Centre for Brain Research, Indian Institute of Science

CBR-MAHE Ph.D. Program - Courses for 2022-23

Semester 1 (September to December 2022)

- CBR101 - Neuroscience I
- CBR102 - Human Genetics, Genomics, Bioinformatics
- CBR103 - Research and Publication ethics

Semester 2 (January to April 2023)

- CBR201 - Neuroscience II
- CBR202 - Research methodology (Lab-specific)

Semester 1

CBR101 – Neuroscience I (3 Credits)

- Timing: 9:00 to 10:00 am - Tuesday, Thursday, and Saturday
- Venue: Classroom, 2nd floor, CBR Building
- Coordinator: Dr. Smitha Karunakaran (smitha@iisc.ac.in)
- Instructors: Prof. Ravi Muddashetty (RM), Prof. Thomas Gregor Issac (TGI), Dr. Smitha Karunakaran (SK), Dr. Chinnakkaruppan Adaikkan (CA), and Dr. Sivaprakasam Ramamoorthy (SR)

Course structure

I. Neural development: Neural induction, polarity and segmentation, genesis and migration, determination and differentiation, axon growth and guidance, development of neuronal connectivity, survival and growth.

Instructor: **RM** | Number of lectures: 2

II. Neuroanatomy: Central nervous system - an overview of meninges; Introduction to spinal cord, medulla, pons, midbrain, cerebellum - external features, internal structure; Cranial nerves: Nuclei, functional components and distribution of cranial nerves. Fourth ventricle: Features, boundaries with special emphasis on floor of fourth ventricle. Cerebrum: External features, functional areas of cerebral cortex. White matter of cerebrum: Types of fibres, internal capsule. Ventricular system: Parts and Boundaries of lateral, third ventricles. Circulation and formation of cerebrospinal fluid. Choroid plexus and fissure. Diencephalon Thalamus: External features, internal structure, connections. Basal ganglia: Nuclei, connections, functions. Limbic system: Components, connection, functions. Blood supply of brain, Blood brain barrier.

Instructor: **TGI** | Number of lectures: 4

III. Neurons and glia: Cajal & Golgi and the history of neuron, The neuron doctrine and the reticular theory, Types of neurons, structure and function. Types of glial cells and function, Myelin sheath.

Instructor: **RM** | Number of lectures: 2

IV. Functional Neuroanatomy: Introduction to various terminologies with reference to the CNS (Brief), Anatomical localisation of various functional regions, Choroid plexus and CSF composition, Homonculus (Sensory and Motor) v), Speech and associated areas (Broca's and Wernicke's), Major regions affected in Neurodegenerative diseases eg. the Limbic system, the Basal Ganglia, Cortex etc., Other important regions: C-shaped structures of the brain, Metencephalon, and Mylencephalon.

Instructor: **TGI** | Number of lectures: 4

V. Neural Communication: Electrical Properties – Resting membrane potential, Ion channels and gated ion channels, Electrical conduction, action potential, Hyperpolarization and depolarization, All-or-none property, Afterpotentials, refractory period. Conduction and propagation of action potential, EPSP and IPSP, spatial and temporal summation.

Instructor: **RM** | Number of lectures: 3

VI. Neural Communication: Chemical Properties – Chemical synapse, Steps in synaptic transmission, Ionotropic and metabotropic receptors, Types of excitatory and inhibitory neurotransmission. Post-synaptic and second messenger processes, Synaptic integration, Modulation of synaptic transmission. Synthesis and trafficking of neuronal protein.

Instructor: **RM** | Number of lectures: 3

VII. Neurotransmitters: What defines a neurotransmitter? Synaptic transmitters and families of transmitters, major excitatory and inhibitory neurotransmitter in the brain, Major neurotransmitter pathways - dopaminergic, cholinergic, Serotoninergic, noradrenergic.

Instructor: **RM** | Number of lectures: 3

VIII. Hormones and the Brain: Major endocrine glands and their functions, General principles of hormone action, Neurocrine and neuroendocrine communication, hypothalamic-pituitary-adrenal axis (HPA axis), Feedback loops, Brain and pituitary regulation (anterior and posterior).

