

Rayat Shikshan Sanstha's
YASHAVANTRAO CHAVAN INSTITUTE OF SCIENCE,
SATARA

(AUTONOMOUS)

CBCS

Reaccredited by NAAC with 'A+' Grade
Syllabus for
Master of Science

Part - II

APPLIED MICROBIOLOGY

Syllabus to be implemented from June, 2021 onwards

M.Sc. Part I

Semester I

Nature of the Course	Paper Code	Name of the Paper
Theory	MAMiT 101	MICROBIAL BIODIVERSITY
	MAMiT 102	RECENT TRENDS IN VIROLOGY
	MAMiT 103	MICROBIAL BIOCHEMISTRY AND PHYSIOLOGY
	MAMiT 104	ESSENTIALS OF GENETICS
Practical	MAMiP 105	PRACTICAL COURSE I: LAB I
	MAMiP 106	PRACTICAL COURSE I: LAB II

Semester II

Nature of the Course	Paper Code	Name of the Paper
Theory	MAMiT 201	ANALYTICAL TECHNIQUES
	MAMiT 202	MICROBIAL METABOLISM
	MAMiT 203	MOLECULAR BIOLOGY AND GENETICS
	MAMiT 204	RESEARCH METHODOLOGY & BIOSTATISTICS
Practical	MAMiP 205	PRACTICAL COURSE II: LAB I
	MAMiP 206	PRACTICAL COURSE II: LAB II

M.Sc. Part II**Semester III**

Nature of the Course	Paper Code	Name of the Paper
Theory	MAMiT 301	MICROBIAL ECOLOGY AND EXTREMOPHILES
	MAMiT 302	ESSENTIALS OF IMMUNOLOGY
	MAMiT 303	PHARMACEUTICAL MICROBIOLOGY
	MAMiT 304 E-1	FOOD AND DAIRY TECHNOLOGY - I
	MAMiT 304 E-2	ESSENTIALS OF BIOINFORMATICS
Practical	MAMiP 305	PRACTICAL COURSE III: LAB I
	MAMiP 306	PRACTICAL COURSE III: LAB II

Semester IV

Nature of the Course	Paper Code	Name of the Paper
Theory	MAMiT 401	INDUSTRIAL MICROBIOLOGY
	MAMiT 402	MICROBIOLOGICAL QUALITY CONTROL AND ASSURANCE.
	MAMiT 403	GENE TECHNOLOGY AND GENOMICS
	MAMiT 404E-1	FOOD AND DAIRY TECHNOLOGY - II
	MAMiT 404E-2	ADVANCED BIOINFORMATICS
Practical	MAMiP 405	PRACTICAL COURSE IV: LAB I
	MAMiP 406	PRACTICAL COURSE IV: LAB II

SEMESTER III
MAMiT 301: MICROBIAL ECOLOGY & EXTREMOPHILES

Learning Objectives:

The student should be able to :-

1. Learn the significance of microbial ecology.
2. Get introduced to ecology as a tool for global sustainability.
3. Understand the applications of extremophiles.
4. Get acquainted with the human microflora and its effects on health.

UNIT I: Basic Concepts of Microbial Ecology

15

A) Microbial Ecology – Concepts, niche, habitat, ecosystem and applications.
Introduction to microbial diversity, types of microorganisms- bacteria, archaea, eukarya, interactions between micro organisms, ecological succession.

B) Development of Microbial Communities:

- i)* Introduction
- ii)* Microbial community dynamics –
 - a)* Population selection within communities
 - b)* Succession within microbial communities
 - c)* Genetic exchange in microbial communities
- iii)* Structure of microbial communities –
 - a)* Diversity and stability
 - b)* Species diversity indices
 - c)* Genetic and molecular diversity indices.
- iv)* Ecosystems –
 - a)* Experimental models
 - b)* Microcosms

UNIT II: Recent Concepts in Microbial Ecology

15

A) Microbial biofilm –

- i)* Physiology, morphology, biochemistry of microbial biofilm formed in natural environment.
- ii)* Mechanism of microbial adherence.
- iii)* Laboratory methods used to obtain biofilm (with respect to physiology, growth, special arrangement, depth, surface physio chemistry)

B) Beneficial and harmful role of biofilms.

C) Biomimicry – Concept and Applications.

D) Bioremediation and Biodegradation -

- i)* Engineering and bioremediation process its needs and limitations. Molecular technique in Bioremediation.
- ii)* Degradation of aromatic and alicyclic compounds- important organisms, use of mixed cultures in common pathways of aromatic degradation, aerobic and anaerobic degradation of aromatic compounds.

UNIT III: Microbiome

15

A) Introduction: Microbiome Ecosystem Ecology

B) Human Microbiome project: Scientific background; Initiation of the HMP;

The goal of the HMP; Implementation of the National Institute of Health HMP; The International Human Microbiome Consortium (IHMC).

C) Healthy Human Microbiome: Typical components and diversity of the microbiome; archaea, viruses, fungi, and other eukaryotes; Geographical variation in the healthy microbiome; Microbiome establishment and early colonization; Hallmarks of health; outlook.

D) Human Microbiome at the interface of health and disease: Influences on the microbiota during host life cycles; Disease links and health implications.

UNIT IV: Extremophiles and their Applications

15

A) Extremophiles

- i)* Concept
- ii)* Thermophiles – Nucleic acids, Membrane adaptations, Proteins.
- iii)* Psychrophiles – Membrane adaptation, Proteins
- iv)* Acidophiles – Mechanism to tolerate acid and metal and acid toxicity.
- v)* Alkalophiles- Bioenergetics adaptations.

B) Extremozymes

- i)* Extremozyme – Characteristics, examples, structure, Biotechnological uses of archaea as extremozymes and applications.
- ii)* Biotechnological, applications of extreme proteins from different groups of methanogens.
- iii)* Polyextremophiles – characteristics, examples and uses

Learning Outcomes:

After learning the theory paper, the student will be able to :-

1. Comprehend the concepts of microbial ecology.
2. Apply recent trends in ecology for global sustainability.
3. Utilize extremophiles as industrial tools.
4. Imbibe basic concepts of the human microbiome.

