CENTRAL UNIVERSITY OF HIMACHAL PRADESH

[Established under the Central Universities Act 2009]
PO Box: 21, Dharamshala, District Kangra - 176215 (HP)
www.cuhimachal.ac.in

SEMESTER III

Course Code: CBB 518
Course Name: Elements of Systems Biology
Instructor Name: Dr Vikram Singh
Credits Equivalent: 4 Credits

(One credit is equivalent to 10 hours of lectures / organised classroom activity / contact hours; 5 hours of laboratory work / practical / field work / Tutorial / teacher-led activity and 15 hours of other workload such as independent individual/ group work; obligatory/ optional work placement; literature survey/ library work; data collection/ field work; writing of papers/ projects/dissertation/thesis; seminars, etc.)

Course Objectives: This course will be centered on (i) the theoretical and practical aspects of modeling in systems biology – both deterministic and stochastic and (ii) the study of biological networks. Students will become acquainted with the key concepts and computational approaches of both these fields.

"Systems Biology" finds its major application in the research field known as "Synthetic Biology" (aiming to design and realize modified or new biological parts). Students will also become familiar with necessary mathematical and computational concepts of Synthetic Biology.

Students having prior knowledge of any programming language will be encouraged to write their own codes for simulating and analyzing model biological systems.

Attendance Requirement:
Students are expected to attend all lectures in order to be able to fully benefit from the course. A minimum of 75% attendance is a must failing which a student may not be permitted to appear in examination

Evaluation Criteria:
1. Mid Term Examination: 25%
2. End Term Examination: 50%
3. Continuous Internal Assessment: 25%
    a. Attendance: 5%
    b. Class-room participation: 5%
    c. Class test: 5%
    d. Presentation and assignment: 10%

Course Contents

Unit 1: Introductory interdisciplinary concepts (8 hours)

- Definition and scope of systems and synthetic biology. Introduction to biological complexity -- Self organization, Emergence, Chaos, Robustness.
- First-order systems: Fixed points and stability, Population growth.
- Bifurcations (with examples) in first order systems: Saddle node, Pitch fork, Transcritical.
- Basic notion of bifurcations in second order systems: Period doubling, Hopf.

Unit 2: Deterministic modelling in systems biology (8 hours)

- Chemical kinetics, Michaelis-Menten kinetics, Hill equations
- Feedback in gene regulation: positive, negative, mutual inhibition
- Deterministic methods of systems modelling (Euler and RK4), with numerical applications on

  a) Simple examples of autocatalysis, linear degradation etc.

  b) Examples from natural systems: Predator-Prey, p53-mdm2.

  c) Examples from synthetic systems: Brusselator, Repressilator.

Unit 3: Stochastic modelling in systems biology (8 hours)

- Introduction to noise in biological systems. Intrinsic vs. extrinsic noise. System behavior and role of noise.
- Stochastic Methods for modelling biological systems (Master equation, Gillespie's stochastic simulation algorithm)
- Application of Gillepsie's SSA on Brusselator, Predator-Prey and other simple examples.

Unit 4: Design principles of biological networks (8 hours)

- Introduction to networks: Hamiltonian path vs. Eulerian path; Basic terminology; Topology of genetic, metabolic and ecological networks.
- Network models: Erdös-Renyi, Small-world, Scale-free.
- Global Properties: Average path length, network diameter, centrality measures, clustering coefficients etc. Modular and hierarchical networks.
- Local Properties: Regulatory motifs and graphlets in networks. Motifs in TRNs: discussion on FFL, SIM and other motifs.

UNIT 5: Analysis of biological networks **(8 Hours)**

- Elementary graph algorithms: Breadth-first search, Depth-first search, Topological sort, Strongly connected components. Growing a minimum spanning tree.
- Finding shortest path: Single source shortest path, All pairs shortest paths
- Network clustering: Clique based clustering, Center based clustering
- Basics of flux balance analysis.