Instructor: **SK** | Number of lectures: 3

IX. General Principles of Sensory Systems: Transduction, Sensory encoding, Neural pathways, Receptive fields, Topographic maps. Touch - Different kinds of receptors, Receptive field, Response properties, Innervation.

Instructor: **SK** | Number of lectures: 2

X. Vision and Visual Perception: Visual pathways in the brain, receptive field. Primary visual cortex, Receptive fields of cells (Hubel & Wiesel), Orientation and direction selectivity.

Instructor: **SK** | Number of lectures: 2

XI. Audition: Auditory system pathway, Direction of sound movement – afferent and efferent pathways, Neurotransmitters involved.

Instructor: **SK** | Number of lectures: 1

XII. Olfactory and gustatory systems: Morphology of Taste Buds and Cell Types, Taste stimuli, Propagation of a Neural Code to the Gustatory Center. Morphology of Olfactory Mucosa and Cell Types, Transduction of Olfactory Stimuli, Neural Pathway into the Olfactory Cortex.

Instructor: **SK** | Number of lectures: 1

XIII. Motor System: Motor cortex, Motor unit, Motor neurons and neuromuscular junction, Pyramidal and extrapyramidal systems. Movement controls at different levels of nervous system. Motor learning and remapping of motor cortex, Mirror neurons, Neurotransmitter systems in movement.

Instructor: **SK** | Number of lectures: 3

XIV. Learning and memory: Theories of memory, Classification, short-term and long-term storage of memory, Retrieval, Memory consolidation, anterograde and retrograde amnesia, Different types of plasticity, LTP, LTD, Cell & molecular basis of learning and memory, Neural oscillations basis of learning and memory.

Instructor: **CA** | Number of lectures: 4

XV. The Neurobiology of Emotion: Papez and limbic lobe, Limbic circuit, Delineating anatomy of emotion, hippocampus, amygdala, prefrontal cortex. Papez/Maclean circuit, pitfalls of limbic system theory, Modern approach to study emotional brain eg: Fear learning circuit, Experiments by Phelps, LeDoux, Damasio, Fanselow.

Instructor: **SK** | Number of lectures: 3

XVI. Executive Functions of the Frontal Lobe: Phineaus Gage, Major functions of the prefrontal cortex. Experiments to study frontal lobe function such as Delayed response (working memory), Experiments by Goldman Rakic, Funahashi and Bruce, Cellular basis of working memory, Task shifting.

Instructor: **SR** | Number of lectures: 3

Recommended reading

- Neuroscience, edited by Purves, Augustine, Fitzpatrick, Hall, LaMantia, Mooney, Platt and White. Sinauer (2018) Sixth Edition.
- Neuroscience: exploring the brain. Bear, M., Connors, B.W. and Paradiso, M.A. 3rd edition Lippincott, Williams and Wilkins (2001)
- Principles of Neural Science by Kandel
- Development of the Nervous System by Sanes (selected chapters).
- Textbook of Neuroanatomy by Inderbir Singh

CBR102 – Human genetics, Genomics, Bioinformatics (3 Credits)

- Timing: 9:00 to 10:00 am - Monday, Wednesday, and Friday
- Venue: Classroom, 2nd floor, CBR Building
- Instructor: Prof. Bratati Kahali (bratati@iisc.ac.in)

Description

Introduction to algorithms, statistical methods and data analysis techniques relevant for understanding the role of genomic variations in human health and disease, and how to conduct high-throughput large-scale human genomics research. The class consists of three main components: lectures, hands-on sessions, and student course projects. The lecture topics cover genome and protein databases, statistical and numerical methods in human genetic data analysis, genome-wide association studies (GWAS), sequence (Next Generation Sequencing) analysis, human evolutionary and population genetics, network biology, and other relevant current topics. The course includes practical sessions for the concepts taught in class.

Course structure

I. Databases and Software for Genome Biology:

Bioinformatics databases, Nucleotide sequence databases, NCBI, EMBL, Gene Bank, DDBJ; Secondary nucleotide sequence databases, SWISSPROT, TrEMBL, PIR, Sequence motif databases -Pfam, PROSITE. Epigenome databases. Protein structure databases, Protein Data Bank, SCOP, CATH, KEGG, Chembank, Sequence, structure and function relationship. Profile HMMs for Protein Family Modeling. Pathway and GO annotation systems. Protein-protein interaction network and their characteristic features.

