LIGAND BINDING AND ENZYME CATALYSIS

The purpose of this handout is to describe some of the features of the related processes of ligand binding and enzyme catalysis. We will use two closely related equations to help in our examination of these processes. The equations are best used simply by “playing around” with them: consider different cases (L really big, L=K, etc.) to confirm your intuitions about the processes.

**Binding of a ligand to a protein** - The ligand is the molecule that is binding to a site on a protein. It could be anything: a sugar molecule, and neurotransmitter, a drug, even another protein: anything that is binding to a site. We call the ligand L. Lets call the protein B, since it is doing the binding. Proteins can have multiple sites for multiple ligands, but we’ll just think about the simple (and often encountered) case of one site for L on each protein molecule. Let’s represent the binding of L to its site on B with the cartoon below. The individual molecules of L are the squares, and the binding site is a tailor-made square pocket (Isn't biology amazing!). The binding is in equilibrium, and this is indicated by the double-headed arrow.

![Binding cartoon](image)

Although only one B is shown, in a real situation there will be a number of B molecules, each providing one site, and some amount of L. At equilibrium a constant number of L molecules will be bound. An identical way to say this is that a constant number of B sites will be occupied. Of course, on the molecular level, L molecules are continuously binding to or leaving sites on B, but at equilibrium the number of bound L is constant because the two processes balance out. The main question is: how does the amount (concentration) of total L present affect the binding equilibrium? To think about this, picture the following situation. We have a set number of B sites (a set concentration of B molecules) at different concentrations of L. In each case, some of the L’s are bound, and some are free. The limiting cases are easy to picture. When no L is present, there will be no bound L, and there will be no occupied B sites. When L is really concentrated, many of the sites will be occupied, and the higher L gets, the more likely it is that all the B sites will have a resident L bound there. Remember, it is still an equilibrium. L’s are constantly coming and going from sites, but as the total concentration of L gets higher, the chances of a site on B staying unoccupied gets lower and lower. A simple equation describes the behavior of this kind of simple binding. That equation is shown above. It is called a binding isotherm, and is very general. The binding isotherm can be even further simplified. It is consists of two terms. The value B is really the concentration of total binding sites available, since there is one per
protein molecule. So B is the maximum binding capacity possible. The term in front of B (written alone in the box below) is the fraction of total sites that will be occupied at that concentration of L.

Notice that this expression can only go between 0 and 1. The higher L gets, the closer we get to one. So increasing L increases the fraction of sites that will be occupied. When L = 0 (no L around), the fraction of total sites that are bound is zero, and the concentration of bound L is zero (when there is no L, none of it can be bound). As the concentration of L increases, the fraction of total sites approaches 1, meaning that as much L as possible is bound. That is, \( L_B = B \). This kind of behavior is very general, so binding isotherms like this appear all over the place in biology, physics and chemistry. The shape of these curves is characteristic and is drawn below. The total binding starts at zero and increases as L increases up to the maximum possible, in which every B has a bound L. This behavior is called **saturability**, and is a central feature of things in biology that are dependent on binding, like responses to drugs, cellular adhesion, neurotransmitter action, and enzyme catalysis, as we’ll see below. The shape of the curve is totally determined by the size of K. When Kd is very small, L binds to its site very efficiently, and the binding saturates at lower levels of L. This is shown in the graph by comparing the binding of two ligands with K's that are very different. So the smaller Kd is, the better L binds to its site. Kd is a measure of the thermodynamic equilibrium constant for the dissociation of the L-B complex into free L and B. In any case, K is a constant property of the system. Notice that the fraction \( \frac{L}{L + K_d} \) is equal to 0.5 when L = Kd. So Kd is the concentration of L that is needed to get 50% saturation of the sites. This helps one to think about what Kd means: the value of Kd tells the concentration of L that you need to get 50% saturation. The lower Kd is, the better L likes to bind to its site, and the less it takes to get significant binding. From our discussions of binding, you can imagine that a site that can establish a lot of bonds to a ligand in exactly the right configuration would be able to bind that ligand tightly. So Kd is an indication of the "fit" of a

\[
\frac{L}{L + K_d}
\]

The term in front of B: fraction of bound sites
ligand to its site. The better the fit, the tighter the binding, and the lower you might expect $K_d$ to be.