Text Books:

17. **Steven H. Strogatz (1994),** Nonlinear Dynamics and Chaos: With Applications to Physics, Biology, Chemistry, and Engineering. Perseus Books, Massachusetts.
18. **Szallasi *et al.* (2010),** System Modelling in Cellular Biology. MIT Press.
19. **Junker and Schreiber (2008),** Analysis of Biological Networks. Wiley-Interscience, New Jersy.

Additional Readings:

1 **Uri Alon (2006),** an Introduction to the Systems Biology. Chapman and Hall.
2 **Mark Newman (2010),** Networks: An Introduction. Oxford University Press.
3 **Klipp *et al.* (2009),** Systems Biology in Practice. Wiley-VCH.
4 **BO Palsson (2006),** Systems Biology. Cambridge University Press.
5 **Press *et al.* (2007),**Numerical Recipies in C. Cambridge University Press.
6 **Singh and Dhar (2015),** Systems and Synthetic Biology, Springer

CENTRAL UNIVERSITY OF HIMACHAL PRADESH
[Established under the Central Universities Act 2009]
PO Box: 21, Dharamshala, District Kangra - 176215 (HP)
www.cuhimachal.ac.in

SEMESTER III

Course Code: CBB 515
Course Name: Computer Aided Drug Discovery
Course Instructor: Dr P. Aparoy
Credits Equivalent: 4 Credits (One credit is equivalent to 10 hours of lectures / organised classroom activity / contact hours; 5 hours of laboratory work / practical / field work / Tutorial / teacher-led activity and 15 hours of other workload such as independent individual/ group work; obligatory/ optional work placement; literature survey/ library work; data collection/ field work; writing of papers/ projects/dissertation/thesis; seminars, etc.)
Course Objectives:
This course will be centred on**:**

- When to use CADD methods in your research (and when not to).
- Which methods are best to use to solve your particular research problems.
- Structure Based and Ligand based drug design approaches and examples.
- Role of Scaffold Hopping in modern drug discovery

Attendance Requirement:
Students are expected to attend all lectures in order to be able to fully benefit from the course. A minimum of 75% attendance is a must failing which a student may not be permitted to appear in examination.
Evaluation Criteria:

1. Mid Term Examination: 25%
2. End Term Examination: 50%
3. Continuous Internal Assessment : 25%
    a) Class room participation 5 %
    b) Assignments 5 %
    c) Class test 10 %
    d) Presentations 5 %

Course contents:
Unit –I: Introduction to Drug Discovery and Proteins **(5 classes)**

- Introduction : Drug Discovery process
- Differences between traditional and computational drug discovery
- Proteins: Amino acids; Levels of Protein Structure
- Anfinsen's experiment and dogma

Unit –II: Introduction to Molecular Modelling (**10 classes**)

- Force Field
- Intermolecular interactions
- Energy minimization; Local and global minima
- Types of energy minimization methods

Unit –III: Structure Based Drug Design **(10 classes)**

- Protein Structure Prediction; Homology modelling
- Docking and its applications : Various search algorithms and scoring functions
- *De novo* drug design methods
- Virtual screening and its applications
- Molecular Dynamics

Unit –IV: Ligand Based Drug Design **(10 classes)**

- QSAR
- Pharmacophore Modelling
- Pseudoreceptor Modelling
- Scaffold Hopping

Unit –V: Clinical Trials and Drug Discovery **(5 classes)**

- Success stories of CADD
- Clinical trials

Reference books:

- Andrew Leach (2009) Molecular Modelling: Principles and Applications, Pearson Education (ISBN-13: 9788131728604).
- Kenneth M. Merz, Dagmar Ringe, Charles H. Reynolds (2010) Drug Design: Structure- and Ligand-Based Approaches, Cambridge University Press (ISBN-13: 9780521887236)
- Lipkowitz, KB, Boyd, DB, Eds (1997) Reviews in Computational Chemistry; John Wiley & Sons, Inc.: Hoboken, NJ, USA (ISBN: 9780471192480)