References:-

- 1) R.M. Atlas, R. Bartha (2008) Microbial Ecology: Fundamentals and Applications, 4th Ed. Pearson India Education Services – **UNIT I, II, III.**
- 2) Charles Greday, Nicolas Glansdorff.(2007) Physiology and Biochemistry of Extremophiles, ASM Press. **UNIT IV.**
- 3) Rajendran P, Gunasekaran P. (2011) Microbial Bioremediation, MJP Publishers, Chennai – **UNIT II.**
- 4) Odum Eugene (2004) Fundamentals of Ecology, Cengage Learning – **UNIT I.**
- 5) The Human Microbiome : At the Interface of Health and Disease – Ilseung Cho and Martin J. Blaser, Nature Journal – **UNIT III**

MAMiT 302: ESSENTIALS OF IMMUNOLOGY

Lectures: 48

Learning Objectives:

The student should be able to :-

1. Understand various immunotechniques.
2. Advanced concepts in immunology.
3. Learn immunodeficiency diseases.
4. Learn cell signaling pathways

MAMiT 302: ESSENTIALS OF IMMUNOLOGY

Lectures: 48

UNIT I Cell signaling and Apoptosis

Lectures: 12

A) Cell Signaling

- 1) Signal receptors in immune system
- 2) Signal Transduction Pathway-
 - a) JAK-STAT Pathway
 - b) Phosphotidyl Inositol Pathway
 - c) RAS-MAPK Pathway
- 3) IL 2 Signaling Pathway
- 4) Chemokine Signaling Pathway

B) Apoptosis

- 1) Molecules involved in apoptotic cell death
- 2) Mechanism of apoptosis
 - a) Extrinsic Pathway
 - b) FAS signaling pathway
 - c) Intrinsic Pathway

Unit II :- MHC complex and experimental systems

Lectures: 12

- 1) Major Histocompatibility Complex
 - a) General Organization and Inheritance of the MHC
 - b) MHC molecules and genes.
 - c) Detailed genetic map of MHC genes.
 - d) Cellular distribution of MHC molecule
 - e) Regulation of MHC expression
 - f) MHC and immune responsiveness.
- 2) **Experimental Systems-**
Experimental animal models & cell culture system .

Unit III :-Tumor immunology and immunotechniques

Lectures: 12

- 1) **Immunity to tumors**
 - a) Tumor of immune system
 - b) Tumor antigen
 - c) Immune responses to tumor- T cell , antibodies ,NK cell, Macrophages
 - d) Evasion of immune response by tumors .
 - e) cancer immunotherapy.
- 2) **Immunotechniques**
 - a) Flow Cytometry
 - b) Immuno gold labelling for electron microscopy
 - c) Immune PCR
 - d) Mixed lymphocyte reaction.

Unit IV:-Immunodeficiency Disorders

Lectures: 12

- 1) Primary immunodeficiencies
 - a) Lymphoid immunodeficiencies
 - i) Humoral Deficiencies- XLA, XHM
 - ii) Cell mediated Deficiencies – DiGeorge Syndrome,
 - iii) Combined Deficiencies – Severe SCID
 - b) Immunodeficiencies of the myeloid lineage
 - i) Phagocytic Deficiencies- CGD, reduction in neutrophils count

d) Complement defects- Defects in C3 component

2) Secondary immunodeficiencies

a) Causative factors of secondary immunodeficiency diseases

b) AIDS – Target cells infection by HIV, HIV-1 Latency, Factors promoting HIV Provirus (Refer Abbas) Mechanism of immunodeficiency

3) Treatment of Immunodeficiency Diseases

4) Immunotechniques and their applications, Principle, Procedure, Application, Advantages and disadvantages.

LEARNING OUTCOME:

- Students should understand immune system and its relation with various microbes.
- Students should know advances in the field of immunodeficiency.
- Students should learn about immune response to diseases and tumors.
- Student should be updated with techniques and experimental systems required in immunological research.

REFERENCE BOOKS:

1) **UNIT – I, II, III:** Cellular and Molecular Immunology – Abul

K. Abbas. (5th Edition)

2) **UNIT – I, II, III:** Kuby Immunology – Kindt Goldsby & Osborne. 3) **UNIT – IV:** Immunology – Tizard.

4) **UNIT – IV:** Immunology – C. Vaman Rao.

5) **UNIT – I, II, III & IV:** Essential Immunology – Roitt I.M. 3

6) **UNIT – IV:** Basic and clinical Immunology – Danie P. Stites, John Stobo, H. Fudenberg.

MAMiT 303: PHARMACEUTICAL MICROBIOLOGY

Learning Objectives:

The student should be able to:-

1. Get basic knowledge on community medicine.
2. Get acquainted with the recent research on drug discovery and development.
3. Understand the tools and techniques used in antimicrobial testing.
4. Learn about emerging trends in biopharmaceuticals.

UNIT- I: Community Medicine and Epidemiology

15

A) Fundamentals of Community Medicine

- i)* Definition of health, dimensions of health.
- ii)* Determinants and indicators of health.
- iii)* Concept of well- being.

B) Basics of Epidemiology

- i)* Concept of causation: Germ theory, epidemiological triad, multifactorial causation, web of causation.
- ii)* Natural history of disease- prepathogenesis and pathogenesis phase.
- iii)* Changing pattern of disease.

UNIT II: Drug Discovery and Development:

15

A) Introduction

- i)* Contributions and postulates of Paul Ehrlich
- ii)* Significance of terms - lead optimization, candidate selection

B) Drug Discovery and Design

- i)* Conventional Process of bioprospecting (medicinal chemistry)
- ii)* Extraction and purification principles,
- iii)* Purification and characterization of bioactive molecules from natural sources
- iv)* Rational Drug Design – Principle (Structure Activity Relationship-SAR)

And Tools (applications of High Throughput Screening, Combinatorial Synthesis, Pharmacogenomics)

C/ Drug Development

- i)* Preclinical Development – Toxicity Testing: Acute, Sub-acute and Chronic.
- ii)* Clinical Development – Clinical Trials: Aims, Objectives, Conduct, Phases of Clinical Trials – I, II, III, IV.

UNIT III: Antimicrobial Testing Systems

15

A/ Introduction:

Antimicrobial agents, broad types, therapeutic ratio, MIC and MBC.

B/ Antimicrobial Susceptibility Testing

- i)* Use of liquid and solid media.
- ii)* Factors affecting susceptibility testing, guidelines issued by CLSI.
- iii)* Diffusion methods –
 - a)* Agar Dilution Technique
 - b)* Gradient Plate Technique
 - c)* E-test
 - d)* Kirby Bauer Method
 - e)* Stokes Method
- iv)* Susceptibility Testing for –
 - a)* Anti-mycobacterial agents.
 - b)* Anti-fungal agents.
 - c)* Anti-protozoan agents.

d) Anti-viral agents.