**Inhibition of binding** - What if more than one ligand can bind the same site? That is, what if there are two molecules that each can fit into the single binding site on B? You can imagine that a binding site might be able to recognize more than one ligand if each had the appropriate molecular features (you know, things like OH's in the right places, charges where they should be, etc.). I'm not talking about a binding site that can hold more than one ligand at the same time. I mean a site that will bind either of two ligands. Like this:

![Diagram showing inhibition of binding](image)

So what happens if you have both present? Let's consider the same experiment as before, where we varied $L$ and measured the amount of bound $L$ ($L_B$). but now we also have present a set concentration of another ligand, $I$ (with the strange shape) that also can occupy the site on B. So now Y is present at a set concentration and you start adding more and more of $L$. As before, the $L$ (the one you're adding) will "win out" as its concentration becomes more and more dominant: as $L$ gets higher and higher, the chances of an empty B site bumping into an I instead of an L get lower and lower. (That's why its so hard to meet that special someone at a really crowded party). But it is harder for $L$ to saturate since there is always the chance that an I will bind instead of $L$. It turns out that the effect of an alternate ligand like $I$ on the $L$ binding curve is very simple: the binding of $L$ will still be of the form $L_B = [L/(L+K)]$, but the $K$ that describes the shape of the curve will be bigger than the $K_d$ for the interaction of $L$ and B alone, or in other words, the binding of $L$ to its site will appear to be less strong. This is not because the I alters the interaction of $L$ with a site on B. The shifted $K$ is entirely due to probabilistic effects that a
set concentration of $I$ will have on the equilibrium values of $L_B$ at a given concentration of $L$. The graph shows the saturation of B sites by L in situations where competing ligand $Y$ is present. Each curve has a characteristic "$K\text{"}$, as determined by the 50% saturation point. As predicted from the discussion, the more $Y$ present, the slower $L$ is to saturate. The actual molecular processes that allow the binding of $L$ are exactly the same, but the apparent Kd's are different because $Y$ makes it harder for $L$ to find $B$. This type of inhibition, in which the final saturation value is the same but the binding curve rises more slowly (but still has the $[L/(L+K)]$ form is called competitive inhibition, and is encountered all over biology and medicine. A substance like $Y$ that causes such a change in a $L$'s binding isotherm is called a competitive inhibitor.

**A medical example:** People inject street heroin with little information about the amount that is present in an illicit sample. The actions of this substance when injected are very fast, and can bring about life-threatening respiratory depression in minutes if the dose is too high. When such a patient is lucky enough to end up in an emergency room, they are given a drug called naloxone, or a related substance. Naloxone is structurally related to heroin (see picture), and binds to the same receptor that the heroin binds to (called the opiate receptor). That is, naloxone is a competitive inhibitor of heroin binding. However, unlike heroin, naloxone does not turn on the receptor, it just sits there. Thus, a sufficiently high does of naloxone displaces the heroin from its receptor sites, and almost instantly shuts off the effects of the heroin overdose. The effects of this treatment are astonishing, and can take a patient from death’s doorstep to the ER exit door in less than 5 minutes.

