Annexure No.	**42 I**
SCAA Dated	**29.02.2008**

BHARATHIAR UNIVERSITY, COIMBATORE 641046

PG DIPLOMA IN GENOMICS (Affiliated Colleges)

For the students who are admitted from the academic year 2007-08 batch and onwards.

DURATION: ONE YEAR (TWO SEMESTERS)

SUBJECT	THEORY PAPERS	PRACTICAL PAPERS
I semester	4x75=300	1x100=100
II semester	4x75=300	1x100=100
Total marks	600	200

SCHEME OF EXAMINATIONS:

SEMESTER	SUBJECT	Instr Hrs	University Exams	
			Duration hrs.	Max. Marks *
FIRST				
Paper I	GENOME DIVERSITY AND GENE MANIPULATION	75	3	75
Paper II	PLANT AND MICROBIAL GENOMICS	75	3	75
Paper III	HUMAN GENOMICS	75	3	75
Paper IV	INTRODUCTION TO BIOINFORMATICS	75	3	75
PRACTICAL I	BASICS OF GENOMICS	60	-	-
SECOND				
Paper V	STRUCTURAL GENOMICS	75	3	75
Paper VI	FUNCTIONAL GENOMICS	75	3	75
Paper VII	PHARMACOGENOMICS	75	3	75
Paper VIII	BIOETHICS, BIOSAFETY AND IPR	75	3	75
PRACTICAL I	BASICS OF GENOMICS		3	100
PRACTICAL II	APPLIED GENOMICS	60	3	100

∗ Includes 25% continuous internal assessment marks.

Paper I - GENOME DIVERSITY AND GENE MANIPULATION

Unit I:
Organization of genome projects- human, plant, animal and microbial genome. EST sequencing strategies, whole genome assembly.

Unit II:
Characterization of transcriptome- micro arrays, DNA chips and SAGE technology.
Proteomics- protein arrays and structural genomics, functional genomics and comparative genomics.

Unit III:
Evolutionary biology concepts, computational biology review. Epidemiology and recombination. HIV molecular systematic,Paralogous evolution. Phylogenetic analysis: Support measures and phylogenetic concepts. Gene duplication. Support measures and hypothesis testing. Domain evolutions.

Unit IV:
The neutral theory of molecular evolution. Detecting natural selection. Comparative genomics, protein evolution and domain architecture. Homology modeling. Structural genomics.

Unit V:
Basic Techniques in Gene Manipulation: Isolation and purification of Nucleic Acids - Agarose Gel Electrophoresis - Southern, Northern and Western blotting - Polymerase Chain Reaction: Methods and advancements - Enzymes in Molcular Biology: Nucleases, Restriction endonucleases, DNA Ligases, topoisomerases, gyrases, methylases, other modifying enzymes – Bacterial Transformation: Principles and methods

REFERENCES:
1. Peuzner, P.A., Computational molecular Biology, An algorithmic approach.
2. Misener, S and Krawetz, S.A (Eds), 2001. Bioinformatics: Methods and protocols, Replica Press private limited, New Delhi.
3. Mount, D.W, 2001. Bioinformatics: sequence and Genome analysis, Cold spring harbor laboratory press, New York.
4. Taylor, W (Ed), 2000. Bioinformatics: Sequence, structure and databanks. Oxford University Press, Oxford

Paper II - PLANT AND MICROBIAL GENOMICS

Unit I

Plant genome and genomics- An overview, measuring gene activity during plant development; programmed morphogenesis and genome expression profiles; Expressed sequence tags (EST's)- Tools of plant genome analysis- seed germination, dormancy and genetic homogeneity of seeds; seedling vigour- expression of seed germination related functions in cereal grains- GA3 and alpha amylase activity profiles; involvement of induction and transduction of hormone signals.

Unit II

Host-pathogen interactions; suscesptibility/resistance to disease causing plant pathogens; hypersensitive response and manifestations of disease resistance in higher plants; ROS and expression of scavenger functions in relation to disease occurrence. Senescence and programmed cell death, Genome analysis during *in vitro* responses.