UNIT IV: Biopharmaceuticals

15

A/ Introduction:

Concept and significance of biopharmaceuticals.

B/ Regulations and Recommendation

- i) Regulatory authorities and their role – the FDA.
- ii) The concept of Pharmacopoeia – USP, EP, BP and IP.

C/ Drug Formulation Studies

- i) Drug formulations – carriers and delivery systems.
- ii) Targeted drug delivery and sustained release.
- iii) Pharmacokinetics – ADME / Bioavailability studies.

Learning Outcomes:

After learning the theory paper, the student will be able to:-

1. Understand the importance of community medicine.
2. Imbibe the basic concepts of drug development.
3. Practically perform antimicrobial testing.
4. Comprehend the concept of biopharmaceuticals.

References:-

1. K. Park (2009), Park's Textbook of Preventive and Social Medicine (20th Edition) – **UNIT I.**
2. Konrad J. Karczewski, Roxana Daneshjou, Russ B. Altman (2012) Chapter 7. Pharmacogenomics PLOS – **UNIT II.**
3. Franklin T.J. and Snow G.A., (1975), Biochemistry of Antimicrobial Action, Chapman and Hall, London – **UNIT III.**

- 4.** Gale E.F., Cundliffe E., Reynolds P.E., Richmond M.H. and Waring M.J., (1972), The molecular basis of antibiotic action, John Wiley and Sons, London – **UNIT III.**
- 5.** Goldstein A., Aronow L. and Kalman S.M. (1969) Principles of Drug Action, The Basis of Pharmacology, Harper International Edition, New York – **UNIT III.**
- 6.** Manfred A. Holliger, (2008) Introduction to Pharmacology, 3rd Edition, CRC Press – **UNIT IV.**
- 7.** Kokate C. K., Purohit A.P., Gokhale A.B. (2000) Pharmacology, 4th Edition, Nirali Prakashan – **UNIT IV.**

MAMiT 304 E-1 DAIRY AND FOOD MICROBIOLOGY – I

Learning Objectives:

The student should be able to:-

1. Learn the significance of microbiology in food and dairy technology.
2. Study the usage of different microorganisms.
3. Understand the tools and techniques used in genetic engineering.
4. Learn about emerging trends in gene technology.

UNIT I: Microorganisms in Dairy

15

A) Naturally Present Microorganisms

Sources and beneficial role of microorganisms.

B) Spoilage Causing Microorganisms

i) Mechanism of spoilage.

ii) Causative agents and control measures of: natural curdling, gas production, ropiness, proteolysis, lipolysis.

C) Milk Borne Diseases

i) Milk borne infections: Salmonellosis, Botulism, Aflatoxicosis.

ii) Milk borne diseases: Listeriosis, TB.

D) Starter Culture

i) Introduction and Background

ii) Role, Nature and Types: single strains, mixed strains, multiple strains.

iii) Factors affecting starter culture.

iv) Starter culture defects.

v) Evaluation of starter culture.

vi) Genetics and metabolism of starter culture.

UNIT II: Milk Processing and Milk Products

15

A) Processing of Milk

i) Introduction, type and standards of market milk

ii) Microbiological quality of market milk

iii) Processing steps-

a) Pre-processing: Pumping, Filtration, Cooling, Centrifugal clarification, standardization, Homogenization

b) Processing: Pasteurization LTH, HTST and Sterilization: Complete in bottle, 2 stage, UHT.

c) Post processing: Cooling, packaging, distribution.

B) Processed milk products

Cheese and allied products.

UNIT III: Microbiology in Foods

15

A) Microorganisms in foods- Role, Significance

B) Microorganism in food spoilage:

i) Types of foods and their spoilage

ii) Microbial, biochemical aspect of food spoilage

iii) Physiology of food spoilage organisms : Importance, Response of microbes, future prospectus.

C) Food Borne Diseases

i) Bacterial diseases: *E. coli* EHEC o157:H7 and other strains, *L. monocytogenes*, *H. pylori*.

ii) Fungal, algal, viral, prions and other non-bacterial forms.

D) Food Preservation

i) Control of spoilage: By physical removal, heat, low temperature, reduced aw, low pH, organic acids, modified atmosphere, anti-microbial preservatives, irradiation, canning.

ii) Control by combination of methods (Hurdle concept)

iii) Novel emerging techniques of preservation – Bacteriocin- Introduction, types, mode of action, applications.

UNIT IV: Microorganisms in Food Processing

15

A) Fermented & Processed Foods

Indian fermented foods: Idli, Jilebi, Dhokla, Tofu.

- i)* Oriental mold modified foods: Soya sauce, Miso, Hamanatto, Sufu.
- ii)* Fermented meats and fish: sausage, fish sauce.
- iii)* Fermentation: wine, vinegar.

B) Genetically Engineered Microorganisms in the Food Industry

- i)* Concept, advancements, principles
- ii)* Role of genetically engineered microbes in the food industry.

Learning Outcomes:

After learning the theory paper, the student will be able to :-

1. Understand the role of microorganisms in food and dairy industries.
2. Practically apply the techniques of food & dairy technology.
3. Comprehend the processing and preservation of milk and dairy products.

References:-

- 1.** K. Vijaya Ramesh (2007) Food Microbiology, MJP Publishers, Chennai – **UNIT I, II.**
- 2.** Swaminathan M (1974) Essentials of Food and Nutrition (2nd Edition) Ganeshand Co. – **UNIT I, II.**
- 3.** Modi H.A. (2009) Dairy Microbiology, Pointer Publishers, India – **UNIT III, IV.**
- 4.** J.S. Yadav, Grover S., Batish V.K. (1993) Comprehensive Dairy Microbiology, Metropolitan Book Cooperative Pvt. Ltd. – **UNIT III, IV.**
- 5.** Frazier W, Westoff D. (2013) Food Microbiology (5th Edition) Tata McGrawHill Education – **UNIT I, II.**

MAMiT 304.E-2 – ESSENTIALS OF BIOINFORMATICS

Learning Objectives:

The student should be able to :-

1. Learn basics of the networking and the internet.
2. Get introduced to the fundamentals of bioinformatics.
3. Learn about the tools and techniques employed in the field of bioinformatics.
4. Get acquainted to various concepts constituting bioinformatics.