Additional Readings

1. David L. Nelson, Michael M. Cox (2017) Lehninger Principles of Biochemistry 7th Edition, WH Freeman publisher

2. Laurie AT, Jackson RM. Methods for the prediction of protein-ligand binding sites for structure-based drug design and virtual ligand screening. Curr Protein Pept Sci. 2006 Oct; 7(5):395-406. Review. PubMed PMID: 17073692.
3. Krieger E, Nabuurs SB, Vriend G. Homology modeling. Methods Biochem Anal. 2003;44:509-23. Review. PubMed PMID: 12647402.
4. Dias R, de Azevedo WF Jr. Molecular docking algorithms. Curr Drug Targets. 2008 Dec;9(12):1040-7. Review. PubMed PMID: 19128213.
5. Oda A, Tsuchida K, Takakura T, Yamaotsu N, Hirono S. Comparison of consensus scoring strategies for evaluating computational models of protein-ligand complexes. J Chem Inf Model. 2006 Jan-Feb;46(1):380-91. PubMed PMID: 16426072.
6. Warren GL, Andrews CW, Capelli AM, Clarke B, LaLonde J, Lambert MH, Lindvall M, Nevins N, Semus SF, Senger S, Tedesco G, Wall ID, Woolven JM, Peishoff CE, Head MS. A critical assessment of docking programs and scoring functions. J Med Chem. 2006 Oct 5;49(20):5912-31. PubMed PMID: 17004707.
7. Bissantz C, Kuhn B, Stahl M. A medicinal chemist's guide to molecular interactions. J Med Chem 53 (2010) 5061-5084.
8. Sun H. Pharmacophore-based virtual screening. Curr Med Chem. 2008;15(10):1018-24. Review. PubMed PMID: 18393859.
9. Hans-Joachim Böhm, Alexander Flohr, Martin Stahl, Scaffold hopping, Drug Discovery Today: Technologies, Dec 2004; 1 (3) :217–24.

CENTRAL UNIVERSITY OF HIMACHAL PRADESH
[Established under the Central Universities Act 2009]
PO Box: 21, Dharamshala, District Kangra - 176215 (HP)
www.cuhimachal.ac.in

SEMESTER III

Course Code: CBB 516
Course Name: Molecular Evolution and Biodiversity
Course Instructor: Dr. Satpal
Credits Equivalent: 4 Credits (One credit is equivalent to 10 hours of lectures / organized classroom activity / contact hours; 5 hours of laboratory work / practical / field work / Tutorial / teacher-led activity and 15 hours of other workload such as independent individual/ group work; obligatory/ optional work placement; literature survey/ library work; data collection/ field work; writing of papers/ projects/dissertation/thesis; seminars, etc.)

Course Objectives: The course is designed to:

- Make students familiar with laws of genetics.
- Understand mechanism behind the process of molecular evolution.
- Study various techniques which are used to study genetic patterns and evolutionary history.
- Study genetic processes that result in biodiversity.

Attendance Requirement:
Students are expected to attend all lectures in order to be able to fully benefit from the course. A minimum of 75% attendance is a must failing which a student may not be permitted to appear in examination

Evaluation Criteria:
1. Mid Term Examination: 25%
2. End Term Examination: 50%
3. Continuous Internal Assessment: 25%
    a) Presentation 10%
    b) Class Participation 10%
    c) Attendance 5%

Course Content:

UNIT I: INTRODUCTION TO MOLECULAR EVOLUTION (8 hours)
Introduction to Molecular evolution: Meaning and importance of Molecular evolution, heredity and variation, Variations- nature and types, Genetic basis of evolution, Mendelian laws of inheritance, Exceptions in Mendel ‘s laws and organization and structure of gene, evolution of Genetic code, Molecular clock, phylogeny

