

## NEUROBIOLOGY - SEMINAR I

1. Wie entsteht das Ruhepotential einer Nervenzelle? Wie kann man es berechnen?
  - unequal distribution of sodium and potassium on both sides of the membrane
  - Nernst equation: concentration of potassium ions intra-/ extra-cellular, chloride, calcium
2. Wie entsteht ein Aktionspotential? Durch welche Ionenströme wird es getragen?
  - stimulus  $\rightarrow$  sodium channels (voltage gates) open, depolarization  $\rightarrow$  potassium channels (voltage gated) open, repolarization, hyperpolarization
  - all-or-none-response, no AP if depolarization below threshold
3. Wie kann man aus der Primärstruktur eines Proteins Rückschlüsse auf seine Membrantopologie ziehen?
  - membranetopology: how is the protein integrated in the membrane
  - amino acid sequence analysis
  - proteins are highly hydrophilic molecules  $\rightarrow$  how can they become deeply embedded into the hydrophobic core as so called integral membrane proteins?
  - proteins widely differ in their side chain properties, some have highly hydrophobic side chains  $\rightarrow$  integration possible
  - find such transmembrane segments by computer aided screening
4. Mit Hilfe welcher Messanordnung kann man bei Nervenzellen Ionenströme messen?
  - voltage clamp technique
  - inject certain current (not voltage), measure response of cell
  - difference between patch clamp and voltage clamp: contains only one single ion channel
5. Wie sind spannungsunabhängige Ionenkanäle aufgebaut?
  - material: amino acids
  - K<sup>+</sup> channel consist of 4 subunits, Na<sup>+</sup> channels consist of one protein consisting of 4 domains (chemically connected)
  - each: 6 transmembrane segments (connected by loops), hydrophilic pathway between two transmembrane segments (hairpin loop between 5 and 6)
  - charged S4 segment  $\rightarrow$  voltage sensor  $\rightarrow$  opening of channel
  - inactivation particle between (loop) III and IV, closes the channel from inside (automatically linked to opening)  $\rightarrow$  if not: too long signal  $\rightarrow$  has to be fast, short signals
  - S4 segment returns to original position during repolarization
  - remove of inactivation particle  $\rightarrow$  hyperpolarization  $\rightarrow$  end of refractory period
  - disadvantage of refractory period: limited range of APs per second
  - signal strength coded by frequency; advantage of possibility of use of high frequencies: slight differences can be recognized
6. Nennen Sie die wichtigsten Bauteile einer Nervenzelle! Welche Funktionen haben diese? Worin unterscheiden sich die beiden Haupttypen von Zellfortsätzen voneinander?
  - axon, synapse, dendrites, soma, nucleolus
  - axon (neurite): sends out electrical signals, uniform diameter, can be very long
  - dendrite: receives signals from other nerve cells, highly branched
  - synapse: chemical or electrical signal transfer to target cells, specialized structures at nerve endings
  - soma: keeps everything together, contains nucleolus (with DNA), mitochondria  $\rightarrow$  ATP (for pump), endoplasmic reticulum (for protein production), Golgi-apparatus (produces vesicles)
  - one protein only produced in nerve cells: neurofilaments  $\rightarrow$  how is the selection made to produce them (from whole DNA)? – gene activation mechanism initiated by transcription of m-RNA regulated by proteins (transcription factors)
7. Welche intrazelluläre Stützstrukturen besitzen Nervenzellen? Wie ist deren molekularer Aufbau?
  - microfilaments consist of protein actin: keep vesicles apart from membrane to prevent exocytosis (in synapse)
  - microtubules consist of protein tubulin: component of cytoskeleton, guide fast axonal transport
  - neurofilaments: also component of cytoskeleton
  - $\Rightarrow$  all three: stabilize the extensively branched cellular structure, allow structural flexibility and material transport
  - fast axonal transport goes in both directions
  - slow transport: for generation of cells (axons are built of cytoskeleton material and membrane proteins)
  - mechanism of slow transport: not yet known
8. Welchen Vorteil bietet die Patch-clamp Technik? Auf welchem Prinzip basiert sie?
  - works similar to voltage-clamp technique
  - measure the current of a single ion channel
  - does not manipulate the cell
9. Worin unterscheiden sich Gliazellen von Nervenzellen?
  - astrocytes (taking up glucose, cleaning up potassium in the extracellular space, uptake of neurotransmitters in the CNS)
  - without removal: nerve cell fires 10 seconds  $\rightarrow$  10.000 APs, membrane potential becomes depolarized by accumulation of potassium
  - oligodendrocytes (myelination in the CNS)
  - Schwann Cells (myelination, regeneration, potassium removal in the PNS)
  - microglial cells (immune cells of brain (no others in the brain, because of blood brain barrier) – CNS)
  - $\Rightarrow$  most of the glial cells are able to divide throughout life, typically possess a uniform set of cell processes, usually smaller than neurons; physiological dependence, function cooperation between glial and nerve cells (similar in their complex morphology)
10. Weshalb haben Mitochondrien bei Nervenzellen eine besonders große Bedeutung?
  - sodium-potassium-pump  $\rightarrow$  regenerates the ionic gradients (which are constantly disturbed by APs)
  - fast axonal transport: support kinesin and dynein with ATP
  - 90 % of body energy is used in nerve cells