Unit III

Chloroplast DNA- Genes for genetic and photosynthetic apparatus, D1 protein, herbicide resistance, interaction of chloroplast and nuclear genes, Rubisco- stress responses in chloroplast DNA, repair mechanism, radiation induced changes, photorepair, adaptive mutagenesis. Comparative study of plant genomes- *Marchantia*, rice, *Arabidopsis thaliana.*

Unit IV

Microbial genomics: Chromosomes, genes, and proteins - Prokaryotes vs Eukaryotes - Genome size - Chromosome organization Mutaions: DNA damage mechanisms Mutagens - DNA repair mechanisms - Direct repair: photolyase and Ada - Mismatch repair: mutSLH - Recombinational repair: recA, recFOR, and recBCD - SOS and translesion synthesis: umuCD - Mutator genes

Unit V

Microbial Genomics: Genetic analysis : Complementation - In vitro complementation: Cross-feeding - In vivo complementation: dominance and cis/trans tests - Genetic recombination

Genetic exchange : Mechanisms of genetic exchange: transformation, conjugation, and transduction - Genetic exchange in nature - Genetic exchange in the lab - Mobilization and transfer - Transposable elements - Transposons and evolution

References:

1. Buchanan, Grussem and Jones (eds)- 2000. Biochemistry and Molecular Biology of Plants.
2. Yu *et. al.* (2002). A Chaft sequence of the rice genome(*Oryza sativa, O. indica*) Science, 296: 79-92.
3. Hwang and Sheen (2001). Two component circuitry Arabidopsis cytokinin signal transduction. Nature 413: 383-89
4. Lansing M.Prescott, John P.Haarley, Donald A.Klein, 1990. Microbiology.

Paper III - HUMAN GENOMICS

Preamble

Scope: Understanding the basics in the human genome will help to design and develop new drugs for the various human disorders and the treatment based on gene therapy

Objective: To expose the students to study the human disorders in molecular level.

Goal: After completion of this paper students will have thorough knowledge in various human disorders and molecular mechanism behind it. This will enhance their knowledge in further discovery and characterization of new drugs

UNIT I

Human Genome Project: Genesis – the Alta summit - Tracking the Genes - Forward Genetics approach, Reverse genetics approach, Human Chromosomes. Important genes associated with each chromosomes - Mendelian and sexlinked traits in human inheritance. Genetic diseases due to defects in autosomal and sex linked genes.

UNIT II

Disease Diagnosis: DNA/RNA Probes and monoclonal antibodies in disease diagnosis. Detection of genetic diseases – Amniocentesis, Detection of genetic disorders: Karyo type analysis, RFLP analysis, Hybridization with Oligonucleotide Probes.

UNIT III

Identification of genes Causing genetic diseases, Pedigree analysis, PFLP studies , STR linkage mapping, Identification: Cystic fibrosis, beta thallasaemia, albinism, duchenne muscular dystrophy, atherosclerosis, retinoblastoma, sickle cell anemia, cancer, Diabetes, obesity, tuberculosis, malaria.

UNIT IV

DNA Profiling/DNA fingerprinting: DNA Markers in disease diagnosis and finger printing: RFLPs, VNTRs, Microsatellites, SNPs, Current Technology for DNA Finger printing.

UNIT V

Gene based therapies: Types of gene therapy, Augmentation of Gene therapy – Targeted Gene Transfer, Genetic Counseling. Gene based therapies for disorders of nervous system, cardiovascular system. Immunology in gene therapy: bone marrow transplantation in leukemia.

Reference:

1. Human Genetics: A modern Synthesis by Gordon Edlin; Jones and Barlett publishers, Borton, 1990.
2. Basic Human Genetics by Elaine Johansen Mange and Arthur P.Mange; Sinauer Associates, Inc, Publishers, Sunderland, Massachusetts, 1994.
3. The Human Genome Project; Deciphering the blueprint of heredity ; Edited by Necia Grant Cooper; University Science books, CA, USA, 1994.
4. Biotechnology by Satyanarayana, Books and Allied (P) Ltd.2005.
5. Transducing the Genome; Information, Anarchy and Revolution in Biomedical Sciences by Gary zweiger. Tata McGraw-Hill Publishers, 2003.

Paper IV - INTRODUCTION TO BIOINFORMATICS

Scope: This paper involves the study of computer assisted management of data that is generated for biotechnological application which helps to make use of data that are fast accumulating in massive databases.

Objective: To expose the students to study various databases and tools

Goal: It is prerequisite for the students to do research by using the various Data bases and bioinformatics tools for the analysis of biomolecules at the sequence level.Exposure to the tools and databases will help them to design research and their application

Unit – I

Principles of computing: Operating systems, application and advantages of Unix/Linux in bioinformatics. Basic word processing and database management soft wares.

Unit – II

Data acquisition and management: Types of data-DNA, RNA and protein sequences, protein structure data, gene and protein expression data. Databases: the public biological databases (Ex. Genbank, SWISSPROT, PDB, etc)- searching and retrieving data form databases- FASTA and BLAST and PHI-BLAST).

