Weird Geometry and Protein Cages

Proteins are the workhorses of life. While DNA carries the "instructions" for life it is the proteins that actually carry out the reactions. Researchers have realized this and,in a major biotechnological revolution,, are trying build artificial versions of these natural nano-machines through protein engineering with the grand vision of building new enzymes, materials and drug delivery systems. One of the most useful shapes is the protein "sphere". Typically these are just a few tens of nanometer in diameter and, hollow, just like a football. They are made up of many copies of one or more proteins and because of this they are not really spheres but, just like a football, or a gaming dice, are made up of shapes that are tiled together (in the case of a football this is typically pentagons surrounded by hexagons). Technically these types of shape are referred to as "convex polyhedra".

Perhaps the most important class of convex polyhedral proteins in nature are the outer coats of viruses, called "capsids". These are the "bodies" of the virus, which hold, in their hollow core, the RNA or DNA instructions. Viruses use the capsids to travel into cells where they then release their genetic material which can be copied or even inserted into the host`s own DNA. If we could make artificial versions of these capsids we may be able to tailor-make our own devices for gene delivery. Artificial protein spheres could also be a safe way of developing vaccines; where only a non-toxic part of a disease-causing organism attached to the many copies of the sphere protein. Artificial sphere proteins could also be designed to utilize the hollow core as nano-reaction vessels for making many different kinds of particles such as quantum dots; the possibilities are endless.

In order to make such structures we must understand in detail how the individual proteins fit together to make the convex polyhedron shape. As the football example shows, there are rules of geometry that limit the kinds of shape you can make. For polyhedra where each face is made up of single identical polygon for example, there are in fact only 5 possible shapes (these are called Platonic solids and are familiar to us all, such as the cube). Slightly more advanced rules allow the 13 "Archimedean solids" which reach as far as the 20-sided icosahedron (familiar to any role-playing game fan) while more complex structures still are the 92 "Johnson Solids". These 110 shapes constitute all of the possible convex polyhedral.

These rules come from geometrical considerations where shapes must fit together exactly. We asked "can these rules be broken?" If different kinds of convex polyhedral could be made that require a distortion so small that it lies with in the normal flexibility of a protein or variation in a chemical bond, might they not be possible? The answer seems to be yes: We used an 11-sided protein called TRAP as a building block. An 11-sided shape should under no circumstances be able to form a convex polyhedron Although the details of the structure need to be confirmed, we found that when TRAPs were connected to each other in an arrangement where each TRAP sat at a position equivalent to the corners of a snub cube (a shape made by expanding a cube), they fit together to form a convex polyhedron (called "TRAP-cage") with errors so small as to be insignificant. The TRAP-cage is about 20 nanometres in diameter (a nanometer is a billionth of a metre, about one hundred thousand times less than the thickness of a human hair). This completely new way of fitting proteins together could lead to the development of other new kinds of biological nanostructures not seen in nature. *We are now trying to understand the structure of this and related proteins in more detail (using a type of microscope called an electron microscope) and we want apply geometry and mathematics to understand the rules underlying these structures so that their formation can be predicted.*

Another very interesting part of the work was the method whereby the TRAP proteins were connected together. Naturally occurring protein cages are typically held together by quite weak bonds known as hydrogen bonds and hydrophobic ("water hating") interactions. TRAP-cage however seems to be held together by the strongest type of bond (covalent bonds) which gives it extreme stability. Interestingly these bonds can only be formed if tiny particles of gold (called gold clusters) are present. Each cluster contains only 55 gold atoms and is just 1.4 nanometres across. Gold is generally thought to be inert but recent discoveries have shown that these small gold clusters can be extremely reactive. The reasons for this are still unclear but may have to do with the way that the gold atoms are held together. Using gold clusters to link proteins together is a new application for the material and may be a useful protein "glue" allowing scientists to build new, previously inaccessible protein shapes.

So how might these findings be used? The results showing a new kind of geometry and a new form of gold-protein chemistry will allow transformative technologies. For the TRAP-cage specifically the answer may come from another intriguing finding: Despite its high general stability, the TRAP-cage easily breaks apart in conditions equivalent to those inside cells. This raises the possibility of filling the centre of the cage with a drug molecule and using it to safely deliver the cargo to the inside of cells where it will be automatically released: Something to think about the next time you role a dice!