## NEUROBIOLOGY - SEMINAR II

### 1. Wie entsteht das Endplattenpotential an der neuromuskulären Verbindung? Welche Bedeutung hat es?

- neuromuscular junction → muscle considered as target cell
- transports information from nerve-ending to muscle
- depolarization of postsynaptic membrane
- neurotransmitter: ACh → opens sodium channels
- voltage gated sodium channels opened by epsp → induction of muscle AP → contraction

### 2. Was versteht man unter einem Agonisten, was unter einem Antagonisten eines Neurotransmitters? Welche cholinergen Agonisten/Antagonisten kennen Sie?

- Agonist → epsp (only replacement)
- Antagonist → ipsp (blocker: replacement, allosteric inhibition)
- nAChR: agonist nicotine, antagonist curare
- mAChR: agonist muscarine, antagonist atropin
- glutamate: neurotransmitter ≠ agonist (NMDA)
- bicuculline = agonist of GABA

### 3. Worin unterscheiden sich chemische von elektrischen Synapsen? Welche Vor- und Nachteile besitzen sie jeweils?

- no synaptic vesicles, no synaptic cleft → fast (no refractory period), (often) bidirectional
- direct ion-channel formed by pores in each membrane (a gap junction consists of 2 connexons, each consisting of 6 connexins (subunits built of 4 transmembrane segments))
- used to synchronize activity of populations of neurons
- chemical synapse: delayed response, neurotransmitter, unidirectional (only in the presynapse we've got synaptic vesicles)

### 4. Welche Neurotransmitter kennen Sie? Welche Eigenschaften haben die zugehörigen Rezeptoren

- muscarine one subunit, 7 transmembrane segments (metabotropic, G-Protein-coupled) → ipsp
- nicotine channel-like: 6 subunits, 4 transmembrane segments each → binding opens → epsp
- dopamine, noradrenaline (= biogenic amines; inactivation by MonoAmineOxidase): metabotropic G-Protein-receptors
- GABA<sub>A</sub> ionotropic: Cl<sup>-</sup> influx → ipsp (channel built of 5 subunits (pentamer), 4 transmembrane segments each)
- GABA<sub>B</sub> metabotropic (7 tm segments): α subunit - GTP binding, β, γ subunit - activation of K<sup>+</sup> channels (outflow) → ipsp
- serotonin sensitization of Aplysia → G-Protein coupled receptors
- glutamate (ionotropic) NMDA receptors (silent synapses) Ca<sup>2+</sup> influx
- non-NMDA receptors K<sup>+</sup>, Na<sup>+</sup> channels (mainly K<sup>+</sup> outflow, little Na<sup>+</sup> influx)
- metabotropic glutamate receptors → largely inhibitory (mGluR1, ..., mGluR8)

