

Biomimicry of Herpes Simplex Virus-1 through DNA nanostructure formation for drug delivery

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Objective/Goal

The objective of this project is to create a DNA nanostructure modeled after Herpes Simplex Virus-1 to be used as a drug delivery tool.

Introduction

Without effective drug delivery techniques, drugs be difficult to dose, inefficient, unpleasant, and dangerous.¹ One common issue is biocompatibility, and using DNA as a delivery tool ensures the structure is biocompatible while also allowing us the freedom to create complex and dynamic structures.¹⁻³ In this project we sought to use flat-faced triangles to form an enclosed icosahedron. To create this structure, we used a technique called DNA origami, in which one long strand of DNA, called a scaffold strand, is shaped with shorter strands of DNA, called staple strands.⁴ This allows structures to self-assemble using only on the sequence of the DNA used.⁴ DNA origami has been used in the past to create complex polyhedral structures as wire frames, as well as creating flat-faced triangles that are able to connect to one-another, but no reliable technique for creating complex enclosed structures exists.^{5,6} Using enclosed structures allows drugs to be attached to the surface or be contained within the structure, allowing for a greater diversity of drugs that can be transported in the body.^{7,8}

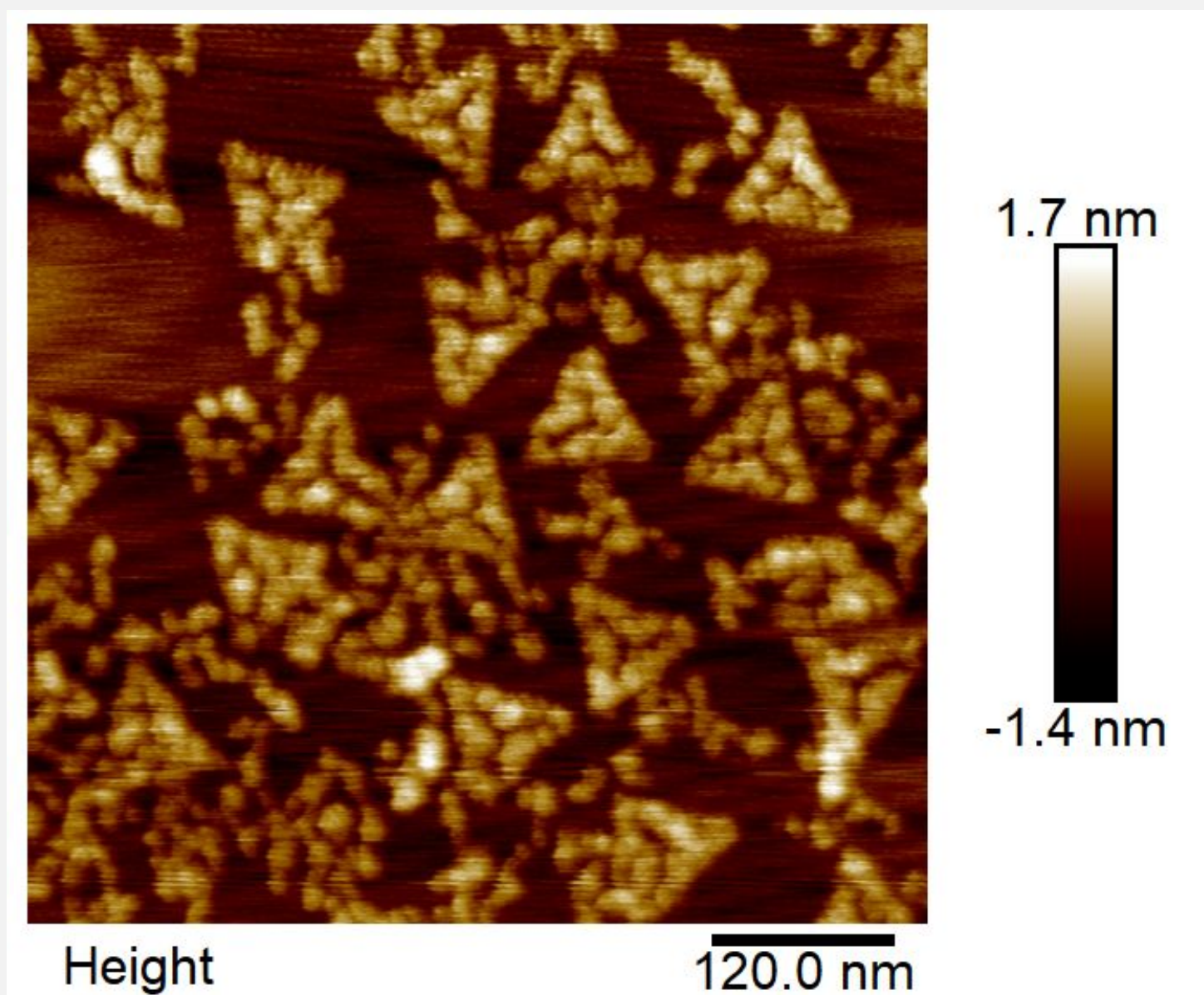


Fig. 1 Atomic Force Image of anticipated result.⁹

Structure

Our structure is modeled after Herpes Simplex Virus-1, which has evolved effective techniques to enter cells and deliver their DNA.^{10,11} The virus can also target cells that are difficult to reach, including neurons and immune cells.^{12,13} Thus, mimicking the structure of HSV-1 could allow for more effective targeting of these cells, as well as more effective drug delivery.

