Alternative arrangements: using artificial biological nanoparticles to probe the importance of three dimensional organisation in biological molecular interactions

Life is action. What is true for us at the large scale is also true of the interactions at the microscopic scale. For example, when our cells interact with other cells and viruses they typically do so via proteins on the cell surface that stick to molecules on the partner. These cellular proteins are embedded in the fatty, lipid layer, or membrane that surrounds the cell. The receiving molecules themselves are usually proteins and these interactions are elegant, precise and often referred to as being like a lock fitting into a key.

There are many types proteins and many types of interactions. Cells can, for example, bind other similar cells to form tight layers such as those forming our blood vessels. Cells can also secrete binding proteins into their surroundings. Cells of our immune system famously do this – releasing antibodies that can latch onto pathogenic viruses and bacteria to neutralise them. Pathogens themselves of course exploit similar systems to their advantage, binding to cell surface receptors to trigger their own uptake.

Learning more about these protein-protein interactions would clearly be very useful for a deeper understanding of the various important life processes that they mediate. With this this understanding we maybe able to either block the interactions (e.g. stopping pathogens from entering cells).

Unfortunately this is more difficult that night first be imagined not least because the “lock and key” analogy is in many cases overly simplistic – it turns our tat the interaction between cell surface proteins and their partner proteins is often not just a simple1:1 interaction but can depend on their number, density and three dimensional arrangement. For example, it is known that multiple copies ordered with high density have to be present on the surface of vaccine particles for best efficacy.

Finding out what kind of spacing and arrangement of proteins in 3D space is optimal for a given surface protein is difficult: These molecules are much too small to be physically moved around and arranged by us and living systems, with their huge complexity, are virtually impossible to manipulate to achieve this.

In our project we will address the basic questions of how the three dimensional arrangement of proteins affect their activity. We will be able to precisely design and control the exact arrangement of the proteins by using synthetic biological nanoparticles. These are precisely structured particles somewhat resembling viruses (but completely safe) that we can design and make using DNA or protein. Because these are artificial particles we can precisely design exact points on their surfaces for attaching or the proteins we are investigating. In this way we can control the number, arrangement and spacing of such proteins and see how this affect their ability to do their job.

We hope that our project will answer the question of how the protein arrangement affects function. We may be able to exploit this information to give our artificial particles useful abilities such as neutralisation of disease-causing viruses and bacteria or even to deliver important therapeutic molecules to cells.