What is the ion type flowing through GABA(A) receptor channels? Use the Nernst equation to compute the reversal potential for this ion type at physiological temperature (intracellular: 4mM, outside 100 mM). Draw an I-V plot and mark the reversal potential.

**Chloride.** $E_{Cl} = -86.67 \text{ mV}.$

Which GABA receptor types do you know. Discuss the differences and similarities.

**GABA(A) and GABA(C) are ionotropic receptors permeable to chloride ions, they mediate fast inhibition. GABA(B) receptors are metabotropic receptors which open potassium conductances via activation of G-proteins, they mediate slow inhibition.**

Which toxins block the GABA(A) receptors?

**Picrotoxin, Biccuculine, Penicillin.**

What happens if one of the above toxins would cross the blood –brain barrier?

**The person is likely to develop seizures.**

Discuss the action of Benzodiapines including possible medical applications.

**Benzodiazepines increases affinity of GABA(A) receptors for GABA. They therefore prolong the duration of inhibitory postsynaptic potentials. They have sedative, anxiolytic, anticonvulsant, and muscle relaxant properties.**

Explain the concept of balanced excitation and inhibition.

**In cortex, excitation and inhibition counteract each other keeping brain activity at a reasonable level. If the balance is shifted towards more excitation (e.g. by blocking inhibition) the brain becomes overly active and therefore seizure prone.**

Discuss the difference between deactivation and desensitization of a ligand gated channel.
Deactivation corresponds to closing of the channels which occurs spontaneously sometime after the transmitter molecule (e.g. GABA) is no longer present in the synaptic cleft. Once deactivated, the ligand gated ion channel can be opened again if presented with the transmitter molecule. Desensitization describes the transition to a closed state in the constant presence of the transmitter.

How would you distinguish an excitatory from an inhibitory synapse in an electron micrograph?

**Excitatory synapses show a pronounced region of electron-dense material on the postsynaptic side** (asymmetric synapse) whereas **inhibitory synapses lack this dense postsynaptic structure** (symmetric synapse).

Why do chemical synapses have mechanisms to either degrade or reuptake transmitter?

**These mechanisms serve to ensure specificity and temporal resolution.**

Describe the reuptake mechanisms for inhibitory synapses. Which substance inhibits this process. Suggest a medical application.

**GABA gets reuptaken into the presynaptic terminal by GAT (GABA transporter). Tiagabine inhibits GAT and therefore can be used for treating epileptic patients.**

Draw an I-V plot for both the early and the late component of an ionotropic excitatory current at a glutamatergic synapse recorded in a voltage clamped neuron. Label the I-V plots with the corresponding receptor type. Discuss the voltage-dependence in case there is any. What pharmacological manipulation would you do to separate the response mediated by the two receptor types.

**See lecture slides. AMPA Receptor mediated currents peak early are show a linear relationship with voltage. NMDA Receptor mediated current peaks later is voltage-dependent because of the Mg2+ block. CNQX blocks AMPA receptors, whereas APV blocks NMDA receptors.**

Explain how an NMDA receptor is a coincidence detector of pre- and postsynaptic activity.

**For an NMDA receptor to activate, the presynaptic neuron needs to release glutamate (after an AP) and the post-synaptic neuron needs to be depolarized for the Mg2+ block to be removed.**
Why would glia cells convert glutamate into glutamine?

*Since glia cell eventually release the uptaken transmitter, the release of glutamate instead of glutamine would interfere with nerve cell communication.*

Discuss all the synapses involved in the stretch reflex. Specify the neurons on the pre- and postsynaptic side and the neurotransmitter(s) released.

<table>
<thead>
<tr>
<th>Presynaptic</th>
<th>Postsynaptic</th>
<th>Neurotransmitter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alpha motor neuron</td>
<td>Muscle fiber</td>
<td>Ach</td>
</tr>
<tr>
<td>Ia afferent</td>
<td>Main dendrite of alpha motor neuron</td>
<td>Glutamate</td>
</tr>
<tr>
<td>Ia afferent</td>
<td>Ia inhibitory interneuron</td>
<td>Glutamate</td>
</tr>
<tr>
<td>Ia inhibitory interneuron</td>
<td>Somata and main dendrites of alpha motor neurons (antagonist)</td>
<td>Glycine; (GABA)</td>
</tr>
<tr>
<td>Alpha motor neuron</td>
<td>Renshaw cell</td>
<td>Ach</td>
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<tr>
<td>Renshaw cell</td>
<td>Homonymous alpha motor neuron</td>
<td>Glycine; (GABA)</td>
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<tr>
<td>Renshaw cell</td>
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<td>Glycine; (GABA)</td>
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<tr>
<td>Gamma motor neuron</td>
<td>Muscle spindle</td>
<td>Ach</td>
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<tr>
<td>Ib afferent (Golgi tendon)</td>
<td>Ib inhibitory interneurons</td>
<td>Glutamate</td>
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<td>Ib inhibitory interneuron</td>
<td>Alpha motor neuron</td>
<td>Glycine; (GABA)</td>
</tr>
</tbody>
</table>

Explain two mechanisms with which subthreshold excitatory postsynaptic potentials can make a postsynaptic cell fire an action potential.

**Spatial summation. Temporal summation.**

List three pharmacological targets to treat depression. Name the corresponding pharmacological agents.

**Monoamine oxydase (MAO).** Monoamine oxydase inhibitors.
**Serotonin transporter (SERT).** Selective reuptake inhibitors.
**Norepinephrine transporter (NET).** Tricyclic antidepressants.

Explain how cocaine and amphetamines work (neurotransmitter system and specific targets)?
Cocaine: Inhibits dopamine transporter (DAT) and therefore increases dopamine availability.
Amphetamines: Inhibits norepinephrin transporter (NET).