Course title: Cellular signal transmission and Repair Mechanisms

Identification number	Workload	Credits	Frequency of occurrence	Duration
M-Neuro-AM6 a-b	270h	9	WS	One semester

1	Type of lessons	Contact times	Self-study times	Intended group size
	a) lecture b) practice	a) 20h b) 64h	186h (Preparation and post-processing of lectures, practical and exam)	a) 5-8 students b) 5-8 students per supervisor

2 **Aims of the module and acquired skills**

The students are to be introduced to the subject areas of...

Structure and electrical properties of membranes

- be able to describe the biophysical properties of excitable membranes and illustrate them quantitatively using important equations (Nernst, Goldman-Hodgkin-Katz), explain the importance of the interplay between inward and outward currents using the example of Na+ and K+ currents of peripheral nerves, and explain the importance of myelination for the passive properties of biomembranes.
- be able to describe the time and potential dependence of important voltage-dependent ion channels on the basis of the representatives expressed at the heart (Na+-K., L- and T-type Ca++-K., transient, fast and slow delayed rectifying, inward rectifying K+ channel, pacemaker channel) and to record their interaction in quantitative models.
- be able to name the short- and long-term effects of electrical excitation in multicellular systems and describe the underlying molecular mechanisms (e.g. for rhythm generation, synchronicity detection, long-term depression and potentiation) and reflect them critically on the basis of the current literature.

Ligand and voltage controlled channels

- describe selected families of ion channels in their molecular structure, composition of subunits and localization of functionally important protein domains.
- They should be able to name the drugs and toxins attacking these channels, where known, localize their molecular target and describe their effect. Where possible, they should derive the effects of drugs and toxins on multicellular and functional units and be able to describe the clinical picture of the effect.
- They should be able to critically reflect on the therapeutic potential of newly developed agents that act on ion channels.

Neurotransmitters: synthesis, storage, release

- can describe the biosynthesis of neurotransmitters. You will get to know the storage vesicles as dynamic cell compartments with highly specialized protein equipment (e.g. VMAT) and function.
- Students should be able to describe the mechanism of physiological transmitter release and demonstrate a detailed understanding of the effects of substances such as cocaine and amphetamine. They should be able to name the pharmaceuticals and toxins attacking these substances, e.g. botulinus neurotoxin, the detailed molecular mechanisms of action, the effects on cells and organs and the clinical picture of the effect.
- They should be able to design new strategies for pharmacological intervention and critically weigh up the advantages and disadvantages on the basis of experimental active substances.

Neurotransmitters: receptors and inactivation

- The students should be able to describe the molecular structure, classification and distribution of G-protein-coupled receptors with a focus on sympathetic nervous system and parasympathetic nervous system. They should be able to molecularly explain phenomena such as negative feedback to pre- and post-synapse, receptor reserve, desensitization, phosphorylation and internalization.

	Students should be able to describe signaltermination mechanisms, i.e. inactivation by transport (NET, DAT, EMT), intracellular (MAO, COMT) or extracellular inactivation (acetylcholinesterase). They should be able to describe the mechanisms of action of the drugs (e.g. tricyclic antidepressants, SSRIs) and toxins (e.g. cocaine, organophosphates) attacking this area and the clinical picture of the effect. • Receptors: molecular structure, localization and dynamics; intracellular reactions • Structure-effect relationships for agonists and antagonists are presented. The binding of receptors to intracellular signaling chains is discussed. • Inactivation of transmitters: transport, metabolism. The functional (e.g. trans-stimulation, transport efficiency) and molecular properties of transport proteins are discussed in detail. **Molecular Biology of Channels and Channelopathies** • The students should learn the analysis of ion channels with the help of molecular biological techniques, recognize how primary structure changes change physiological properties and see clinical relevance based on exemplary diseases (e.g. various myotonies, cystic fibrosis).
3	**Contents of the module** • Structure and electrical properties of membranes • Excitability of biomembranes: Example peripheral nerves • Complex Interplay of Channels: Example of a Heart Muscle Cell • Complex interplay of cells: Example Hippocampus • Ligand and voltage controlled channels • Voltage Controlled Channels : Example Calcium Channels • Ligand-controlled channels: Example GABAA receptor channels • Complex ligand-triggered channels: Example NMDA receptor • Neurotransmitters: synthesis, storage, release • Synthesis pathways of all major neurotransmitters • Properties and Structure of the Memory Spacesicles • Transmitter release mechanisms • Neurotransmitters: receptors and inactivation • Molecular structure, localization and dynamics; intracellular reactions of receptors • Structure-effect relationships for agonists and antagonists • Inactivation by transport and metabolisation • Molecular Biology of Channels and Channelopathies • cloning techniques • Analysis of mutations with PCR and restriction digestion • Expression in HEK cells • Electrophysiological measurements
4	**Teaching/Learning Methods** Lecture/seminar with practice parts
5	**Requirements for participation** Enrollment in the Master's degree course "Experimental and Clinical Neurosciences" at the University of Cologne Contentwise: Previous pharmacological and physiological knowledge corresponding to the contents of the Bachelor programme 'Neurosciences' is required. Practical experience in the modelling of systems, e.g. on the basis of multiple differential equations Basic knowledge of physics and mathematics in the upper secondary school is advantageous.
6	**Type of module examination** Preliminary examination: Regular participation and active cooperation in the exercises and in working on the exercise tasks Final examination: Seminar talk, paper

7	**Requirement for the allocation of credits** Successful seminar talk and paper, regular participation
8	**Compatibility with other Curricula** none
9	**Significance of the module mark for the overall grade** In the Master´s degree course "Experimental and Clinical Neurosciences": 9% of the overall grade (see also appendix of the examination regulations)
10	**Module coordinator** **Teaching coordinator:** PD Dr. Jan Matthes, Tel. 0221-478 5674, jan.matthes@uni-koeln.de **Teachers:** Frau Dr. Elza Kuzmenkina, PD Dr. Jan Matthes, Prof. Dr. Dirk Gründemann
11	**Additional information** **Literature:** • Hille B.: Ionic Channels in Excitable Membranes • Stein WD: Transport and Diffusion Across Cell Membranes. Academic Press • Ashley RH: Ion channels, Oxford University Press