Unit I: Networking and the Internet

(15)

A] Computer Networking:-

Fundamentals of Networking: OSI Referencing Model, TCP/IP, Network topologies and protocols. Networking gadgets (router, switch,etc), Communication links(Wire pairs, coaxial cables, fiber optics, microwave, satellite,etc). Local Area Network (LAN), Wide Area Network (WAN), Metropolitan Area Network (MAN).

B]Network Security:-

Fundamentals, Types of attacks, Firewall, Packet filtering, Classification of data security threats, Protection Mechanism (Authentication, Access Control and Access Rules). Encryption/Decryption techniques.

C]The Internet:-

Introduction, Concept of the Internet, World Wide Web, Browsers – Chrome, Mozilla, Firefox, Opera, Safari, IE/Edge. Search Engines- Google, Bing, Significance of the Net.

Unit II: Introduction to Bioinformatics

(15)

A] Essentials of Bioinformatics:-

Introduction, Definition and History of Bioinformatics, Nature,Scope and Branches of Bioinformatics. Applications.

B/Biological Database Systems:-

Introduction to Database, Database system, Biological Databases, Criteria for Classification of biological databases and their types.

i) Nucleic acid databases(GenBank, DDBJ, EMBL).

ii) Protein Databases(Primary, Secondary and Composite).

iii) Specialized Genome Databases.

iv) Structural Classification Databases(CATH, SCOP).

v) Structural Databases(PDB).

Unit III: Tools and Techniques in Bioinformatics (15)

A] Tools and Formats:-

i) Tools: BLAST, Types of BLAST, Applications.

ii) Formats: Types of Formats, FASTA, SAM, GVF.

Importance.B] Techniques:-

i) Sequence Alignment: Introduction, Types – Global and Local Alignment, Pairwise Sequence Alignment, Multiple Sequence Alignment(MSA) : Progressive and Iterative Methods e.g. Clustal W, Clustal X.

ii) Sequence and Structure Visualization Tools:

Introduction, General Properties of Map Viewer, ORF Finder, Locus Link, Swiss PDB Viewer, Webmol, Rasmol, Chime, MOLMOL, Phymol, SQL.

Unit IV: Concepts in Bioinformatics (15)

Introduction to omics. Concept, salient features and

applications of – Genomics, Proteomics, Metabolomics, Lipidomics,

Glycomics, Foodomics, Transcriptomics, Pharmacogenomics and

Pharmacogenetics. Significance in biological research.

Learning Outcomes:

After learning the theory paper, the student will be able to:-

1. Understand the working of the internet and networking systems.
2. Comprehend the fundamental concepts of bioinformatics.
3. Interpret and analyse computational data using different tools and formats.
4. Master the different concepts constituting the field of bioinformatics.

References:-

1. P. Narayan, Bioinformatics – A Primer – **UNIT I, II,III.**
2. Jin Xiong, Essential Bioinformatics: Genomics and Proteomics(With Practical Exercises) – **UNIT I, II, III.**
3. C. Stan Tsai, Computational Biochemistry, John Wiley and Sons – **UNIT II.**
4. N. Gautam, Bioinformatics – Databases and Algorithms – **UNIT II, III, IV.**
5. V. Rajaraman, Fundamentals of Computers, Phi Learning, ISBN:8120321758, 2001 – **UNIT I.**
6. Tanenbaum Andrew S, Computer Networks, 4th Edition, Prentice Hall PTR, ISBN:8120321758, 2003 – **UNIT I.**
7. Rohit Khurana, Computer Fundamentals and Internet Basics – **UNIT I.**

PRACTICAL COURSES

MAMiP 305

PRACTICAL COURSE – III: LAB - V

Learning Objectives:

The student should be able to:-

1. Learn the different aspects of microbial ecology like biofilm, biodegradation,
2. Get acquainted with the mechanisms employed by extremophiles for survival.
3. Employ various techniques involved in the branch of immunology
4. Explore the different facets of pharmaceutical microbiology by practical analysis and testing.

UNIT – I

A/ Microbial Ecology

- 1) Adhesion of microorganisms to surface by dip slide method.
- 2) Study of siderophore producing microorganisms.
- 3) Isolation of petroleum degrading bacteria and determination of degradation rate.
- 4) Determination of rate of degradation of dye using microbial isolate.

B/ Extremophiles

- 5) Isolation of thermophiles from compost heap.
- 6) Screening of alkaliphilic bacteria from soil/water.
- 7) Isolation and enrichment of psychrophiles.
- 8) Screening of halophilic and halotolerant microorganisms.

C/ Human Microbiome

9) Qualitative analysis of the hand microbiome by suitable method.

10) Isolation of etiological agent of dental caries.

UNIT – II

A) Essentials of Immunology

1) Determination of antibody titer by Ouchterlony double diffusion test.

2) Demonstration of SDS-PAGE technique

3) ELISA- Detection of antigen/ antibody by Sandwich ELISA.

4) Rocket immunoelectrophoresis

5) Radial Immunodiffusion test

6) Purification of H antigen from *S. typhi*

7) Estimation of alkaline phosphatase from patients serum

8) Purification of Antibodies using ammonium sulphate precipitation & column chromatography.

Learning Outcomes

The student will be able to:-

1. Practically comprehend the different concepts of microbial ecology and human microbiome.
2. Practically perform extraction of bioactive drugs
3. Employ various techniques involved in the branch of immunology
4. Explore the different facets of pharmaceutical microbiology by practical analysis and testing

References:-

1. Kokate C. K., Purohit A.P., Gokhale A.B. (2000) Pharmacology, 4th Edition, Nirali Prakashan
2. R. M. Atlas, R. Bartha (2008) Microbial Ecology: Fundamentals and Applications, 4th Ed., Pearson India Education Services

MAMiP 306 PRACTICAL COURSE – III: LAB – VI

UNIT – I

Learning Objectives:

The student should be able to:-

1. Learn the different aspects of microbial ecology like biofilm, biodegradation,
2. Get acquainted with the mechanisms employed by extremophiles for survival.
3. Employ various techniques involved in the branch of immunology
4. Explore the different facets of pharmaceutical microbiology by practical analysis and testing.

A) Pharmaceutical Microbiology

1) Determination of Epidemiological Ratios:

a) Human Development Index, b) Mortality Ratio, c) Morbidity Ratio.

2) Extraction of bioactive ingredients from plant and its activity fraction.