Unit – III

Sequence analysis with acquired data: Sequence comparison with pair wise and multiple sequence alignment. Deducing phylogenetic relationships from multiple sequence alignment. Building phylogenetic trees. Profiles and motifs.

Unit – IV

Bioinformatics in structure analysis: Format of a protein structure data. Retrieving protein structures from PDB. Using molecular visualization tools to study protein structure. Predicting protein structure from sequence by comparative modelling and other methods.

Unit – V

Genomics and proteomics: Use of micro arrays to study gene expression. Genome sequencing projects, 2D-PAGE as a tool in proteomics. Bioinformatics and drug discovery.

References

1. Bioinformatics-A beginner's guide by Jean – Michel Claverie and Cedric Notredame, Wiley- Dream Tech India Pvt. Ltd.
2. Developing bioinformatics computer skills by Cynthia Gibas and Per Jambeck, O' Reilly publications.
3. Introduction to bioinformatics by T.K. Attwood and D.J. Parry –smith, Pearson Education Asia.
4. Bioinformatics by David.W.Mount, CBS publishers and distributers.
5. Instant notes in bioinformatics by D.R. Westhead, J.H.Parish and R.M.Twyman.

Paper V - STRUCTURAL GENOMICS

Scope: This paper will help to determine the nucleotide sequence of whole genome and role in determining the 3 D structure of proteins and its function for the human healthcare and thereby improvement of plants and animals.

Objective: To expose the students to study the basics techniques of molecular biophysics

Goal: Upon completion of this paper will emphasize the students to get the theortical knowledge in X ray crystallography and related techniques will help them doing the further research in the area like molecular modeling and Drug designing.

Unit I:
Structural genomics- definition, historical prospective; objectives and strategies, Protein structure- primary, secondary, tertiary and quaternary structures. Basic forces of interactions, conformation, Ramachandran plot and principle of protein folding.

Unit II:
Protein structure databanks- protein databank, Cambridge small molecular crystal structure databank, internal and external coordinate system.

Unit III:
Protein structure determination: x ray crystallography, protein crystallization, x ray diffraction. Molecular replacement and direct method: atomic coordinates and electron density maps, analysis and correctness of structure.

Unit IV:
Protein structure prediction by homology modeling- fold recognition- ab initio methods for structure prediction.

Unit V:
Methods for comparison of 3D structures of protein. Calculation of conformational energy for biomacromolecules, electrostatic energy surface generation, molecular mechanics and molecular dynamics. Simulations of free energy changes- force fields, model selection structure refinement and structure- function relationship.

REFERENCES:
1. Branden, C and J.Troze, 1999. Introduction to protein structure. Second edition.
2. Baxevanis, A.D and Ouellette, B.F.F (Eds), 2001. Bioinformatics: A practical guide to the analysis of genes and proteins. Wiley interscience. New York.
3. Higgins, D and Taylor, W (Eds), 2000. Bioinformatics: Sequence, structure and databnks.Oxford University Press, Oxford.
4. Misener, S and Krawetz, S.A (Eds), 2001.Bioinformatics: methods and protocols. Replica press private limited, New Delhi.

Paper VI. FUNCTIONAL GENOMICS

Scope: It involves the determination of the function of genes and several innovative techniques available to decipher the function of the genes. The different approaches of functional genomics like comparative genomics and whole genome expression analysis can be used to study the function of genes and their improvement.

Objective: Attempts to make use of the vast wealth of data produced by genomic projects to describe gene and protein functions and their interactions.

Goal: Completion of this paper will pave the way for the student to determine and characterize the function of unknown genes and in polymorphic analysis.

UNIT I

Restriction enzymes for Megabase DNA analysis; Biodatabases – Concept, Protein, Nucleic acid. Sequence analysis of protein and DNA – alignment, Calculation of Parameters, Consensus Sequences. Structural Analysis and homology modeling. Micro array: DNA Micro array, Protein Micro array Transcriptomics, Applications and advantages of Micro arrays.

UNIT II

Proteomics: DNA polymorphisms as expressed in proteomes. Large scale proteomic tools – 2D gels, Mass spectroscopy, Computational pattern, recognition of proteomes – protein networks and pathways.

Human genome project – databases of human genome; Gene cards, Gene larynx and others, Applications of functional genomics: Role of genomics in drug design and in gene discovery, in designing personalized therapies.