UNIT II: EVOLUTION AT MOLECULAR LEVEL (8 Hours)

Mutation and its types: Point mutation, Gene duplication, Chromsomal rearrangement, polyploidy and aneuploidy
DNA Damage and Repair: Types of DNA Repair: Base Excision Repair Nucleotide Excision Repair, Mismatch Repair, Double Strand Break Repair
Protein and DNA alignment, distances among sequences, parsimony, Models of molecular evolution: Neutral and nearly neutral theory, tree as evolutionary hypothesis

UNIT III: MOLECULAR TECHNIQUES (8 Hours)

Molecular techniques: RFLP, RAPD, SSR, AFLP, VNTR, Plasmid Fingerprinting
Hybridization techniques: FISH, Nucleic acid probes or hybridisation probe
Polymerization chain reaction and its various types:Allele specific PCR, Helicase Dependent PCR, Real Time PCR , Assembly PCR, Inverse PCR, Anchor Dependent PCR or solid phase PCR , *In situ* PCR, RT PCR, Nested PCR
DNA sequencing methods: Sanger dideoxy method, Maxam Gilbert method

UNIT IV: MOLECULAR EVOLUTION IN BACTERIAL PATHOGENS (8 Hours)

Molecular epidemiology of pathogenic bacteria, Applications in Epidemiology Diagnostics and Interventions, Strategies of genome evolution, gene acquisition Horizontal gene transfer (HGT)
Evolution in *Mycobacterium tuberculosis* and *M. leprae*
Reductive evolution: Case of *Mycobacterium leprae* and *Yersinia pestis*

UNIT V: BIODIVERSITY (8 hours)

Biodiversity: Genetic, species and ecosystem diversity. Biodiversity at global and national levels.
Genetic variations, genetic drift, factors that affect genetic variations
Approaches to biodiversity conservation: species and landscape approach, Ecosystem approach

PRESCRIBED TEXT AND REFERENCE BOOKS:

1. John H.Gillespie. (2004), Population genetics: A concise guide, (2^{nd}edn), John Hopkins
2. P.Higgs and T.Atwood. (2005), Bioinformatics and Molecular Evolution, John Wiley and Sons
3. Molecular Biology of the gene (2004), Watson, Baker, Bell, Gann, Levine and Losick,(5^{th} edn)

Additional Readings:

1. Purves, Sadava, Orians and Heller, Life-The Science of Biology (7th edn)
2. Bebjamin and Pierce (2005), Genetics, A Conceptual Approach (2nd edn)
3. D.C.Reanney Hicks and Smith. (1973), Molecular Evolution, Frontiers of Biology
4. Richard B. Primack. (2002). Essentials of Conservation Biology (3rd edition)
5. Eldon John Gardner, Michael J. Simmons, D. Peter Snustad. Principles of Genetics (8th edition)
6. T. A. Brown. (2010). Gene Cloning and DNA Analysis: An Introduction (6th edition)
7. T.A. Brown (2002). Genomes 2, BIOS scientific Publishers

Journal Articles

1. Evolution of *Mycobacterium tuberculosis* (2013). *Adv Exp Med Biol.*; 783:81-91.
2. Genomic fluidity and pathogenic bacteria: applications in diagnostics, epidemiology and intervention (2008). *Nat Rev Microbiol.* 6(5): 387-94.
3. *Mycobacterium leprae*: genes, pseudogenes and genetic diversity (2011).*Future Microbiol*6(1): 57–71. Doi: 10.2217/fmb.10.153
4. Studying Genomes Through the Aeons: Protein Families, Pseudogenes and Proteome Evolution (2002). *Journal of Molecular Biology*.
5. Horizontal Gene Transfers in prokaryotes show differential preferences for metabolic and translational genes (2009). *BMC Evolutionary Biology*.