**Cooperative binding: the story of myo and hemo-** The binding isotherm that we discuss above, with the form $[L/[L+K])$, is very common in many processes. So common is it that such a curve has a name. It is called a rectangular hyperbola. Fancy name, but a simple mathematical form. One such protein that shows this sort of binding is called myoglobin, which binds oxygen ($O_2$) and holds it in the muscle tissue until it is used. Myoglobin has a very well-studied structure. It exists as a single molecule, or a monomer, in solution with a heme group covalently nestled between several $\alpha$ helices. The binding of $O_2$ to myoglobin follows a simple binding isotherm. That is shown below. The way that you vary $O_2$ (since its a gas) is by changing the partial pressure of $O_2$, and the effect of $O_2$ pressure on the fraction of myoglobin sites with a bound $O_2$ is totally predictable from a single, unchanging $K$, at any level of $O_2$ from the lowest pressure to the highest. Now let's consider myoglobin's big city cousin hemoglobin. Unlike myoglobin, hemoglobin consists of four very similar subunits arranged as a set of four, or a tetramer. That is, it has a quaternary structure, whereas myoglobin does not. The individual subunits of hemoglobin look a lot like myoglobin. The sequences ($1^\text{O}$ structure) of myoglobin and any of the subunits of hemoglobin have numerous identical amino acids. Furthermore, each of the hemoglobin subunits have folded ($3^\text{O}$) structures that look identical to each other and nearly identical to the single myoglobin
monomer. Finally, each hemoglobin subunit has a bound heme prosthetic group that serves as an O₂ binding site. So from these structural considerations alone, it looks like hemoglobin could be considered a "four pack" of myoglobins. And so we might expect the hemoglobin to show a very similar O₂ binding curve, with a constant K and a the familiar (if tongue twisting) rectangular hyperbolic shape. 

**But NO! The curve is completely different!** The saturation of hemoglobin binding sites with O₂ has a sigmoidal shape (that means "looks like an S"): This is a comparison of the O₂ binding isotherms of hemoglobin and myoglobin. The fraction of total sites bound is plotted against the total O₂ pressure. Whereas the myoglobin curve has a single K that fits every single point on the curve, the sigmoidal shape of the hemoglobin curve means **there is no constant K**. If you calculate an apparent K at each point it becomes clear that the K is quite big at low O₂, and drops to a value that is ~ 300 times less at high O₂. Remember that high K means weak binding, and low K means strong binding. At low levels of O₂, the interaction of O₂ with heme is weaker than the interaction at high level of O₂. So somehow, the hemoglobin's binding properties are being altered by the amount of oxygen in the environment. Hemoglobin is "measuring" the concentration of O₂ in the environment.

Another way of looking at this is that as each O₂ binds to one of the four sites on the hemoglobin, the binding of the next one is strengthened. A good analogy is that if four people swim up to a rowboat, the first one to climb in has a very tough time. The second one climbing in gets help from the first. The third person has an even easier time, since two people can help, and the last one can almost be lifted in! This molecular phenomenon of the concentration of a ligand altering the binding properties of a protein that recognizes it is called **cooperativity**. The example of hemoglobin is called **positive cooperativity**, in which increase concentrations of the ligand increase the strength of the binding. Examples of **negative cooperativity** also exist, where binding grows weaker at higher concentration of the ligand. I guess that in that case, the people in the boat don’t want company so they tend to push out the late comers!

**Quaternary structure and cooperativity**- in thinking about the difference between hemoglobin and myoglobin, the most obvious difference between the two proteins is the fact that myoglobin exists as a lone protein molecule, whereas hemoglobin is an assembly of four separate molecules bound in a single quaternary structure called a tetramer. This quaternary structure is critical and central to the ability of hemoglobin to alter its properties in response to oxygen. In the rowboat analogy, you’ve got to be able to hold more than one person for them to help the next person on board. What actually appears to happen (this is still something that is under study) is that the tetramer can assume two states, a low affinity state and a high affinity state, and the binding of O₂ shifts the equilibrium towards the high affinity state. So its a little different from our boat analogy, but still the same sort of process.
Enzyme Catalysis: getting out of a bind