3) Determination of Minimum Inhibitory Concentration (MIC) of drug.

4) Estimation of antimicrobial activity using CLSI.

5) Determination of phenol coefficient.

6) Study of antimicrobial activity of spices.

7) Determination of microbial load of non-sterile products – ointments, capsules.

8) Determination of drug sensitivity of *Streptococcus mutans*.

UNIT – II

A) Essentials of Bioinformatics

- 1) Study of network IP.
- 2) Connecting computers in a Local Area Network (LAN).
- 3) Searching sequence databases by BLAST
 - a) BLASTn, b) BLASTp.

Learning Outcomes:

After learning the theory paper, the student will be able to:-

1. Explore the different facets of pharmaceutical microbiology by practical analysis and testing.
2. Process to determine MIC of drug
3. Practically perform experiments related to pharmaceutical microbiology.

References:-

1. R. M. Atlas, R. Bartha (2008) Microbial Ecology: Fundamentals and Applications, 4th Ed., Pearson India Education Services.
2. Sandhya Mitra – Genetic Engineering: Principles and Practice, McGrawHill Education (India) Pvt. Ltd.
3. Kokate C. K., Purohit A.P., Gokhale A.B. (2000) Pharmacology, 4th Edition, Nirali Prakashan.

SEMESTER IV

MAMiT 401 – INDUSTRIAL MICROBIOLOGY

Learning Objectives:

The student should be able to:-

1. Learn basic concepts of fermentation technology.
2. Know the significance of microbial sensors.
3. Study the significance and economical aspects of solid state fermentation.
4. Get acquainted with various concepts related to intellectual property.

Unit I: Fermentation Technology

(15)

A) Bioreactor

- i)* Design and operation.
- ii)* Batch culture fermenter : Main parts, peripherals parts and accessories, alternative vessel design, types of instrumentation, common measurement and control system, sensors.
- iii)* Simple continuous culture : Accessories and peripherals.
- iv)* Fermenter preparation and use.
- v)* Inoculation techniques in bioreactor, sampling from fermenter vessel.
- vi)* Maintenance of fermenter components.
- vii)* Type of organism used in fermentation.
- viii)* Sub fermenter system – a new approach.
- ix)* Solution to common problems in fermentation.

Unit II: Microbial Biosensors

(15)

A/ Concept of Biosensors

a) Cell Immobilization - Introduction, Immobilized cellsystem –

- i) Surface attachment of cells.
- ii) Entrapment within porous matrices.
- iii) Containment behind a barrier.
- iv) Self-aggregation of cells

b) Design of immobilized cell reactors –

- i) Mass transport phenomena in immobilized cell system.
- ii) Reaction and diffusion in immobilized cell system
- iii) Bioreactor design
- iv) Physiology of immobilized microbial cells.

B] Types of electrochemical microbial sensors

- i) Optical biosensors.
- ii) Other types.

Unit III: Solid State Fermentation and Fermentation Economics

(15)

A) Solid state fermentation (SSF) :-

Introduction, comparison of SSF and submerged fermentation, Advantages, disadvantages, problems, types, Factors affecting, fermenter design for SSF, Koji manufacturing process, industrial application of SSF, amylase production –case study.

B] Fermentation economics:-

Introduction, economic objectives. Various aspects influencing fermentationeconomics – Strain improvement, High yielding strain, Market potential, fermentation media and raw material, fermentation equipments, recovery cost, water uses

and recycling, effluent treatment.

Unit IV: IPR and Patenting

(15)

A/Intellectual Property Rights

Introduction and concept of IPR, the World Intellectual Property Organization(WIPO), Fields of intellectual property protection, General introduction to patents, copyrights and trademarks.

B/ Patents:

i) Introduction, conditions of patentability, drafting and filing a patent, examination of a patent application, infringement, exploitation of the patented invention, compulsory licenses. Utility models

ii) Indian Patent Act

C/Intellectual Property and Bioethics:

Introduction, general principles and key aspects.

Learning Outcomes:

After learning the theory paper, the student will be able to:-

1. Use and manipulate different types of fermenter and fermentation
2. learn design of immobilized cell reactors
3. Employ the technique of solid state fermentation for laboratory production of metabolites.
4. Utilize bioethical concepts and fundamentals for social welfare.

References:-

1. Mansi E. L. (2011) Fermentation Microbiology and Biotechnology(2nd Edition),CRC Press – **UNIT I, II.**
2. Patil S.C. (2010) Industrial Microbiology, S. Chand and Company – **UNIT II.**

3. Casida J.R. (2016) Industrial Microbiology, New Age International Pvt. Ltd. –**UNIT III.**
4. Pepler H.J., Pearlman D. (1979) Microbial Technology (2nd Edition), Academic Press – **UNIT III.**
5. Stanbury P.P., Whitekar A., Hall S.J. (2008) Principles of Fermentation Technology, Elsevier – **UNIT III.**
6. Intellectual Property Rights in India, Shodhganga, Chapter 2 – **UNIT IV.**
7. WIPO Intellectual Property Handbook (2004) 2nd Edition, Chapters 1 and 2 –**UNIT IV.**
8. Intellectual Property and Bioethics: An Overview – WIPO Booklet – **UNIT IV.**

MAMiT 402– MICROBIOLOGICAL QUALITY CONTROL AND ASSURANCE

Learning Objectives

The student should be able to:

1. Learn specific requirements for production of different products in the pharmaceutical industry.
2. Know the techniques and tools for facility and instrument qualification.
3. Study the concept of clean room technology and culture maintenance and disposal.
4. Learn the essentials of analytical techniques employed in the pharmaceutical industry.

Unit I: Pharmaceutical Industry

(15)

A/ Schedule M:-

i) Part I-A: Specific Requirements for Manufacture of Sterile Products, Parenteral Preparations and Sterile Ophthalmic Preparations.

ii) Part I-B: Specific Requirements for Manufacture of Oral Solid Dosage Forms (Tablets and Capsules).

iii) Part I-C: Specific Requirements for Manufacture of Oral Liquids (Syrups, Elixirs, Emulsions and Suspensions).

iv) Part I-D: Specific Requirements for Manufacture of Topical products

i.e. External Preparations (Creams, Ointments, Pastes, Emulsions, Lotions, Solutions, Dusting Powders and Identical Products).

v) Part I-E: Specific Requirements for Manufacture of Metered Dose-Inhalers (MDI).

vi) Part I-F: Specific Requirements of Premises, Plant and Materials for Manufacture of Active Pharmaceutical Ingredients (Bulk Drugs).