LECTURE PLAN

Lectures	Topics	Prescribed Text Book	Chapter No.
Lecture – 1	Introduction to Molecular evolution: Meaning and importance of Molecular evolution	Book-4	26
Lecture – 2	Heredity and variation	Book-4	9,24
Lecture – 3	Variations- nature and types	Book-4	9,24
Lecture – 4	Genetic basis of evolution	Book-4	26
Lecture – 5	Mendelian laws of inheritance & Exceptions in Mendel ‘s laws	Book-5	2
Lecture – 6	Organization and structure of gene	Book-4	9
Lecture – 7	Evolution of Genetic code	Book-3	15
Lecture – 8	Molecular clock & phylogeny	Book-4	26
Lecture – 9	Mutation and its types: Point mutation	Book-10	14
Lecture – 10	Gene duplication, Chromsomal rearrangement	Book-10	14
Lecture – 11	Polyploidy and aneuploidy	Book-5	9
Lecture – 12	DNA Damage and Repair: Types of DNA Repair: Base Excision Repair	Book-10	14
Lecture – 13	Nucleotide Excision Repair & Mismatch Repair,	Book-10	14
Lecture – 14	Double Strand Break Repair & Protein and	Book-10	14

	DNA alignment		
Lecture – 15	Distances among sequences, parsimony	Book-2	8
Lecture – 16	Models of molecular evolution: Neutral and nearly neutral theory, tree as evolutionary hypothesis	Book-2	8
Lecture – 17	Molecular techniques: RFLP, RAPD,	Book-9	10
Lecture – 18	SSR, AFLP	Book-9	10
Lecture – 19	VNTR, Plasmid Fingerprinting	Book-9	10
Lecture – 20	Hybridization techniques: FISH, Nucleic acid probes or hybridisation probe	Book-9	10
Lecture –21	Polymerization chain reaction and its various types:Allele specific PCR, Helicase Dependent PCR,	Book-9	9
Lecture –22	Real Time PCR , Assembly PCR & Inverse PCR	Book-9	9
Lecture –23	Anchor Dependent PCR or solid phase PCR , *In situ* PCR, RT PCR, Nested PCR	Book-9	9
Lecture –24	DNA sequencing methods: Sanger dideoxy method, Maxam Gilbert method	Handouts & Web Resources	
Lecture –25	Molecular epidemiology of pathogenic bacteria	11,12	
Lecture –26	Applications in Epidemiology	11,12	
Lecture –27	Diagnostics and Interventions	11,12	
Lecture –28	Strategies of genome evolution	Book-4	26
Lecture –29	Gene acquisition	Book-4	26
Lecture –30	Horizontal gene transfer (HGT)	15	
Lecture –31	Evolution in *Mycobacterium tuberculosis* and *M. leprae*	11	
Lecture –32	Reductive evolution: Case of *Mycobacterium leprae* and *Yersinia pestis*	13,14	
Lecture –33	Biodiversity: Genetic	Handouts & Web Resources	
Lecture –34	Species and ecosystem diversity	Handouts & Web Resources	
Lecture –35	Biodiversity at global and national levels	Handouts & Web Resources	
Lecture –36	Genetic variations	Book-1	1
Lecture –37	Genetic drift	Book-1	19
Lecture –38	Factors that affect genetic variations	Book-1	19
Lecture –39	Approaches to biodiversity conservation: species and landscape approach	Handouts & Web Resources	
Lecture –40	Ecosystem approach	Handouts & Web Resources	

CENTRAL UNIVERSITY OF HIMACHAL PRADESH
[Established under the Central Universities Act 2009]
PO Box: 21, Dharamshala, District Kangra - 176215 (HP)
www.cuhimachal.ac.in

SEMESTER III

Course code: CBB 540

Course Name: High Throughput Sequencing Technologies: data analysis and applications

Credit Equivalent: 4 Credits (One credit is equivalent to 10 hours of lectures / organised classroom activity / contact hours; 5 hours of laboratory work / practical / field work / Tutorial / teacher - led activity and 15 hours of other workload such as independent individual/ group work; obligatory/ optional work placement; literature survey/ library work; data collection/ field work; writing of papers/ projects/dissertation/thesis; seminars, etc.)