Enzymes are a special class of proteins that catalyze chemical reactions. That is, they alter the rate of a chemical occurrence (bond making or bond breaking) and are left unchanged to do the same thing again. In every case, there is a molecule that is altered by the enzyme to result in a product. The starting molecule is called the substrate, and the resulting molecule is called a product. A simple example of this is the enzyme phosphoglycerate isomerase. It changes 2-phosphoglycerate (2-PG) into 3-phosphoglycerate (3-PG), like in the reaction below. The enzyme speeds up this process. So in considering the action of phosphoglycerate isomerase in the reaction going in this direction, we would call the 2-PG the substrate and the 3-PG the product.

\[
\begin{array}{c}
\text{substrate} \\
\text{OH} \\
\text{OPO}_3^- \\
\text{OH} \\
2-\text{PG}
\end{array}
\quad \xrightarrow{\text{phosphoglycerate isomerase}} \quad
\begin{array}{c}
\text{product} \\
\text{OH} \\
\text{OH} \\
\text{OPO}_3^- \\
3-\text{PG}
\end{array}
\]

An enzyme will not affect the equilibrium of a chemical reaction. This means that the rates of both forward and reverse reactions will be enhanced to the same extent. So in some circumstances you could just as easily study the reverse reaction. In our case that would mean that the 3-PG would be the substrate and the resulting 2-PG would be the product. It just depends on which specific reaction you are studying. In other cases, the energy change between substrate and product is so great that the reverse reaction will be too slow to observe in the laboratory, even with the help of the enzyme. So in that case, you would probably only study the reaction that you could observe happening.

**Substrate as a temporary ligand** - So how does an enzyme alter the substrate? It turns out that in many, many cases, the action of the enzyme can be broken down into two steps. The substrate first binds to the enzyme, just like a ligand. Then the chemical changes occur and the product is formed, exiting the binding site and restoring the enzyme. So we look at it this way:

\[
\begin{array}{c}
S + E \\
\text{binding} \\
SE \\
\text{chemistry} \\
E + P
\end{array}
\]

Now we have a way to think about this process. The substrate first acts like a ligand by binding to the enzyme. Then something happens to it. This turns out to be a very good, very general way to think about enzyme action. If the substrate must bind to a specific "pocket" or binding site on the enzyme as a prelude to chemical change, then we can make predictions about enzyme action from our now-clear understanding of ligand binding. First, we would predict that enzyme catalysis can be very specific for particular substrates. This is called **specificity** or **selectivity**. There are countless examples of the high specificity of enzymes for...
one particular substrate. For example, the enzyme glucokinase will phosphorylate glucose but not the very similar galactose. Another feature of enzyme action that we would predict is that enzymes are **saturable**. That is, if we keep adding more and more substrate to an enzyme, eventually the rate of product formation will reach a maximum. This is because at high enough substrate concentration, all of the binding sites are occupied, and the other substrate molecules have to wait their turn. Its sort of like a bank with a bunch of tellers. Until each teller has a customer, the rate of transactions (customers served per unit time) will increase as more people arrive. Eventually, when the number of people exceed the number of tellers, the rate of transactions reaches a maximum as each teller always has someone at their station, and we all stand in line, pondering what it feels like to be a substrate in waiting. Finally, we would predict that enzyme catalysis could be **inhibitable**. That is, one might be able to find a molecule that will bind in place of the substrate, and just sit there, because it can not undergo the chemistry that occurs when a substrate is there. Having enough of this inhibitor around would block the conversion of substrate to enzyme because the substrate can't even bind to the enzyme. Just like in ligand binding, an inhibitor that works by occupying the substrate binding site is called a **competitive inhibitor**. All of these similarities between enzymes and ligand binding led people a long time ago to hypothesize that enzymes worked by specifically binding the substrate, and then doing some sort of chemistry. The site on an enzyme that binds substrate is called the **active site**, and now due to the advances in protein structural analysis, the active site is a clear structural reality.

