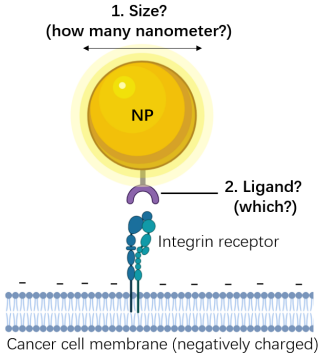
1. During the lecture you heard about the ligands and receptors.
   a) Please draw a cartoon to show how the ligand-receptor binding looks like on the cell membrane, and list 3 types of ligands and receptors

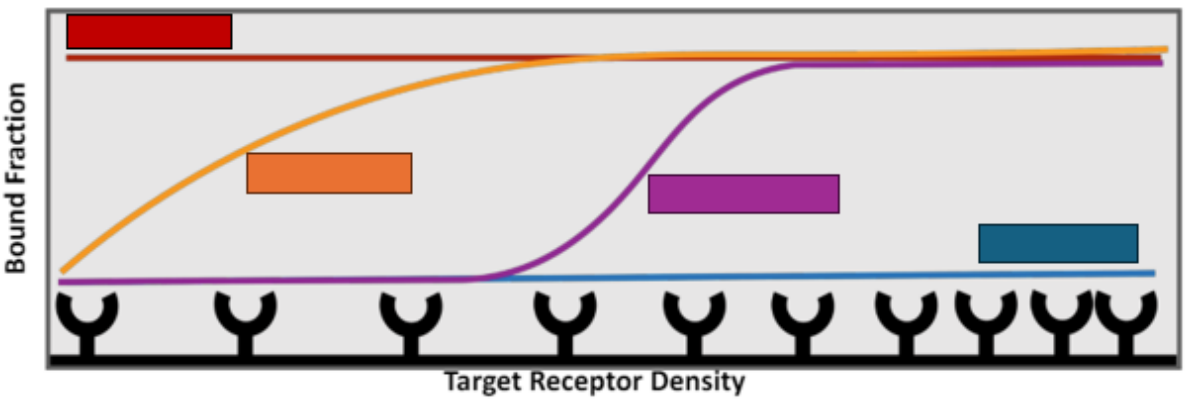
   b) In previous lectures you learned about the Arg-Gly-Asp (RGD) motif, which serves as a ligand for integrin receptors on the surface of cells to mediate cell adhesion. What is the binding mode between RGD-integrin? What are the other binding modes between ligands and receptors?

   c) To maximize the treatment effects biomaterials and avoid their side effects on normal organs/tissues, therapeutic biomaterials (i.e, nanoparticles) need to recognize diseased cells rather than healthy cells. This is typically achieved by either one or both means of targeting: passive or active. What are the differences between passive and active targeting? Which targeting strategy do you think would work better?

   d) Cancer cells overexpress integrin receptors on their surface. Below you can see a nanoparticle (NP) core, that you would like to make into a cancer-targeting nanoparticle. Please supplement the design parameters that you think may improve the targeting efficiency.



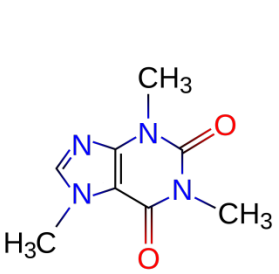
   e) Now considering that all cells overexpress integrin receptors and we want to minimize off-target effects, we aim to design nanoparticles that will only interact with cells expressing integrin receptors above a certain threshold. First, name the different binding types represented on this curve and secondly select the binding type that is suited best for designing this type of nanoparticle.



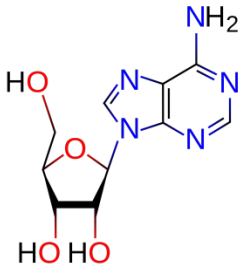
Red:
Orange:
Purple:
Blue:

2. Ligands can be classified into agonists or antagonists according to their efficacy upon their binding to receptors.
   a) What are agonists and antagonists?

   b) During the lecture you heard about adenosine, a natural molecule in our body. Naturally, it binds to adenosine-receptors and makes us feel tired. Often, we drink coffee to feel more awake and alert. Caffeine, a component of coffee, is a ligand for the adenosine-receptor. Based on the structure below, why do you think both adenosine and caffeine can bind to the same receptor?

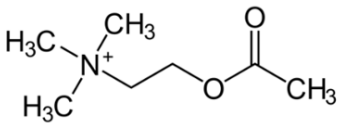


Caféine

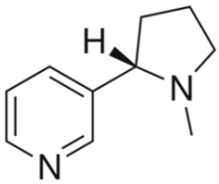


Adénosine

   c) Based on the effect, is caffeine an agonist or antagonist for the adenosine receptor? Explain why?
   d) Both Nicotine and Acetylcholine act as agonists for the nicotinic acetylcholine receptor (nAChRs). The binding between these two molecules and nAChRs could make us feel excited, however Nicotine is also known an addictive drug in tobacco products. Based on the dissociation constant (Kd) shown below, could you explain why tobacco is so addictive?
   - Kd of Nicotine-nAChRs is: 1 nM to 1 pM
   - Kd of Acetylcholine-nAChRs is: 140 µM to 0.1 mM



Acetylcholine



Nicotine

3. In the lecture you heard about the concepts of endo- and exocytosis.
   a) Please describe the general differences between the two processes.
   b) Please give an example for both processes within our body.
   c) Imagine you would like to deliver a nanoparticle like the one in 1d) into the cytoplasm of a specific cell how could this be induced and what features would the nanoparticle need to have to end up at the desired location?
   d) For what applications could such a nanoparticle inside cells be useful for?

4. During the lecture you heard about endosomal escape and potentially you talked already about it in 3c), but we would like to focus in a bit more detail on the aspect of endosomal escape.
   a) Why is it important, that a cargo, that would need to enter a cell escapes the endosome rather early than late?

   b) Please name at least two different ways of how a particle can escape the endosome.

   c) Please draw the chemical structure of this peptide: GRKKRRQRRRPQ

   d) What is the charge of this peptide and what is it used for?

5. Some questions about Kd calculations:
a) At a ligand concentration that equals the **Kd**, what percentage of receptors on a cell would be bound by the ligand?
b) Calculate the concentration of free receptors **[R]** at equilibrium when we know that the total concentration of receptors **[Rt]** and ligands **[Lt]** is 200pM and 300pM respectively and the concentration of ligand-receptor **[LR]** complex is 120pM at equilibrium.

c) Use the concentrations of **[R], [L]** (concentration of the ligand), and **[LR]** to calculate the dissociation constant (**Kd**) for the ligand-receptor interaction.

d) Does the dissociation constant calculated indicate a strong or weak interaction between the ligand and receptor? Does this mean that the receptor is a good target for nanoparticles taking advantage of super-selective binding?