**DNA Origami**

How DNA structures can be used to transport Interleukin-2

Outline

Our research is evaluating the usage of modelling DNA to help deliver drugs around the body. Specifically, we will be assessing the usefulness of this for interleukin-2 (IL-2), a type of cytokine (protein). IL-2 is released by T-cells which can detect cancerous cells antigens and signals to the immune system that there is a threat. Additionally, we shall model our own structure (a star shape) out of DNA using a software called scADNAno to design such a shape. Then, we shall synthesise a shape of DNA at a later date.

Hypothesis

Can “folding DNA” help the distribution of single IL-2 molecules around the body? To test this, we shall consolidate research completed by other sources and evaluate this question. Due to the complexity, we will not directly test this hypothesis as we can not design 3D structures. However, we will be producing a 2D shape to learn how to use designer DNA.

DNA origami

DNA origami is a project that focuses on folding long chains of DNA into useful and interesting shapes. Biologically, it contains the instructions for cells to grow and reproduce. Because DNA comes in pairs of nucleotides that are attracted to each other, we can program them to bond with other strands. Due to the “codable” nature of DNA, material scientists select it for a number of projects where small but precise molecules are required: novel data storage in systems, treating diseases, logic components in computer chips and, the focus of our research, in the transport of drugs around the body [1]. We will explore how this is done (designing a 2D structure) and, more importantly, its real life applications (in drug transportation). It is important to note that in this context DNA is not a double helix but single stranded DNA (ssDNA).

**DNA and how it folds**

Described in other articles, DNA has “base pairs” of chemicals called nucleotides. These combine with the backbone to form the strand of DNA. Adenine (A) bonds with thymine (T) to make a pair of these base pairs and cytosine (C) bonds with guanine (G) to make the other (3). A-T pairs form two hydrogen bonds, whereas C-G pairs form three hydrogen bonds. This means that A-T-rich strands will be slightly weaker but more flexible than C-G-rich strands of DNA. However hydrogen bonds are weak so don’t make much difference to the overall stability of the structure. The attraction of these bonds is useful when we model DNA, as we can put corresponding nucleotides on matching small and long strands of ssDNA to fold and lock the shape into more rigid positions. Therefore, these bonds can give DNA different shapes. There are only certain places the structure can bend (matching AT and CG pairs) so when it is mixed, it will self assemble under the correct conditions [4].

**DNA cages**

DNA is used in designing small structures which is particularly useful for transportation of chemicals. This is because they are very small. For example, interleukin-2 molecule is 2.0 nanometers (converted from kDa to nanometers) [5] whereas a human double helix DNA is 2.0 - 2.5 nanometers [6] in diameter. Additionally, there are a “code” due to the AT CG bonds - a unique feature for something as microscopic. Scientists select DNA for “cages” to carry drugs around the body. This can be to regulate extraneous variables or to stop the molecule interacting with the wrong part of the body. Additionally, DNA cages can be designed to release IL-2 towards targeted places in the body. If we too were to design a cage to do this, it would be a cube (this shape would be very rough as it is so small) with the medicine in the centre.

**Interleukin-2 (IL-2)**

Interleukin-2 was discovered in 1976 by Shugan et al [7]. It works by stimulating the immune system, encouraging the growth and division of white blood cells. It works by activating other immune cells which in turn destroy the cancerous cells by interfering with the growth and multiplication of cells. The chemical is used to treat advanced kidney cancer where it has proliferated. IL-2 is a typical cytokine with a half life of just 20 minutes [8].

**Analysis & conclusions**

After sending the code of our sequences off to IRIS, we have had our model analysed. This has shown us how inherently stable the shape is. The parts in blue (in figures 4 & 5) are fully stable but the parts in red are less stable. Weaker parts of the structure will change due to the twisted nature of DNA. Those are quite clearly along the edges of the design. This would be because the restoring is less secure as we cannot connect the scaffold to other parts of the structures. Partically, we can see that the edges of the designs will twist slightly.

**References**

1. Callington Community College
2. Pippa Dyter
3. Poppy Harrison-Shearer
4. Alice Law
5. Connor Smith

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