*,* Gregory Petsko & Dagmar Ringe, 2008

参考书/Reference book

1. ***Proteins: Structure and Function,*** David Whitford, 2013
2. ***Principles of protein X-Ray crystallography,*** Jan Drenth ; with major contribution from Jeroen Mesters, New York : Springer, c2007