Number of lectures: 4

II. Sequence Alignment in Genomics:

Pair-wise sequence alignment, Scoring schemes, Smith –Waterman algorithm for local alignment, Needleman-Wunsch algorithm, Understanding Statistics of Sequence alignment score, BLAST and FASTA. Multiple sequence alignment, Algorithms for Multiple sequence alignment. Introduction to Phylogenetic analysis. Algorithms for aligning short reads from human NGS, Working principles of Burrows Wheeler Aligner. Examples from Human Genome Project and 1000 Genomes Project.

Number of lectures: 4

III. Introduction to Probability and Biostatistics:

Probability models and distributions. Combinatorial principles. Conditional probability. Independent events. Sampling design. Statistical estimation. Statistical testing. Confidence intervals. Regression analysis. Survival analysis. Classification and discrimination techniques.

Number of lectures: 6

IV. Statistical models and Numerical methods in Human Genetics:

A. Population level

Genetic analysis of naturally occurring variation in humans, detecting natural selection from genomic data, origins and consequences of mutation, as mediated by selection, migration, population structure and drift. Estimation of Allele Frequencies, Population Substructure, Population differentiation at genetic level in humans, Population Stratification, Population Admixture, Modeling the Effects of Population Admixture and Stratification (PCA, genomic control and others), Population Inbreeding, Hardy-Weinberg Equilibrium, Testing for HWE.

Number of lectures: 7

B. Heritability and genetic models

Heritability and segregation analysis, Genetic Markers and Marker Maps, Testing for Linkage or Association, Linkage Disequilibrium and Related Measures Used to Describe Linkage Disequilibrium, LOD scores, Genetic association with Dichotomous disease traits and continuous phenotypes, Additive Genetic Model, Codominant, Recessive and Dominant Models.

Number of lectures: 8

C. Statistics in association testing

TDT, pTDT, and Family Based Association Tests, Multiple testing problem in association studies, Genome-wide association studies, Quality–Control for the Genotype Data, Testing Strategies for Family-Based Studies and population cohort based studies, Replication, Non-replications and Meta-analysis, statistical estimation of haplotypes from genotype data (Phasing), Imputation methods for missing genotypes, merging of imputation reference panels, Common variant and rare variant association studies, gene based tests, SKAT, Gene Environment interaction studies. Introduction to Linux and HPC, Advanced R programming for statistics, Perl and Python for genomics. Scanning genetic databases for understanding variant details and characteristics.

Number of lectures: 9

V. Currently conducted GWAS and Next Generation Sequencing studies across the world:

GWAS of Height and Obesity, Rare disorder WGS in extended families with large pedigrees, Sequencing to understand rare disorder in multiple families, Exome sequencing in clinical scenario. Understanding of the modules of the whole genome sequencing variant calling pipeline for Population based WGS and large disease-based WGS. Practical quality checks and Coding for Sequencing Data.

Number of lectures: 7

VI. Analysis of gene expression and gene regulation data:

Data analysis of Microarrays, RNA-Seq, Single cell transcriptomics analysis, data analysis of ChIP-Seq Experiments.

Number of lectures: 3

Recommended reading

- Bioinformatics and Functional Genomics, 3rd edition- Pevsner (Book).
- Bioinformatics: Sequence and Genome Analysis- David Mount (Book).
- Statistical Genetics- Laird and Lange (Book).
- Relevant current publications in the field will be shared and discussed in class by the instructor.

CBR103 – Research and Publication Ethics (3 Credits)

- Timing: 10:30 to 11:30 am - Monday, Wednesday, and Friday
- Venue: Classroom, 2nd floor, CBR Building
- Coordinator: Dr. Latha Diwakar (latha@iisc.ac.in)
- Instructors: Prof. Ravi Muddashetty (RM), Prof. Thomas Gregor Isaac (TGI), Dr. Jonas S Sundarakumar (JSS), Dr. Reddy P Kommaddi (RPK), Dr. Latha Diwakar (LD), Dr. Chinnakkaruppan Adaikkan (CA), and Dr. Sivaprakasam Ramamoorthy (SR)

