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DNA Origami: A Nanodevice with Mega Potential

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DNA Origami

A Nanodevice with Mega Potential

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Can DNA be used as a machine? With the development of DNA origami, it is used as a nanodevice in numerous applications. Over the summer, I researched protein interactions of DNA origami at Ohio State University, and I was amazed to learn about its many functions. These functions can range from drug delivery to nanorobotics, but the possibilities of this nanodevice are endless because its novelty. This new DNA device can particularly be used cancer treatment and in bioanalysis.

In 2006, Paul Rothumed proposed the first design for DNA Origami. To make the origami, you need a long circular strand of DNA (a "scaffold"), some shorter strands of DNA, a protective solution that's mainly water -- a buffer -- and time. Eventually, the shorter DNA pieces will attach to the scaffold and produce a sculptural structure, like origami, the Japanese art of paper folding. This was originally used as artwork: scientists made stars, smiley faces and even a map of China with their constructed DNA. However, the applications hardly stop here: research was then conducted as to its applications in medicine.

One exciting application of the nanodevice is in drug delivery. Doxorubicin (Dox) is a common chemotherapy drug that kills tumor cells by literally inserting itself into the DNA of a tumor, and obstructing its growth. However, there are numerous adverse effects, one of them being that tumors can develop resistance to Dox. DNA origami though, can circumvent resistance to Dox by targeting the primary mechanism of resistance. One of the most common ways for tumor cells to become resistant to drugs is to inhibit the uptake of drugs, preventing it from being absorbed through the cell membrane. However, Jiang and colleagues demonstrated that DNA origami constructs loaded with Dox developed the biocompatibility of the nanodevice. Unlike other Dox delivery services, the biological nature of the nanodevice allows it to enter the cell, much like a mole infiltrating an enemy spy group. They found that the uptake of Dox in resistant human breast cancer cells was size and shape-dependent. The origami indicated massive potential as a therapeutic because the cancer cells had an increase in uptake of Dox. Because of this circumvention, DNA origami shows great promise are a potential treatment if other studies are succesful.

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DNA origami is also applicable outside of the field of medicine. One of the most significant applications for DNA origami is in bioanalysis, the quantitative measurement of biomolecules in biological systems. One reason for the surge of origami research is its ability to control the distance between molecules on binding sites with a super-fine resolution. This works because binding sites can be imagined as wells in a 3D platform structure. In fact, in this application, DNA origami is literally a platform to build molecules. Under an advanced microscope, we can see finer detail when studying DNA when it's in an origami manifold made specifically for this task.

DNA origami can also be easily customized for single-molecule kinetics experiments. These are experiments where we observe how molecules bind to DNA on the nanodevice platform on a literal single-molecule level. These experiments operate within an interdisciplinary rubric -- at this molecular level, biology, chemistry, and physics are difficult to separate. However, this cannot be done with origami alone; we need to use fluorophore techniques. Johnson-Buck and colleagues utilized these techniques on a single-molecule level to measure how a single-stranded oligo (synthesized DNA) attached to DNA origami affected the kinetics of attaching to its complement target strands. This type of kinetics work with DNA has been utilized by other scientists to study distance interactions with more physiologically relevant molecules.

Over the summer, I researched interactions between oligos and transcription factor (TF) protein found in yeast (Cbf1) using DNA origami. I looked at the distance between binding sites on DNA origami and affinity, or attraction, of Cbf1. Our research was informed by Ben Donovan, who researched Cbf1 accessibility of nucleosomes. Donovan's goal was to understand how Cbf1 binds to DNA when nucleosomes restrict DNA accessibility. Nucleosomes are the skeletal structure of DNA in eukaryotes, including plants and animals, that prevent Cbf1 from having easy access to DNA. This happens because DNA is wrapped around proteins in nucleosomes, which block binding sites from TFs. The research demonstrated that the proteins bind to sites within nucleosomes with a high affinity but dissociate from nucleosomes ~25 fold slower. This gives us an idea as to how TFs bind in cells, but we believe DNA origami can give us a similarly accurate reasoning.

When TFs like Cbf1 bind to gene, they increase the likelihood of gene expression. Their mechanisms for binding are not as well understood due to the density of the cytoplasm, or cell fluid. DNA origami analysis addresses the problem of the density of the cytoplasm by allowing for DNA binding in vitro (outside of a cell). This allows for control of both distance between binding sites and the amount of binding sites attached to the origami structure. The implications of this field of research are that we can now better quantify affinities using DNA origami. From these, we can also solve other problems such as thermodynamic quantities.

DNA origami has nearly limitless potential and could be groundbreaking for a multitude of scientific fields. We can modify DNA with other pieces of DNA and use it for practical applications. The most exciting ones are in drug delivery and bioanalysis. The biological nature of this nanodevice allows it to effectively kill drug resistant cancer cells. Specifically, the nanodevice is biocompatible with the cell and bypasses the shape and size-dependent barriers of the cell where other delivery methods fail. DNA has contributed most significantly to bioanalysis. With the aid of fluorescent techniques, we can observe how biomolecules interact on an Angstrom scale and be able to control how the molecules bond to the platform and to each other. Techniques in electron microscopy can verify this. Fluorescence has also proved effective in providing researchers a tool to determine the kinetics of target strand binding to an oligo assay on an origami platform. DNA origami has already changed multiple disciplines and its development and later use will be thrilling to watch. • • •