**The enzyme isotherm-** If enzymes often work by first binding the substrate, then you might think that the relationship between the concentration of substrate, called $S$, and the rate of product formed might look like a binding isotherm. Indeed that is the case, and it was the extensive quantitative similarities between binding isotherms and enzyme rate data that led to the original idea that substrates find a specific site on the enzyme. So let's do an experiment that is very similar to the binding experiment in the last section. We'll place a set amount of some enzyme in a solution and add different amounts of substrates. We will measure the rate that product $P$ is formed. As you might expect with this elaborate buildup, the rate of $P$ formation is described by the same sort of curve as is binding, with a characteristic constant, $K$, and a maximal rate of product formation. So here is a graph and the corresponding equation:
In this case, the \( K \) that comes out of the data is related to the strength of the binding, and is called the \( K_m \) for the two people (Michaelis and Menten) that first measured it (both had the initial M). Like in the binding equation, the \( K_m \) is an indication of how good the enzyme is at finding the substrate. In fact, the rate of product formation is 50% maximal when the substrate concentration equals the \( K_m \). So the \( K_m \) will tell us what substrate concentration is needed to get 50% of the maximum rate of \( P \) formation possible. So again, the lower the \( K \), the better the enzyme is at finding the substrate. The \( V_{max} \) is amount of enzyme (E) times a constant (\( k_{cat} \)) that reflects the rate at which that particular enzyme will turn a substrate into a product once the substrate is bound. If you like the crowded bank analogy, E tells you how many bank tellers are working, and \( k_{cat} \) indicates how fast each can take care of a customer.

**Inhibition of an enzyme**- A **competitive inhibitor** of an enzyme binds to the active site, and just sits there. The effect of a set concentration of such an inhibitor has exactly the same effects on the rate curve as such an inhibitor would have on a binding curve. Increasing substrate still increases the rate of \( P \) production in the predicted manner, but the apparent \( K_m \) is larger (meaning the curve climbs more slowly). \( K_m \) is still constant over the whole curve, just bigger. Competitive enzyme inhibitors play an extremely important role in modern medicine, and many drugs on the market today work by specifically inhibiting a "target enzyme" in a competitive manner.

**Multiple substrates**- many reactions of enzymes connect two things together, or switch groups between two molecules, so that there may actually be two or more substrates in the reaction. How do you do a study the effect of changing one substrate's concentration when there are actually two that are being processed? Simple. You keep one constant and study the effects of changing only the other one. Suppose \( S_a \) and \( S_b \) are bonded together to form \( P \) and this reaction is catalyzed by an enzyme. Two substrates, one product. The way you would study the effect of changing \( S_a \) on the rate of \( P \) production is to fix \( S_b \) at some concentration, and then vary \( S_a \) over a range. You would also, in a parallel experiment, fix \( S_a \) at some concentration and vary \( S_b \) over a range. The usual way people do this is to keep the fixed substrate at a saturating concentration, so that in the experiment the maximum rate of the reaction is attained in each experiment. So with multiple substrates you simply study them one at a time. In this way, you find out a \( K_m \) for each substrate, that reflects the interaction of that substrate with the enzyme.

**Hemoglobin again? cooperativity in enzyme action**- You might predict that enzymes could also show cooperativity and related fancy behaviors. This is right, and these features of enzyme action are so central to biology the they were called "the second secret of life" by Jacques Monod, the brilliant Nobel prize winning French scientist. I think that he said it more like "Le deuxieme secret de la vie!", but we know what he meant. Why Monod said this will become apparent shortly. As I said earlier, many enzyme rates respond to changes in substrate concentration in the simple manner that we saw above: there is a single unchanging \( K_m \) that can describe the effect of \( S \) concentration on the rate of product formation. So these cases have curves (\( S \) vs rate) that remind us of myoglobin binding: a simple rectangular hyperbola. One \( K_m \), unchanging, whole curve. However, it wasn't very long in the study of enzymes until someone discovered that the relationship between \( S \) concentration and rate of \( P \) production was not always described by a simple constant \( K_m \). Instead, such enzymes show the more complex sigmoidal behavior that would now remind us of hemoglobin. Let's look at the behavior of one of the best studied of all enzymes, called aspartate transcarbamoylase, abbreviated ATCase, since no one can pronounce it! The reaction that ATCase catalyzes is the production of carbamoyl aspartate (CA; that first word is pronounced car-bam-o-ill) from carbamoyl phosphate (CP) and the amino acid aspartate.
Notice that this is a real example of two substrates and one product. We want to study the effect of varying aspartate on the rate of CA production, so we fix the carbamoyl phosphate at a saturating concentration and vary only the aspartate. Thus, we will only consider the effects of the aspartate concentration of the rate of CA production.