Course Objectives: The course is designed to:

- Introduce students to the fundamental of DNA and RNA sequencing
- Introduce to high throughput sequencing (HTS) technologies and algorithms involved.
- Applications of HTS in biology

Attendance Requirements:

Students are expected to attend all lectures in order to be able to fully benefit from the course. A minimum of 75% attendance is a must failing which a student will not be permitted to appear in examination.

Evaluation Criteria:

1.Mid Term Examination: 25%

2.End Term Examination: 50%

3.Continuous Internal Assessment: 25%

(a) Assignment: 10%

(b) Class test: 5%

(c) Presentation: 10%

Course Contents:

Unit-I: First generation sequencing technologies (4 hours)

- Introduction
- Maxam-Gilbert sequencing
- Sanger sequencing
- Limitations of first generation technologies

Unit-II: High Throughput Sequencing Technologies (HTS) (10 hours)

- Introduction to HTS
- Overview of HTS platforms
- Future sequencing technology
- Comparison of available HTS techniques
- NGS file formats
- NGS databases

Unit-III: Genome sequence assembly (8 hours)

- Reference based genome assembly
- *De novo* genome sequence assembly
- Challenges in genome assembly
- Single-End reads and Pair-End reads in assembly
- Data preprocessing methods and sequence read correction methods
- Assembly errors and evaluation of assembly methods

Unit-IV: Assembly algorithms (8 hours)

- The overlap graph approach
- De Bruijin graph approach
- Classification of *De Novo* assembly algorithms
- Greedy algorithms
- Overlap Layout Consensus (OLC) algorithms
- De Bruijin Graph-Based algorithms
- Comparison of algorithms

Unit-V: Application of HTS (10 hours)

- Comparative genomics
- Functional genomics
- Diagnostic and exome sequencing
- RNA-seq (transcriptomics) and ChIP-seq
- Disease gene identification
- Metagenomics and Microbiome studies
- Microarray and Metabolomics

TEXT BOOKS:

1. Masoudi-Nejad, Ali, Zahra Narimani, and Nazanin Hosseinkhan. *Next generation sequencing and sequence assembly: methodologies and algorithms*. Vol. 4. Springer Science & Business Media, 2013.

Other References (Review articles)

1. Hert, D. G., Fredlake, C. P., & Barron, A. E. (2008). Advantages and limitations of next□generation sequencing technologies: a comparison of electrophoresis and non□electrophoresis methods. *Electrophoresis*, *29*(23), 4618-4626.

2. Wang, Z., Gerstein, M., & Snyder, M. (2009). RNA-Seq: a revolutionary tool for transcriptomics. *Nature reviews genetics*, *10*(1), 57.

3. Werner, T. (2010). Next generation sequencing in functional genomics. *Briefings in bioinformatics*, *11*(5), 499-511.

4. Prakash, T., & Taylor, T. D. (2012). Functional assignment of metagenomic data: challenges and applications. *Briefings in bioinformatics*, *13*(6), 711-727.

5. Metzker, M. L. (2010). Sequencing technologies—the next generation. *Nature reviews genetics*, *11*(1), 31.

6. Compeau, P. E., Pevzner, P. A., & Tesler, G. (2011). How to apply de Bruijn graphs to genome assembly. *Nature biotechnology*, *29*(11), 987.

7. Reuter, J. A., Spacek, D. V., & Snyder, M. P. (2015). High-throughput sequencing technologies. *Molecular cell*, *58*(4), 586-597.

8. Cao, Y., Fanning, S., Proos, S., Jordan, K., & Srikumar, S. (2017). A review on the applications of next generation sequencing technologies as applied to food-related microbiome studies. *Frontiers in microbiology*, *8*, 1829.