UNIT III

Landmarks of Human Genome: Morbid anatomy of genome comprising Allelic disorders, relation to oncogene, malformation syndrome, specific susceptibility/resistance Maternal-fatal incompatability, their functional attributes and other disorders associated with chromosome 1 to 10

UNIT IV

Landmarks of Human Genome: Morbid anatomy of genome comprising Allelic disorders, relation to oncogene, malformation syndrome, specific susceptibility/resistance Maternal-fatal incompatability, their functional attributes and other disorders associated with chromosome 11 to 22

UNIT V

Landmarks of Human Genome: Morbid anatomy of genome comprising Allelic disorders, relation to oncogene, malformation syndrome, specific susceptibility/resistance Maternal-fatal incompatability, their functional attributes and other disorders associated with X and Y chromosome.

References:

1. Pavel A. Perizner, Computational Molecular Biology – An algorithmic Approach.
2. Alan G. Atherly, Jack R.Griston, John F McDonald (1999). The Science of Genetics, Saunders College PublishingCo. Newyork.
3. Mount Bioinformatics Sequence and Genome analysis.
4. Baxevanis and Ouellette (2000), Bioinformatics.
5. Peter D.Snustard and Michael J Simmons 1999, Principles of Genetics, Second edition, John Wiley and Sons Inc., New York.
6. Human gene disorders compiled by Dept. of Genetics, Johns Hopkins University in collaboration with the Journal of NIH Research, Washington, D.C.
7. http://www.ornl.gov/sci/techresources/Human_Genome/posters/chromosome/chooser.shtml

Paper VII. PHARMACOGENOMICS

Scope: Understanding the genetic polymorphism provides a strong scientific basis for optimizing drug therapy and the basis of each patient's genetic constitution – personalized medicine.

Objective: To expose the students to study various branches of pharmacogenomics like chemogenomics , toxicogenomics and structural genomics.

Goal: Upon completion of this paper will emphasize the students to develop rational means to optimise drug therapy, with respect to the patients' genotype, to ensure maximum efficacy with minimal adverse effects. Such approaches promise the advent of "personalized medicine",.

Unit I

Pharmacogenomics overview and background;**Genetics:** Linkage analysis: Classic examples of pharmacogenetics, pedigrees, recessive traits, positional cloning of drug-induced arrhythmia gene (Long QT); genetic polymorphisms and maps.

Unit II

Genetics: Association analysis; beta receptor polymorphism, criteria for successful association analysis (power analysis, choice of cases and controls, Hardy-Weinberg equilibrium), application to pharmacogenetics; candidate gene versus whole genome association studies; haplotypes versus individual markers. **Genomics:** expression arrays to study drug response; SNP genotyping methods and technology

Unit III

Determinants of drug response: Pharmacokinetics and pharmacodynamic factors involved in drug response, gender and ethnic differences in drug response, molecular mechanisms for alterations in drug response.

Pharmacogenetics: Enzymes: Thiopurine methyltransferase deficiencies, pedigree analysis, autosomal recessive traits, CYP 2D6 polymorphisms, genetic basis of polymorphisms, effects on drug response

Unit IV

Pharmacogenetics: Transporters: MDR1 studies in knockout mice, human polymorphisms, effects on drug response, haplotypes, Other transporter polymorphisms.

Transcription factors: Nuclear receptors, PXR, FXR and CAR.

Implications of pharmacogenetics healthcare delivery; ethics and clinical study design: Cost of pharmacogenetic testing to process

and to costs, types of clinical protocols, consent forms, the Committee on Human Research, ethical implications of pharmacogenetic studies

Unit V

Model organisms in pharmacogenetic studies: use of yeast, *C. elegans*, zebrafish and mice in pharmacogenetic studies; pharmacogenomics as a public health tool; nonscientific challenges for pharmacogenomics.

References:

1. Howard L McLeod1 andWilliam E Evans (2001). PHARMACOGENOMICS: Unlocking the Human Genome for Better Drug Therapy. Annu. Rev. Pharmacol. Toxicol. 2001. 41:101–21

2. Evans WE, RellingMV. 1999. Pharmacogenomics: translating functional genomics into rational therapeutics. *Science* 286:487

3. Satoskar, R.S., Bhandarkar, S.D and Annapure, S.S (1999), Pharmacology and pharmacotherapeutics, popular prakashan, Mumbai.

4. Mycek, J., Harvey, A.R and Champe, P.C (1997), Pharmacology, 2nd edition, Williams and Wilkins publishers.

PAPER VIII. BIOETHICS, BIOSAFETY AND IPR

Scope: Knowing the biosafety guidelines and rules on transgenic research would help the student in carry out their research in transgenic organisms and products.

Objective: To expose the students on the biosafety of transgenic products and transgenic research guidelines and rules.

Goal: The major part of the transgenic research deals with the recombinant DNA technology and metabolic engineering , completion of this paper will become mandatory to the students to take the precautionary measures during research and checking the transgenic products.