Looks sigmoidal (s shaped)! We interpret this the same way we interpreted the fancy hemoglobin curve: the apparent $K_m$ is changing as the substrate changes. The protein is measuring the concentration of substrate and changing its physical properties to be better at producing product. Sort of like the bank teller who sees that the bank is crowded, gets scared, and starts working harder. Similar to the case with hemoglobin, this effect of substrate on enzyme action is called **positive cooperativity**. Remember that the key feature of hemoglobin that allowed for this kind of information processing was the quaternary structure. So in speculating about this similar behavior in an enzyme, we might guess that ATCase has quaternary structure with multiple substrate binding sites. Sure enough, ATCase is huge, composed of 12 proteins, including 6 identical copies of the enzyme protein itself, along with 6 identical copies of a regulatory protein that has no catalytic role. Like with hemoglobin, it is the quaternary structure of ATCase that allows for cooperativity. With ATCase, you can demonstrate this directly. The ATCase quaternary structure can be gently taken apart in the laboratory into individual proteins. This version of ATCase (called dissociated ATCase) can still catalyze the reaction, but now the resulting curve is our (not so) old friend with a simple hyperbolic shape and a single $K_m$ that describes the whole curve. This data is also on the graph, as indicated, in the dotted curve. So ATCase is a little machine that now only changes S...
into P, but is can adjust its actions in changing environments. The ATCase enzyme is so well studied that people have actually seen (using X-ray crystallography) how the mechanism of aspartate-dependent changes in catalytic action works. It turns out, like in hemoglobin, that the quaternary structure can assume (at least) two different shapes, and the aspartate alters the equilibrium between these forms. So as the ATCase finds itself in more and more aspartate, it continually changes from one form into the other. Remove that quaternary structure, and you lose the cooperative behavior. At present, we have not looked at enough enzymes to know if quaternary structure always underlies cooperative behavior, but at present it is certainly a good bet.

**Cooperativity, allostery effects, and the cellular internet** - There is a basic way to describe the cooperative behavior of the proteins above, whether its binding or enzyme catalysis that we are looking at. The interaction of something with a protein can affect an occurrence somewhere else on that protein. For example, the binding of an oxygen molecule to hemoglobin will alter the interaction of the other binding sites with the next O$_2$ molecules. Similarly, the binding of aspartate to ATCase will affect the catalytic activity of the enzyme towards other aspartate molecules that land on the remaining binding sites. So the main idea is that a small molecule (such as O$_2$ or aspartate) can bind to a protein and alter an occurrence at another site on the same protein. This sort of action is called an allostery effect. It comes from *allo-* different and *steric-*space or site. So it just means "different space" or "different site", and refers to the fact that the binding of something to a protein can affect a process (binding, catalysis) at a "different site" on the same protein. So far we have only talked about when the molecule that causes the change and the molecule that is affected are of the same type: O$_2$ affects the binding of other O$_2$'s, or aspartate affects the processing of other aspartates. But there is no reason that this can't work for molecules that have nothing to do with each other. All you need to have is a binding site for each, and a structure that allows the binding of one to alter the binding of the other. We'll do an abstract case first, and then some real ones. R-ase, my favorite enzyme, catalyzes the conversion of B into R. So the reaction looks like this.