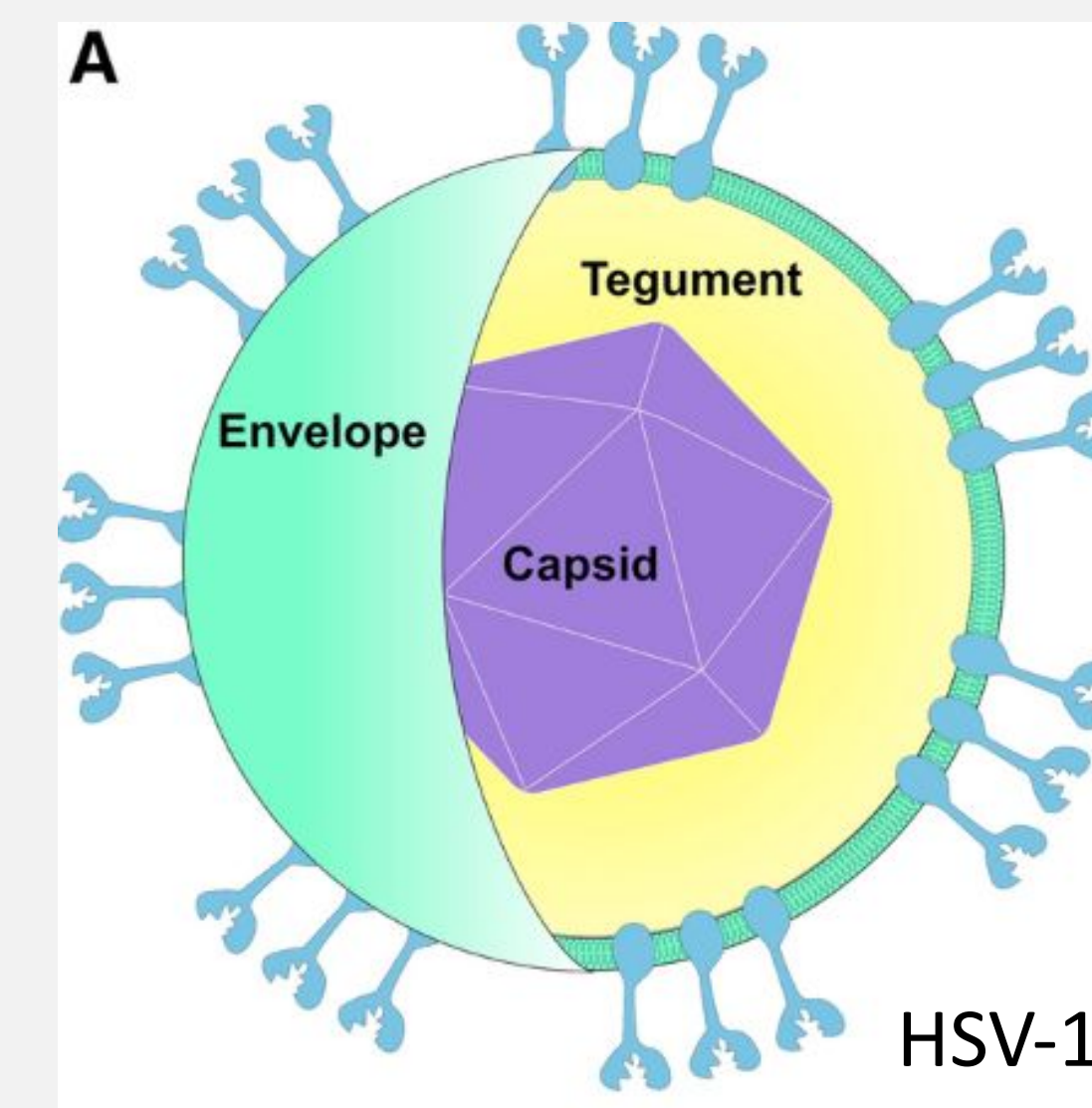


Fig. 2 HSV-1 is about 155-240nm across spherical capsid measuring 125nm across.¹⁴ Outside this capsid is a layer of proteins held between an outer envelope that allows the cell to uptake the virus.¹⁴

