COURSE OUTLINE: BS3008

Course Title	**Computer Aided Drug Discovery**		
Course Code	**BS3008**		
Offered	Study Year 3, Semester 2		
Course Coordinator	Mu Yuguang (Assoc Prof)	YGMu@ntu.edu.sg	6316 2885
Pre-requisites	BS1002 OR BS1012 OR CM1001		
AU	3		
Contact hours	Lectures: 26, Laboratories: 9, Tutorials: 9		
Approved for delivery from			
Last revised	16 Dec 2022, 13:26		

Course Aims

This course aims to equip you with both the physical foundations of biomolecular dynamics simulation methods and practical training in use of these methods. It helps you to understand the structure of biomolecules and more importantly link the structure and dynamics together. In the course you will develop skills in describing structure and dynamics in a quantitative way which enables rational drug discovery in later courses.

Intended Learning Outcomes

Upon successfully completing this course, you should be able to:

1. Use Linux operating system to manipulate files, and run programs
2. Write AWK programs to analyse data
3. Set up and run molecular dynamics simulations using GROMACS
4. Perform virtual screening of small molecule library using Autodock vina
5. Manipulate small molecule formats using open_babel
6. Identify protein-drug interaction using pymol
7. Represent small molecules using Charmm-GUI tools

Course Content

Introduction to molecular modelling

Molecular force fields

Application of molecular force fields in research

Methods of energy minimization

Methods of molecular dynamics simulation

Methods of Monte Carlo Simulations

Basic Statistical Mechanics

Data analysis

Methods of molecular docking

Electrostatics and Dielectric continuum models, Poisson-Boltzmann (PB) model

Coarse grained (CG) models

Donnan salt exclusion effect, DNA-ligand binding, DNA helix-coil transition

DNA hydration and ion interactions

Virtual screening of small molecule library

Check protein-drug binding stability by molecular dynamics simulations

Assessment

Component	Course ILOs tested	SBS Graduate Attributes tested	Weighting	Team / Individual	Assessment Rubrics
Continuous Assessment					
Laboratories					
Presentation	1, 2, 4, 6, 7	**1.** b **2.** c, e, g **3.** a, b **5.** c, d, e **7.** a, c	25	individual	See Appendix for rubric
Written Report	1, 2, 4, 5	**1.** b **2.** c, e, g **3.** a, b **5.** c, e **7.** a, c	25	individual	See Appendix for rubric
Examination (2.5 hours)					
Short Answer Questions	1, 2, 3, 4, 5, 6, 7	**1.** b **2.** c, e, g **3.** a, b **5.** c, d, e **7.** a, c	50	individual	See Appendix for rubric
		Total	**100%**		

These are the relevant SBS Graduate Attributes.

1. **Recognize the relationship and complexity between structure and function of all forms of life, resulting from an academically rigorous in-depth understanding of biological concepts**

   b. Explain the relationship between structure and function of all forms of life at the molecular level

2. **Critically evaluate and analyze biological information by applying the knowledge, scientific methods and technical skills associated with the discipline**

   c. Create abstract models of data

   e. Analyze the validity of qualitative and quantitative scientific data

   g. Evaluate the results of their own experiments and decide on the next step

3. **Develop and communicate biological ideas and concepts relevant in everyday life for the benefit of society**

   a. Simplify and explain scientific concepts and results of experiments to a non-biologist (avoiding jargon)

   b. Display and explain scientific results clearly and persuasively to peers both verbally and in writing (includes the ability to graph data appropriately and accurately).

5. **Develop communication, creative and critical thinking skills for life-long learning**

   c. Demonstrate critical thinking skills such as analysis, discrimination, logical reasoning, prediction and transforming knowledge

   d. Question the assumptions, sources, and contexts of scientific investigation

   e. Demonstrate good observation skills and a curiosity about the world

7. **Demonstrate information literacy and technological fluency**

   a. Locate and evaluate information needed to make decisions, solve problems, design experiments, and understand scientific data

c. Evaluate and use biological databases (literature and public datasets)

Formative Feedback

During the tutorials/lectures I will give comments and corrections of your answers to the questions usually uploaded a week before. You try to solve the problems by yourself first and show your results on the whiteboard in turn. In such a way learning outcomes 3,4,5,6 and 7 will be covered.

During the oral presentation you will explain the simulation data and your own analysis you got during the lab sessions. Comments and corrections will be given by me to explain more details how to interpret the simulation data and what methods should be used to analyze the data. Thus the learning outcomes 1,2,4,5 and 6 are covered.

Learning and Teaching Approach

Lectures (26 hours)	Lectures make use of animated movies to explain some abstract concepts such as ensemble and force field. This helps you to achieve the learning outcomes of 3,5,6 and 7.
Laboratories (9 hours)	Laboratories give you hands-on experiences in computational biology exercises, which help you to achieve the learning outcomes 1, 2 and 4.
Tutorials (9 hours)	Show detailed steps to solve some difficult problems, such as learning outcomes 2, 4,5,6 and 7.

Reading and References

1. Tamar Schlick, Molecular modeling and simulation : an interdisciplinary guide , Springer, c2002.(QD480.S344),ISBN 978-1-4419-6351-2

2. Alan Hinchliffe, Molecular Modelling for Beginners, First Edition, November 2003, John Wiley & Sons Inc; ISBN 0 470 84309 8 (Hardback)

3. Hans-Dieter Höltje ,Molecular modeling : basic principles and applications,2nd Edition, John Wiley, 2003.(QH506.M718MMB),ISBN 3527305890 (Paperback).

4. Christopher J. Cramer, Essentials of Computational Chemistry, John Wiley, 2002, ISBN: 978-0-470-09182-1

Course Policies and Student Responsibilities

During the lectures you are encouraged to ask any questions related to the lecturing contents.