The rate of R formation depends on the concentration of B, and by now, that should be no surprise. That curve is shown as a solid line. For this particular enzyme, if you add inhibitor to it (triangle), the rate of R formation is drastically decreased (right side, dotted line). What is strange is that the inhibitor looks totally different form the structure of B, which is not triangular (ha ha). The inhibitor does not bind to the B active site. So it is not a competitive inhibitor. Instead, the inhibitor acts by binding to a different site on R-ase, that causes changes in the processing of B into R. We say that the triangular inhibitor regulates the enzyme in an allostery fashion, as the little model shows. So we call this molecule an allostery inhibitor. The square is another molecule that looks nothing like B or R. It binds to yet another site on
the enzyme. When the square molecule is around, the B to R reaction works better (middle, thick line)! Again, this square molecule is an allosteric regulator, but it increases the rate at a given substrate concentration. So we call it an **allosteric activator**. The effects of these two allosteric regulators on Rase would be expected to look something like this:

This is not just a cute idea. It is a common and broadly observed occurrence in enzymes and proteins. Not only are there many examples of allosteric regulators operating on enzymes in biology, but often, a given enzyme will have multiple activators and inhibitors that each have their own binding sites. In this way, some enzymes, by virtue of their ability to "measure" the concentrations of various molecules, integrate a great deal of metabolic information in the process of adjusting their catalytic rates.

Once again, allosteric regulators of enzymes appear to work through causing changes in the quaternary protein structure. But enough of these generalities! Here is an example. The amino acid isoleucine is synthesized from the amino acid threonine by a series of enzymatic reactions. Each reaction's product is used as the next reaction's substrate. Sort of like a production line. Exactly like one, in fact. This is called a metabolic pathway. The first reaction of this particular pathway is the removal of the amino group (and the OH group) to give A. Then A is converted to B, B to C, etc. all the way to isoleucine. Five separate enzymes.

It was discovered a long time ago (late 50's) that isoleucine, the final end product of this production line, inhibits the first enzyme in the pathway. Isoleucine does this by binding to its own separate site on the enzyme. This is a real life example of an allosteric inhibitor, and one in which the use is clear. The allosteric site, by binding the final product (isoleucine) measures the amount of the product that the pathway is making, and turns down the first enzyme when there is enough product already around. You don't need to be Henry Ford to know that if you want to make fewer cars, you don't stop the last machine in the factory! So here, the use of an allosteric inhibitor as a way to control a cellular function is clear and real.

What is amazingly powerful and important about this type of regulation is its broad utility. By having the right allosteric binding site, you can control any protein's function with any molecule.
That means, in theory, that you can connect any cellular function to the level of any molecular signal in the cell. That's why I called it the cellular internet. Allosteric interactions allow the existence of elaborate networks of communication between cellular proteins. Remember, that along with the allosteric inhibitors that we just examined, allosteric activators can also exist. So the potential for different uses of this mode of regulation is huge! For example, different metabolic pathways can be linked by measuring each other's products with appropriate allosteric sites. Branched metabolic pathways can be adjusted so the products from each branch are made in equal amounts. Molecular signals outside the cell can be measured by attachment to binding site on the part of a membrane protein that is outside the cell, and transmitted to the inside of the cell by allosteric changes that pass along the regions of the proteins that go through the membrane (see cartoon "allosteric signaling").

More examples? A transporter can be turned off when enough cargo builds up inside the cell by signaling through an allosteric site. Two cells can communicate by mutual binding of allosteric receptors on each other's surfaces. The assembly and disassembly of entire cell structures can be triggered by allosteric interactions with molecules that indicate the needed change. In this way, allosteric regulation allows the possibility of every protein to read and respond to molecular information. Of course, not all proteins are allosteric, some are and some aren't. But I believe that the allosteric mode is simply one of the ways that cellular information is managed and transmitted, and that many surprises remain to be discovered!