Unit I

Inttroduction to ethics/bioethics – framework for ethical decision making; biotechnology and ethics – benefits and risks of genetic engineering – ethical aspects of genetic testing – ethical aspects relating to use of genetic information – genetic engineering and biowarfare

Unit II

Ethical implications of cloning: Reproductive cloning , therapeutic cloning ; Ethical, legal and socio-economic aspects of gene therapy, germ line, somatic, embryonic and adult stem cell research- GM crops and GMO's – biotechnology and biopiracy – ELSI of human genome project

Unit III

Introduction to biosafety – biosafety issues in biotechnology – risk assessment and risk management – safety protocols: risk groups – biosafety levels – biosafety guidelines and regulations (National and International) – operation of biosafety guidelines and regulations – types of biosafety containment

Unit IV

Introduction to intellectual property and intellectual property rights – types: patents, copy rights, trade marks, design rights, geographical indications – importance of IPR - world intellectual property rights organization (WIPO)

Unit V

what can and what cannot be patented? – patenting life – legal protection of biotechnological inventions – Patenting in India: Indian patent act.

References:

1. Principles of cloning, Jose Cibelli, Robert P. lanza, Keith H. S . Campbell, Michael D.West, Academic Press,2002
2. http://books.cambridge.org/0521384737.htm

3. http://online.sfsu.edu/%7Erone/GEessays/gedanger.htm
4. http://www.actahort.org/members/showpdf?booknrarnr=447_125
5. http://www.cordis.lu/elsa/src/about.htm
6. http://www.csmt.ewu.edu/csmt/chem/jcorkill/bioch480/bioLN98.html
7. http://www.accessexcellence.org/AE/AEPC/BE02/ethics/ethintro.html
8. http://lawlib.samford.edu/cio/ciofeb03.pdf
9. http://www.biomedcentral.com/content/pdf/1472-6939-2-2.pdf
10. http://lifesciences.cornell.edu/vision/accelerating_focus05.php
11. http://thompson.com/libraries/fooddrug/
12. http://assets.cambridge.org/0521792495/sample/0521792495WS.PDF
13. http://europa.eu.int/eurlex/pri/en/oj/dat/1998/I_213/I_21319980730en00130021.pdf
14. http://www.clubofamsterdam.com/content.asp?contentid=281
15. Biosafety issues related to transgenic crops,DBT guidelines, Biotech Consortium India Limited, New Delhi

SEMESTER I
PRACTICAL 1 – BASICS OF GENOMICS

Scope: Getting trained in practical knowledge on these experiments would help the students in further research.

Objective: To expose the student in practical knowledge in advanced techniques in molecular biology and bioinformatics tools.

Goal. Upon completion of this course will emphasize the students to get the Practical knowledge this will help them doing the further research

S.No.	Title of the practical
1.	Isolation of plasmid DNA (pBS/pTaq) from *E.coli.*
2	Isoaltion of Genomic DNA from *Bacillus subtilis/thuringiensis*
3	Restriction analysis of plasmid/phage DNA
4	Elution of DNA from Agarose gel (Electro elution/Coloum/Alternate methods)
5	Cloning in E.coli: ligation and transformation
6	Gene expression and analysis of gene (cry/Taq polymerase) product
7	Western blotting
8	Production of His-tag protein and purification
9	Protein- DNA interaction using mobility shift assay; Poly amine stability Gel filtration to study ligand-protein interactions eg: phenol red-BSA mixture (Preparation of sephadex G-25 column, 1.5X15 cm; Scatchard plot of V/L versus V)
10	Polymerase chain reaction and RAPD

11	Site directed mutageneisis
12	Sequence comparison through Bioinformatics (BLAST & FASTA)
13	Analysis of Protein structure in Silico (Swiss – PDB veiwer
14	Multiple sequence alignment
15	Phylogenetic tree construction
SEMESTER II PRACTICAL 2 – ADVANCED GENOMICS	
1.	Isolation of DNA from blood
2	Isolation of DNA from animal tissue by non enzymatic method
3	Liposome mediated transformation in animal cells
4	Isolation of RNA from blood
5	Production of His-tag protein and purification
6	Assay of TNFα release from activated macrophages
7	Southern blotting (Colony hybridization/Dot blotting)
8	rRNA library construction
9	MTT assay
10	DNA ladder formation
11	*GUS* assay using histochemical method.
12	*Agrobacterium tumefaciens* mediated transformation
13	Total genomic DNA isolation from plants by CTAB method
14	Isolation total RNA from plants by Trizol method
15	Analysis of transgenic plants by PCR.
16	cDNA synthesis by RT-PCR