Course structure

I. Philosophy and Ethics

Instructor: **RM/JSS** | Number of lectures: 4

II. Scientific Conduct

Instructor: **RPK** | Number of lectures: 4

III. Publication Ethics

Instructor: **LD** | Number of lectures: 7

IV. Open Access Publishing

Instructor: **CA** | Number of lectures: 4

V. Publication Misconduct

Instructor: **SR** | Number of lectures: 4

VI. Database and Research Metrics

Instructor: **TGI/CA** | Number of lectures: 7

Semester 2

CBR201 – Neuroscience II (3 Credits)

- Timing: TBD
- Venue: TBD
- Coordinator: Prof. Ravi Muddashetty (ravimshetty@iisc.ac.in)
- Instructors: Prof. Ravi Muddashetty (RM), Dr. Jonas S Sundarakumar (JSS), Dr. Reddy P Kommaddi (RPK), and Dr. Latha Diwakar (LD)

Course Structure

I. Neurodevelopmental disorders: Neurodevelopmental disorders-introduction, Autism spectrum disorders (ASD), Monogenetic cause of ASD, Molecular pathways involved in ASD

Instructor: **RM** | Number of lectures: 12

II. Neurobiology of disease: Introduction, Organic mental disorders (includes symptomatic disorders due to medical conditions), Mental disorders due to psychoactive substance use, Psychotic disorders (Schizophrenia, delusional and acute psychotic disorders), Mood Disorders (Bipolar and depressive disorders), Anxiety disorders-I (GAD, panic disorder, phobias, OCD), Anxiety disorders-II (Somatoform and other stress-related disorders), Behavioral syndromes associated with physiological disturbances and physical factors (eating, sleep, sexual dysfunction, menopause, etc.), Disorders of adult personality and behavior, Behavioral and Psychiatric Symptoms of Dementia (BPSD), Psychotropics-I (neuroleptics, antidepressants, mood stabilizers), Psychotropics-II (anxiolytics, hypnotics, cognitive enhancers, neurotoxins)

Instructor: **JSS** | Number of lectures: 12

III. Prototypical Neurodegenerative disorders:

Neurodegeneration- introduction, classification, dementia, factors involved in dementia.

Alzheimer's disease, Lewy body dementia, Frontotemporal dementia, Mixed dementia: Pathology and pathogenesis, genetics, clinical manifestations, molecular mechanisms, and treatment.

Parkinson's disease, Parkinson syndromes, Wilson & Menkes Disease, Huntington's disease: History, pathophysiology, genetics, sporadic and familial forms, clinical manifestations, diagnosis, molecular mechanisms, current treatments

Amyotrophic lateral sclerosis: Epidemiology, pathogenesis, genetics, neuropathology, molecular mechanisms, in vitro and in vivo disease models.

Prions (Proteinaceous infectious particles) – Brain pathology of prion diseases, abnormal protein aggregates, transmissible neurodegenerative diseases. Etiology, pathophysiology and molecular mechanisms.

Instructor: **RPK** | Number of lectures: 12

IV. Vascular disorders

Brain Vasculature, Anatomy and Structure, Veins, Arteries, Microcirculation, Neurovascular unit, Perivascular circulation, Cerebral blood flow, Barriers of CNS, Blood Brain Barrier, Structure, Function, Drug delivery. Role of BBB in Neurodegenerative Disorders.

Stroke - Mortality, Incidence, Prevalence, Stroke Subtypes, Sex differences.

Vascular dementia, Vascular cognitive impairment, Cerebrovascular diseases, genetic cause, Role in Mixed dementia, and AD

Molecular mechanisms, Animal models of large vessel and small vessel vascular insults

Instructor: **LD** | Number of lectures: 12

Recommended reading

- Neuroscience, edited by Purves, Augustine, Fitzpatrick, Hall, LaMantia, Mooney, Platt and White. Sinauer (2018) Sixth Edition
- Neuroscience: exploring the brain. Bear, M., Connors, B.W. and Paradiso, M.A. 3rd edition Lippincott, Williams and Wilkins (2001)
- Principles of Neural Science by Kandel
- Development of the Nervous System by Sanes (selected chapters)
- Textbook of Neuroanatomy by Inderbir Singh

CBR202 – Research Methodology (4 Credits)

The syllabus for this course is lab-specific.