Unit II: Facility and Instrument Qualification

(15)

A] Introduction:-

URS, IQ, OQ, PQ.

B] HVAC Qualification:-

Heating Ventilation Air Conditioning System, Constituents of the System
– Temperature, Relative Humidity, Air Velocity, Differential Pressure and Room to Room Air Balancing, HEPA Filtration, LAF, Viable Count.

C] Utility Qualification:-

Purified Water System and Pharmaceutical Air Monitoring.

D] Instrument Qualification:-

1) Autoclave, 2) Dry heat sterilizer, 3) Incubator and 4) Laminar Air Flow Cabinet.

Unit III: Maintenance of Clean Room & Microbiological Laboratory

(15)

A] Facility Requirements:-

Introduction and guidelines.

B] Gowning Requirements:-

Introduction and

guidelines.

C] Disinfectant Qualification:-

Introduction, Types of Disinfectants, Disinfectant Efficacy Testing.

D] Clean-in Place(CIP) and Sterilize-in Place(SIP):-

Introduction, Principle, Protocol and Applications of CIP and SIP.

E] Culture Maintenance:-

Reference cultures used in the pharmaceutical industry, maintenance.

F] Disposal Systems:-

Disposal protocols and systems for cultures and media.

Unit IV: Essentials of Analytical Techniques in Pharma Industry (15)

A] Media Preparation, Sterilization and Growth Promotion.

Guidelines for a) Media Preparation, b) Sterilization and c) Growth Promotion.

B] Environment Monitoring.

Introduction, Need for EM, Procedure and Significance.

C] Endotoxin Testing

Introduction, Gel Clot Method, Kinetic Assays, Medical Devices.

D] Antibiotic / Vitamin Assay.

General Information, Equipment, Test Organism, Inoculum preparation And Standardization, Antibiotic/Vitamin Standard and Sample Solution Preparation, Growth Media and Additional Test Solutions, Potency Testing –Plate Method and Tube Method. Calculations.

E] Bioburden Estimation of Medical Devices.

Definition of Bioburden, FDA Guidelines, *Significance*.

F] Microbiological Examination of Non-Sterile Products.

Product storage and handling, gowning requirements, Growth promotion and inhibitory properties of the media

Suitability of the test method, test procedure, interpretation of the results.

G] Preserving Efficacy Testing(PET).

Media, Growth promotion of the media, suitability of the counting method in the presence of product, test organisms, preparation of the inoculum, procedure and interpretation.

Learning Outcomes:

After learning the theory paper, the student will be able to:-

1. Understand specific requirements for production of different products in the pharmaceutical industry.
2. Comprehend the techniques and tools for facility and instrument qualification.
3. Imbibe the concept of clean room technology and culture maintenance and disposal.
4. Master the various analytical techniques employed in the pharmaceutical industry.

References:-

1. Pharmaceutical Microbiology Manual (PMM), United States Food and Drug Administration (USFDA), ORA.007, Version 1.2, 2014.
2. Indian Pharmacopoeia (IP), Volume II (P-Z, Reference Spectra and Appendices), Ministry of Health and Family Welfare, Government of India, 1996.
3. Manohar A. Potdar, Pharmaceutical Quality Assurance, 2nd Edition, Nirali Prakashan, 2007.

MAMiT. 403: GENE TECHNOLOGY AND GENOMICS

Learning Objectives:

The student should be able to:-

1. Get basic knowledge on gene technology
2. Get acquainted with the recent research in the sphere of gene technology.
3. Understand the tools and techniques used in genetic engineering.
4. Learn about emerging trends in gene technology

UNIT –I: DNA Libraries

15

A) Introduction and types-

Genomic and cDNA library.

B) Preparation of Genomic Library-

Isolation of genomic DNA, generation of suitable sized fragments, cloning in suitable vector systems, and transformation in suitable host.

C) Preparation of cDNA library-

Isolation of mRNA, preparation of cDNA fragments, cloning in suitable vector systems, and transformation in suitable host.

D) Screening of Libraries-

Criteria to identify particular gene from gene library –

1. DNA sequencing
2. Expression of particular protein with immunological epitope
3. Enzymatic activity

UNIT –II: Directed Mutagenesis and Protein Engineering

15

A) Directed Mutagenesis:

Oligonucleotide directed mutagenesis with M-16 phage, PCR-amplified oligonucleotide directed mutagenesis, error-prone PCR, Random insertion and deletion mutagenesis, selection of mutant peptide – phage display and cell surface display

B) Protein Engineering:

Adding disulfide bonds, changing asparagine to other amino acids, reducing number of free sulfhydryl residues, increasing enzymatic activity, modifying metal cofactor requirement, decreasing protein sensitivity, modifying protein sensitivity increasing enzyme stability and specificity, altering multiple properties.

UNIT –III: Genetic Engineering in Plants and Animals

A] Plants

- i) Plant transformation with Ti and Ri plasmid.
- ii) Ti plasmid derived vector systems.
- iii) Physical methods for transformation.
- iv) Chloroplast engineering.

B] Animals

- i) Gene transfer vectors
- ii) Transfection – a) Physical, b) Chemical.
- iii) Production of transgenic mice ,
- iii) Production of transgenic mice
- iv) Applications of transgenic mice

UNIT –IV :Recent Trends in Gene Technology

15

A] Genomics-

Concept, Introduction, Comparative genomics of bacteria

B] Proteomics-

Concept, Introduction, Expression analysis and characterization of *proteins*

C] CRISPR / Cas9 in Genome Editing-

Concept, Introduction, Applications.

Learning Outcomes:

After learning the theory paper, the student will be able to:-

1. Access various genomic libraries.
2. Comprehend recent trends in protein engineering.
3. Utilize the applications of genetic engineering to industrial use.
4. Understand the significance of gene technology for biological research.

