DNA has a secret – it is not only the blueprint for life but is also a rather **good building material** and the **tiny machines** that it can construct may well revolutionise human health. When the double helical structure of DNA was first revealed, it was a revelation: DNA was shown to consist of long strands wrapped around each other, with bonding between each strand following a very simple rule of bonding between chemical groups on the strand called bases: A binds to T and C binds to G. We can therefore carry out simple designs, for example making a DNA consisting entirely of "A"s, we can make double helix by synthesizing another strand composed entirely of "T"s, called complementary strand. For over 30 years scientists have been tinkering with DNA in order to make it assemble into structures other than the double helix.

The idea of using DNA strands as building block to build complex structures received a major boost in 2006 when Paul Rothemund invented **"DNA origami"**. This is a system that allows researchers to easily design and build arbitrary DNA structures. It uses one long strand of DNA which is forced into the desired shape by a complementary strands that is broken up into many smaller lengths, called "staples". The technique has become popular and many two dimensional and complex 3D designs were constructed. In parallel, a second technology **"DNA aptamers"** was developed whereby a trial and error testing of random short DNA sequences is used to find those sequences that show specific binding to a molecule (e.g. a disease-associated molecule) of interest. This molecule could be termed a "ligand".

The next big breakthrough came in 2012 When Douglas group combined two technologies to make a **programmable DNA nanorobot**. They **designed a container from DNA origami** that was locked by a DNA aptamer sequence. If the ligand is present, the DNA aptamer will bind to its ligand and in doing so unbind from the structure. Thus the lock will be broken and the DNA origami container will open. This is an example of programmability because the opening of the container is conditional on presence the ligand.

Research in DNA origami has been rapid but this is a very new field and many questions and possibilities remain unexplored. We are interested in seeing what more can be done to expand this technique. One innovation is to **produce a DNA origami system that consists of two containers, each filled with a different "cargo".** This may prove useful in **novel drug delivery systems**. We are trying to enclose an inactive form of a **thrombolytic drug** and the enzyme that activates it into the two boxes. Thrombi are of course an important cause of heart disease and acute heart attack, still a very major killer. This DNA origami container would be modified with one aptamer that binds to a specific protein that is associated with thrombi (called E-selectin) and so ensures that the origami device stays in the area that the thrombus is forming. Lock aptamers on the two origami containers will bind specifically to fibrin ligands. Fibrin is the main constituent of a blood clot. Therefore, when fibrin is present it is envisaged that the containers will open, inactive thrombolytic agent and the enzyme that activates it will be released. The enzyme will do its job and activate the thrombolytic which will then digest the clot. The fact that drug is released only where needed should allow larger more controlled doses to be used and there fore should reduce side effects.

We hope that our research will provide a good foundation for further development of DNA origami towards eventual endpoints of **smart nanorobots for medical use**.