During the tutorials you are requested to show your own answers before I discuss them.

During the lab sessions you will do computational setup step by step and do basic data analysis on your own simulation data.

During the oral presentation, you are recommended to make note of my suggestions on your presentation and later to improve your lab report accordingly.

Academic Integrity

Good academic work depends on honesty and ethical behaviour. The quality of your work as a student relies on adhering to the principles of academic integrity and to the NTU Honour Code, a set of values shared by the whole university community. Truth, Trust and Justice are at the core of NTU's shared values.

As a student, it is important that you recognize your responsibilities in understanding and applying the principles of academic integrity in all the work you do at NTU. Not knowing what is involved in maintaining academic integrity does not excuse academic dishonesty. You need to actively equip yourself with strategies to avoid all forms of academic dishonesty, including plagiarism, academic fraud, collusion and cheating. If you are uncertain of the definitions of any of these terms, you should go to the Academic Integrity website for more information. Consult

your instructor(s) if you need any clarification about the requirements of academic integrity in the course.

Course Instructors

Instructor	Office Location	Phone	Email
Mu Yuguang (Assoc Prof)	04s-46a	6316 2885	YGMu@ntu.edu.sg

Planned Weekly Schedule

Week	Topic	Course ILO	Readings/ Activities
1	Introduction to molecular modelling	1	lab practice
2	Molecular force fields	1, 2, 3	do tutorial questions and lab practice
3	Application of molecular force fields in research	2, 3, 4	do tutorial questions
4	Methods of energy minimization	3, 4, 5	do tutorial questions
5	Methods of molecular dynamics simulation	3, 4, 5	do tutorial questions
6	Methods of Monte Carlo Simulations	3, 4, 5	do tutorial questions
7	Basic Statistical Mechanics	3, 4, 5, 6	do tutorial questions
8	Data analysis	2, 6, 7	do tutorial questions and some basic programing
9	Methods of molecular docking	3, 4, 5, 6, 7	do tutorial questions
10	Electrostatics and Dielectric continuum models, Poisson-Boltzmann (PB) model	6, 7	do tutorial questions
11	Coarse grained (CG) models	3, 4	do tutorial questions
12	Donnan salt exclusion effect, DNA-ligand binding, DNA helix-coil transition	6, 7	do tutorial questions
13	DNA hydration and ion interactions	6, 7	do tutorial questions

Appendix 1: Assessment Rubrics

Rubric for Laboratories: Presentation (25%)

You are required to present data analysis results of the simulation study of a protein by using GROMACS tools. The simulation setup, data analysis and nice figures are needed to illustrate your results. The total score will be scaled to 25%.

Points:

5 - Far exceed standard, 4- exceed standard 3 - meets standard, 2 - Nearly meets standard, 1 - Does not meet standard

Category	Criteria	Points
General Presentation and communication skills	Effectively uses eye contact	5
	Speak clearly and effectively using suitable volume and pace	5
	Use of words correctly	5
	Time control	5
	Introduces topic clearly and creatively	5
	Presentation in a logical sequence	5
	Visual aids are well prepared	5
	Confident in presenting own ideas	5
Content (Introduction)	Correct use of references	5
	Smooth Transitions between topics	5
	Introduction is well organized with appropriate amount of information and lays out the problem well/hypothesis	5
	Introduction contains accurate information	5
Content (Result & Discussion)	Describe principle of experiments correctly	5
	Presentation of data in professional manner	5
	Analysis data professionally	5
	Integrate knowledge from other modules for data analysis	5
	Combines and evaluates existing knowledge and data to form new insights	5
	Future direction with high originality and creativity	5
Q&A	Demonstrate extensive knowledge of the topic by responding confidently and precisely	5
	Integrate knowledge from various sources to answer the questions	5
Total		100

Rubric for Laboratories: Written Report (25%)

You are required to write a detailed report of the simulation study of a protein by using GROMACS tools. The simulation setup, data analysis and nice figures are needed to illustrate your results. The total score will be scaled to 25%.

Criteria / Marks	Strong	Medium	Weak
Content (70% weight)	Strong depth in terms of thinking and/or technical achievement All facts are correct and arguments logically sound	Moderate depth in terms of thinking and/or technical achievement. Most facts are correct and arguments logically sound	Superficial in terms of thinking and/or technical achievement. Poor factual knowledge with illogical arguments
Organization (10% weight)	Clear and easily understandable sentences. Supporting points are presented sequentially	Somewhat clear but difficult to understand. Supporting points lack sequential order	Total lack of clarity and no sense of organization
Use of Language (10% weight)	Precise and consistent use of terminology / semantics	Somewhat imprecise / consistent in the use of scientific lingo	A complete lack of regard for common working vocabulary
Spelling and grammar (10% weight)	No or few grammatical and/or spelling errors.	Several grammatical and/or spelling errors but still understandable	Major grammatical and/or spelling errors and incomprehensible

Rubric for Examination: Short Answer Questions (50%)

The short answer questions will involve solving physics problems relating to biological processes. You will need to show full mathematical derivations and explain or interpret the results you find. The total score will be scaled to 50%.

Criteria	Standards		
	Fail standard(0-4 marks)	**Pass standard(5-7 marks)**	**High standard(8-10 marks)**
Correctness of the answers	Wrong answers or without any formula and reasoning	Correct answers but lack full equations or any further discussions.	Correct answers with clear formula and equations and further discussions

Appendix 2: Intended Affective Outcomes

As a result of this course, it is expected you will develop the following "big picture" attributes:

An appreciation of the quantitative aspects of biological processes, e.g. binding, protein folding

A dynamic 3D picture of biological molecules

Appreciate computer modeling tools in drug discovery process