### 5. Welche Funktion wird dem Hippocampus zugeschrieben?

- long term memory; new features are put into memory (selectivity filter)
- How do we know? It was cut out of a man's brain → he could not keep in mind anything new

### 6. Worin unterscheiden sich NMDA von nicht NMDA-Rezeptoren?

- NMDA-receptors → silent synapse (Mg<sup>2+</sup>-block must firstly be removed by depolarization of membrane)
- → chemically and voltage gated ion channel
- highly permeable for Ca<sup>2+</sup> (influx)

### 7. Welchen postsynaptischen Effekt bewirkt das Kalzium bei der Langzeitpotenzierung?

- activation of CaM-kinase II → autophosphorylation → stabilization → long time effect (enzymes named substrate + -ase: Calcium-calmodulin-kinase (calmodulin = calcium-binding-protein, calcium sensor))
- → recruitment of non-NMDA receptors (AMPA-type) → increase of activity (since not dependent on depolarization)
- activation of another enzyme → Nitric Oxide (retrograde neurotransmitter) → facilitation of neurotransmitter release (presynapse)

### 8. Was ist ein Reflex? Zeigen die wesentlichen Elemente eines Reflexbogens auf (Bsp. Kniesehnenreflex).

- stereotypic reactions to certain stimulus (via spinal cord)
- sensory input → motor output (cannot be influenced voluntarily (duty), takes about 1 ms (fastest possible reaction))
- tendon connects muscle to patella → stretch-signal in muscle → activation of sensory fibres (dorsal root)
- specialized neuron: dorsal root ganglia (entrance pathway = dorsal part); highly specialized: pseudounipolar cell
- periphery → grey matter → target neuron (motoneuron) possibly interneurons exist (advantage: modify or specify reaction)
- afferent collateral inhibition → inhibitory interneuron (flexor inhibited while extensor excited)
- → neurotransmitter: GABA would be possible, in PNS rather glycine (Chloride-channel)

### 9. Worin unterscheidet sich ein autonomer Reflexbogen von einem somatischen?

- spinal cord: white matter: fat from myelin; grey matter: neurons
- grey matter: tree compartments: ventral core → motoneurons → ventral roots; dorsal horn → sensory entrance of spinal cord (both needed for somatic reflex arc); intermediate region → autonomic reflex arc (takes same paths as somatic neurons)
- two branches operating: parasympathetic - rest and digest, sympathetic - flight or fight (effect depends on target organ)
- specific wiring properties: start: command neurons (efferent neurons), somatic: motoneurons
- difference compared to somatic reflex: terminate in ganglia instead of target organ
- sympathetic-ganglia: chain along spinal cord → postganglionic fibres connect to target organs
- nAChR → ganglia → mAChR → inhibition
- parasympathetic-ganglia: close to target organ nAChR → ganglion → noradrenaline → excitation (coherent emotional informational environmental activity needs a lot of crosstalk)

### 10. Schildern Sie die zellulären Grundlagen des Kiemenrückziehreflexes bei Aplysia.

- typical monosynaptic reflex: sensory cell (gills), effect (withdraw); only based on ganglion, no spinal cord
- presynaptic nerve terminals act as ganglion for other fibres
- decrease of activity while repeated stimulation → desensitization (habituation)
- strong stimulation: → activation of adenylylcycles → cyclic AMP → relevant for synaptic plasticity
- intracellular pathway: activation of Proteinkinase A → phosphorylation of K<sup>+</sup> channels → reduces conductance → prolonged APs
- → increase of neurotransmitter-release → sensitization