Results

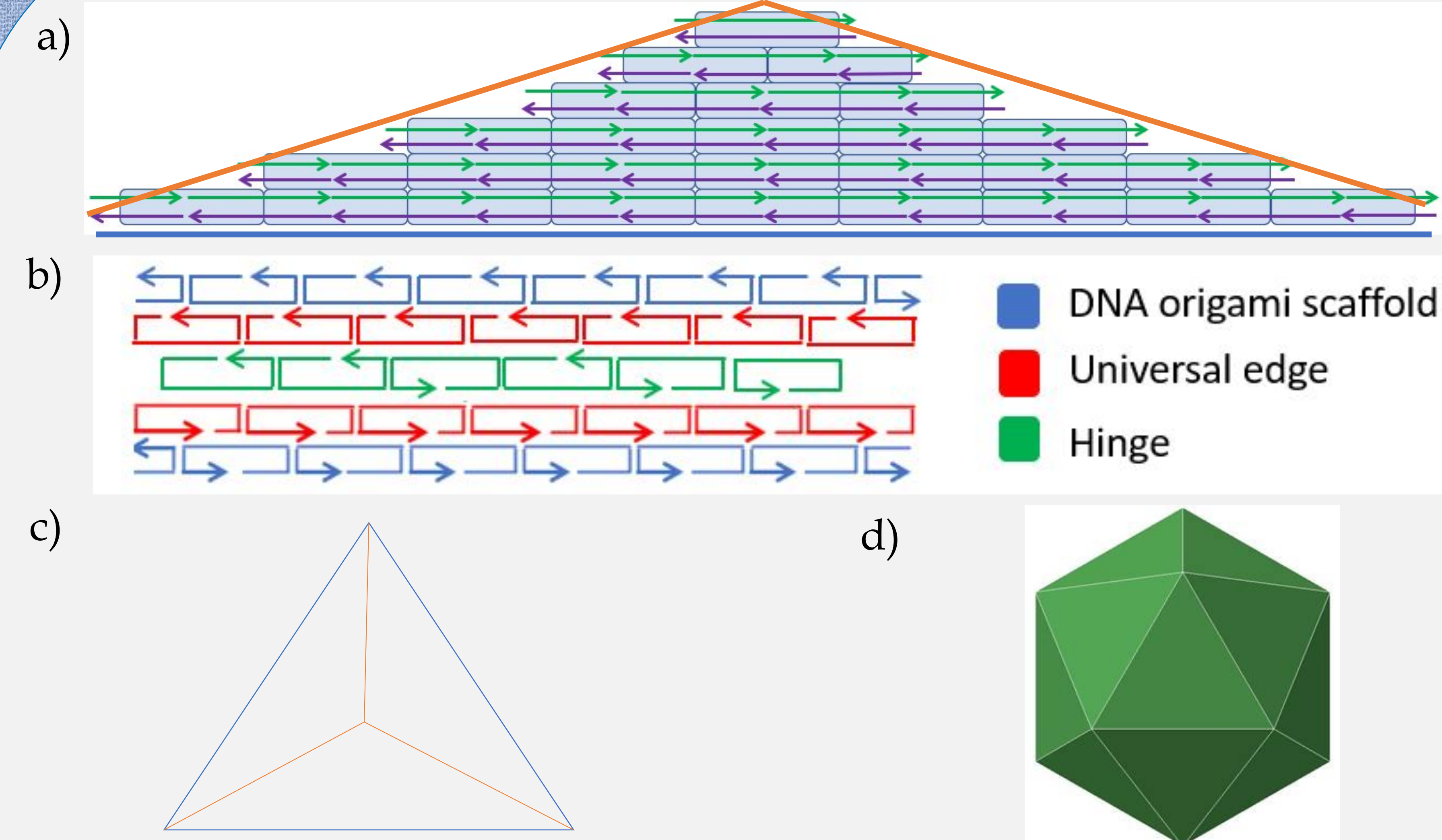


Fig. 3 a) Simplified structure of the triangle. It contains one scaffold strand (light blue blocks – the strand itself runs along their perimeter) and numerous staple strands (purple and green) that help the scaffold strand maintain its shape and connect the triangles together as shown in Fig. 3c. The bottom edge is 232 nucleotides long (~79 nm). b) Junction between 2 triangles. The universal edge (red) allows any edge from any triangle to connect to any other edge from any other triangle. The hinge (green) strengthens the bond between triangles, maintains the bond angle of a regular icosahedron (138.19°), and is also universal. c) The equilateral triangle that will be tessellated to form an icosahedron. Each colored side corresponds to the color of lines drawn into Fig. 3a. d) What the final structure will look like (an icosahedron). Side lengths of ~79 nm will create an icosahedron ~120 nm across.

Discussion

- This technique allows us to make a structure that is analogous to Herpes Simplex Virus-1 (HSV-1) with relative ease
- The structure self-assembles, so it is not labor intensive to create
- Filled surfaces allow more and more diverse drugs to be delivered
- The universal edge maximizes yield because any one triangle is able to connect to any other triangle
- The hinge maximizes yield by strengthening bonds between triangles while also controlling the bond angle, encouraging the 3-dimensional structure to form
- Using edge lengths of ~80 nm allows us to create a structure with comparable size to the capsid of HSV-1 (~120 nm)

Conclusions

- This design allows us to accurately mimic the structure of Herpes Simplex Virus-1 (HSV-1) with biocompatible materials (DNA)
- This technique opens the door to a new approach for creating DNA nanostructures

Future work

- Build the structure and make any necessary design adjustments
- Test its drug delivery efficacy using various drugs
- Test its cell targeting ability by adding surface proteins from HSV-1.

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