References:-

- 2) Sandhya Mitra – Genetic Engineering: Principles and Practice, McGraw Hill Education (India) Pvt. Ltd – **UNIT I.**
- 3) Glick, Pasternak, Patten –(2010) Molecular Biotechnology: Principles and Applications of Recombinant DNA Technology (4thEdition) ASM Press – **UNIT I, II, III.**
- 4) S.B. Primrose, R. M. Twyman – Principles of Gene Manipulation and Genomics (7th Edition) Blackwell Publishing – **UNIT I, II, III, IV.**
- 5) Hartl and Jones – Genetics: Analysis of Genes and Genomes (8thEdition) Jones and Bartlett Learning – **UNIT I.**
- 6) Review Article: CRISPR/CAS 9 in genome editing by Haifeng Wang, Marie-La Bussa, Lei S. Qi – **UNIT IV.**
- 7) Recent trends progress in CRISPR technology by Yue Mei, Yan Wang –Journal of Genetics and Genomics (2016) – **UNIT IV**

Learning Objectives:

The student should be able to:-

1. Learn concepts regarding nutraceuticals and probiotics.
2. Know the rules and regulations regarding food safety and hygiene.
3. Know the techniques for physicochemical and microbiological analysis of milk.
4. Learn the essentials of quality and waste management in the dairy industry.

Unit I: Nutraceuticals and Probiotics

(15)

A) Nutraceuticals and Functional Foods

- i)* Concept, biological significance of nutraceuticals and nutrigenomics.
- ii)* Nutraceuticals and dietary supplements.
- iii)* Functional food in disease prevention :Angiogenesis and cardiovascular diseases, cancer, diabetes, cholesterol management and obesity.
- iv)* Health benefits of nutraceuticals. Pigments – chlorophyll, carotenoid, anthocyanin, isoflavonoids, omega 3 and omega6 fatty acids.

B) Probiotics:

- i)* Introduction, Concept, Microorganisms
- ii)* Criteria for selecting microbes as probiotics
- iii)* Beneficial health effects and daily intake of probiotic cultures
- iv)* Safety issues
- v)* Examples of probiotic foods

Unit II: Food Safety

(15)

A) Food Safety

- i)* Principles of food safety as per WHO.

B) Microbiological Standards for Food Safety and Hygiene.

- i)* FSSAI
- ii)* ISO

C) Food Safety Management System Plans.

- i)* FSMS – Meat and Meat Products (Poultry)
- ii)* FSMS – Bakery and Bakery Product

Unit III: Physicochemical and Microbiological Testing of Milk and Dairy Products (15)

A) Physicochemical Testing of Milk and Dairy Products

- i)* Introduction
- ii)* Analysis of milk: Fat, total solids in milk, titrable acidity, specific gravity, figure, chloride value, estimation of lactose, heat stability test, adequacy test, protein.
- iii)* Test for added water.
- iv)* Preservatives.
- v)* Adulterants and tests for detection.
- vi)* Analysis of butter: Moisture, fat, added salt, total titratable acidity, added Boric acid.
- vii)* Analysis of ice-cream: fat, acidity, total solids, reducing sugars.
- viii)* Analysis of cheese: Moisture, fat, added salt, acidity.

E) Microbiological Testing of Milk and Dairy Products

- i)* Introduction.
- ii)* Standard Plate Count.
- iii)* Breed Counting method / DMC.
- iv)* Tests for determining bacteriological quality of different dairy products.

Unit IV: Quality and Waste Management in the Dairy Industry (15)

A) Quality Management in the Dairy Industry

- i)* Introduction
- ii)* Need of microbiological quality control
- iii)* Role of microbiological standards
- iv)* National and international agencies

v) Microbiological standards for dairy products :Sources of contamination, control methods and assessment of –air, water, packaging material, equipment hygiene, personnel hygiene.

vi) Hazard Analysis Critical Control Point – HACCP.

B) Waste Management in the Dairy Industry

i) Introduction.

ii) Sources of waste.

iii) Effects of wastes on receiving streams/ sewers.

iv) Treatment of dairy waste.

v) Outline design for 2,00,000 lit/day capacity effluent treating plant.

Learning Outcomes:

After learning the theory paper, the student will be able to:-

- Understand the concepts of nutraceuticals and probiotics.
- Comprehend the standards and regulations related to food safety.
- Analyse the quality of milk with regards to physicochemical and microbiological aspects.
- Master the different concepts related to quality management and control in the dairy industry

Reference books

1. Robert E.C. Wildman, Handbook of Nutraceuticals and Functional Goods (2nd Edition) Routledge Publishers – **UNIT I.**
2. Review Article : Nutraceuticals : A review, Skylar A. Souyoul, Katharine P. Saussy, Mary P. Lupu – **UNIT I.**
3. Manual of Methods of Analysis of Foods – Microbiological Testing – Food, Safety and Standards Authority of India, Ministry of Health and Family Welfare, Government of India, New Delhi (2012) – **UNIT I**

4. Modi H.A. (2009) Dairy Microbiology, Pointer Publishers, India –**UNIT III, IV.**
5. J.S. Yadav, Grover S., Batish V.K. (1993) Comprehensive Dairy Microbiology, Metropolitan Book Cooperative Pvt. Ltd. – **UNIT III, IV.**

MAMiT 404.E-2 – ADVANCED BIOINFORMATICS

Learning Objectives:

The student should be able to:-

1. Learn the fundamental concept of phylogenetics and its significance.
2. Know the basics of cheminformatics.
3. Study the techniques for molecular modeling and simulations.
4. Learn the essentials of structural biology.

Unit I: Phylogenetics (15)

Phylogeny: Phylogenetic analysis, Definition and description of phylogenetic trees and various types of trees, Method of construction of Phylogenetic trees [distance-based method (UPGMA, NJ), Maximum Parsimony and Maximum Likelihood method].

Unit II: Basics of Cheminformatics (15)

Introduction to cheminformatics, evolution of cheminformatics, History of chemical information science, uses of cheminformatics, prospects of cheminformatics. History of medicinal chemistry. Prodrugs and soft drugs, Drug targets, Drug solubility, Natural resources of lead compounds, Pharmacokinetics & drug metabolism. Biological testing and bioassays, Preclinical testing and clinical trial, Synthesis.

Unit III: Molecular Modelling & Simulations (15)

Overview of molecular modeling, molecular modelling methods. Semi-empirical methods, empirical methods, molecular mechanics.

Conformations: global vs. local force fields: expressions for stretch, bond, torsion, etc. Description of various force fields: MM3, Dreiding, AMBER, CHARMM. Mechanics of Bio-macromolecules.

Molecular Dynamics - Newton's equations for many particles, Verlet and related algorithms, types of dynamics, simulations: adiabatic, constant T, simulated annealing, etc. Conformational searching using MD and other methods. Free energy calculations. Dynamics of Bio-macromolecule. Electrostatics of biomolecules

Unit IV: Structural Biology

(15)

Macromolecular Structure , Protein - Primary, Secondary, Supersecondary, Tertiary and Quaternary structure, Potential energy maps, Ramachandran map, Nucleic acid – DNA and RNA, Carbohydrates, Co-ordinate systems, Overview of experimental techniques to study macromolecular structures. Methods to study 3D structure: X-ray, NMR, Cryo-

Electron microscopy. Validation using Procheck, Prosa II , Principles of protein folding and methods to study protein folding , Macromolecular interactions, Protein – Protein, Protein – Nucleic acids, Protein – Carbohydrates. Structure of Ribosome, Prediction of protein structure secondary structure prediction methods - First, second and third generation methods. Tertiary structure prediction. Homology modeling, fold recognition and ab initio methods.

Learning Outcomes:

After learning the theory paper, the student will be able to:-

1. Understand the fundamentals of phylogenetics.
2. Comprehend the concepts of cheminformatics.
3. Interpret and analyse computational data using molecular modeling and simulations.
4. Master the different concepts related to structural biology.

References:-

1. Friesner Richard A. Computational Methods for Protein Folding: advances in Chemical Physics Volume 120 Kindle Edition. Publisher: New York, John Wiley & Sons. 2002. ISBN: 0471209554
- **UNIT III, IV.**
2. Jin Xiong, Essential Bioinformatics: Genomics and Proteomics(With Practical Exercises)
– **UNIT I.**

3. Heilmeyer L., Friedrich P. Protein Modules in Cellular Signalling.

Publisher: Amsterdam, IOS Press. 2001. ISBN: 1586031805 – **UNIT II, III.**

4. Branden ,Tooze John. Introduction to Protein Structure. Publisher:

New York, Garland Publishing Inc. 1999. ISBN: 0815323050 –

UNIT II, III, IV.

MAMiP 405 PRACTICAL COURSE – IV: LAB VII

Learning Objectives:

The student should be able to

- 1.. Learn the different components of fermentation technology and microbial biosensors.
2. Understand the nuances of solid state fermentation and its applications.
 4. Study the various facets of intellectual property.
 5. Practically learn analytical techniques employed in the microbiological quality control.

UNIT – I

A) Fermentation Technology and Biosensors

- 1) Determination of blood glucose by glucometer.
- 2) Laboratory production of alkaline protease by solid state fermentation using bacteria.
- 3) Protein Assay by tyrosine curve.
- 4) Laboratory production of citric acid by solid state fermentation using fungi and its estimation.
- 5) Financial survey of fermentation economics of small-scale Company

.B) Intellectual Property

- 6) Group Discussion on: a) Patent and Copyright, b) Bioethics.

UNIT - II

A) Microbiological Quality Control and Management

- 1) Determination of bioburden on textile material by AATCC 101-2004 method.
- 2) Determination of Thermal Death Point (TDP) and Thermal Death Time (TDT) of microorganisms.
- 3) Evaluation of sanitary status of eatery by swab technique.
- 4) In-house determination of aerobic count of microbial load by settle plate technique.
- 5) Sterility testing of autoclave using *Bacillus stearothermophilus*.
- 6) Determination of efficacy of isopropyl alcohol.
- 7) Preservative Efficacy Testing.
- 8) Instrument Qualification of: a) Incubator, b) Hot air oven.
- 9) Detection of leaky substances from bacterial cells.

Learning Outcome:

The student will be able to

- 1.. Learn the different components of fermentation technology and microbial biosensors.
2. Understand the nuances of solid state fermentation and its applications.
3. Study the various facets of intellectual property.
4. Practically learn analytical techniques employed in the microbiological quality control

References:

1. Pepler H.J., Pearlman D. (1979) Microbial Technology (2nd Edition), Academic Press
2. Pharmaceutical Microbiology Manual (PMM), United States Food and Drug Administration (USFDA), ORA.007, Version 1.2, 2014
3. Kokate C. K., Purohit A.P., Gokhale A.B. (2000) Pharmacology, 4th Edition, Nirali Prakashan.

MAMiP 406 PRACTICAL COURSE – IV: LAB -VIII

Learning Objectives

The student should be able to:-

1. perform isolation of plasmid by chemical method
2. Perform analytical techniques employed in the microbiological quality control.
3. Practically analyze biological data using tools and techniques of bioinformatics.
4. Perform experiments related to food and dairy microbiology.

UNIT – I

A) Gene technology and genomics

- 1) DNA amplification by PCR.
- 2) In-vitro seedling growth and multiplication of carrot.
- 3) Isolation of plasmid by chemical method.
- 4) Plasmid curing.
- 5) Isolation of lysozyme from egg white.
- 6) Preparation of protoplast using lysozyme and protoplast fusion.
- 7) Study of bacterial transformation.
- 8) Demonstration of Southern Blotting.

B) Bioinformatics

- 3) Determination and visualization of protein structure by Rasmol
- 4) Construction of phylogenetic tree by MEGA.
- 5) Sequence analysis by Multiple Sequence Alignment.

UNIT - II

A/ Food and Dairy Microbiology

- 1) Estimation of antioxidants by spectrophotometric method.
- 2) Estimation of antinutritional factors (tannic/phytic acid).
- 3) Detection of food adulteration.
- 4) Estimation of sodium benzoate from food.
- 5) Detection of aflatoxins from food.
- 6) Detection of lactic acid from curd.
- 7) Estimation of beta amylase from sweet potatoes.
- 8) Estimation of pectin from plant material.

Learning Outcomes:

The student will be able to:-

1. perform isolation of plasmid by chemical method
2. Perform analytical techniques employed in the microbiological quality control.
3. Practically analyze biological data using tools and techniques of bioinformatics.
- 4.. Perform experiments related to food and dairy microbiology.

References:-

4. Peppler H.J., Pearlman D. (1979) Microbial Technology (2nd Edition), Academic Press
5. Pharmaceutical Microbiology Manual (PMM), United States Food and Drug Administration (USFDA), ORA.007, Version 1.2, 2014.

6. Manual of Methods of Analysis of Foods – Microbiological Testing –Food, Safety and Standards Authority of India, Ministry of Health and Family Welfare, Government of India, New Delhi (2012)
4. Friesner Richard A. Computational Methods for Protein Folding: advances in Chemical Physics Volume 120 Kindle Edition. Publisher: New York, John Wiley & Sons. 2002. ISBN: 0471209554

