BE/CS 196a Lab 12: Design and analysis of a DNA origami tile array that reconfigures from a sword to a rattlesnake

Objective

(i) design a pattern on a square DNA origami tile, (ii) design a set of DNA origami tiles that self assemble into the shape of a sword, and (iii) design and analyze two invader structures that reconfigure the sword to a rattlesnake.

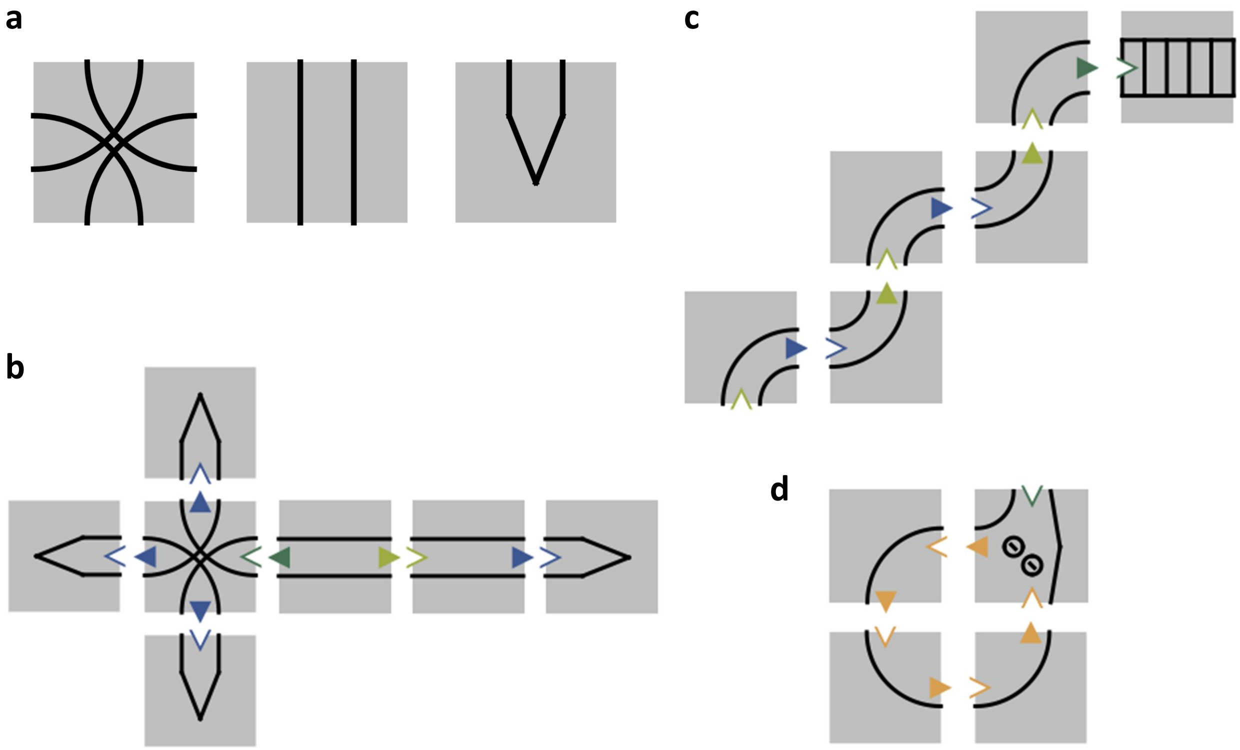

Figure 1: **A reconfigurable tile array.** **(a)** Three tile patterns. **(b)** A 7-tile structure resembling a sword. When implemented with DNA origami tiles, giving edges (with extended staples) and receiving edges (with truncated staples) are indicated by solid triangles facing outward and hollow triangles facing inward, respectively. **(c)** An invader structure that reconfigures the blade of the sword to a snake tail. **(d)** An invader structure that reconfigures the handle of the sword to a snake head. Credit: Kellen Rodriguez.

1 Design a pattern on a DNA origami tile (30 min)

Choose one of the three tile patterns shown in Fig. 1a and use FracTile Compiler to design a pattern on a square DNA origami tile that approximates the pattern of your choice.

- Choose a .png file of any of the three tiles provided with this lab and upload it to the FracTile Compiler (select canvas size 1x1 and then upload image). An initial layout will be automatically generated. A total of 136 pixels are available on a single square DNA origami tile. Each pixel corresponds to the 3' end of an interior staple strand. Because bridge and edge staples play more essential roles in the self-assembly process, they are typically left unmodified and not used for creating a pattern.
- Modify the layout by manually selecting or removing dots. It is desirable to have lines that are at least two-pixel thick so that they can be clearly visualized in AFM imaging. Save a layout file (.txt) for part 2 of this lab.
- Compile the tile layout to DNA sequences and protocols (by clicking the Sequences & Protocols icon), and save the manual protocol as a .txt file (by clicking the Save Manual Protocol button).
- Use the first Mathematica notebook (Lab12_plot_plate) provided with this lab to import your protocol file and generate plate diagrams for all staples involved in the origami tile with your designed pattern. As in Lab 11, this step requires a spreadsheet of all stock plates ("origami_square.xlsx") to be in the same folder, which contains the well position, name, and DNA sequence of each staple strand.
- Double check the correctness of your interior and pattern staples: every staple location should appear exactly once, either as an interior or as a pattern staple. This means every well in the plate diagrams should be marked exactly once either in plate 1 or in plate 5, and either in plate 2 or in plate 6.

2 Design a DNA origami tile array (30 min)

Revise the tile array design shown in Fig. 1b so that each tile has either all-giving or all-receiving edges, and use DTD Designer to create the four unique DNA origami tiles involved in the sword array.

- Follow the instructions given in the DTD Designer to design the DNA origami tiles with desired edges, considering the following criteria:
  - The toehold and branch migration domains of a tile displacement reaction will have 4 and 7 edge staples, respectively (Fig. 2).
  - All pairs of complementary edges that do not participate in a tile displacement reaction will have 11 edge staples.

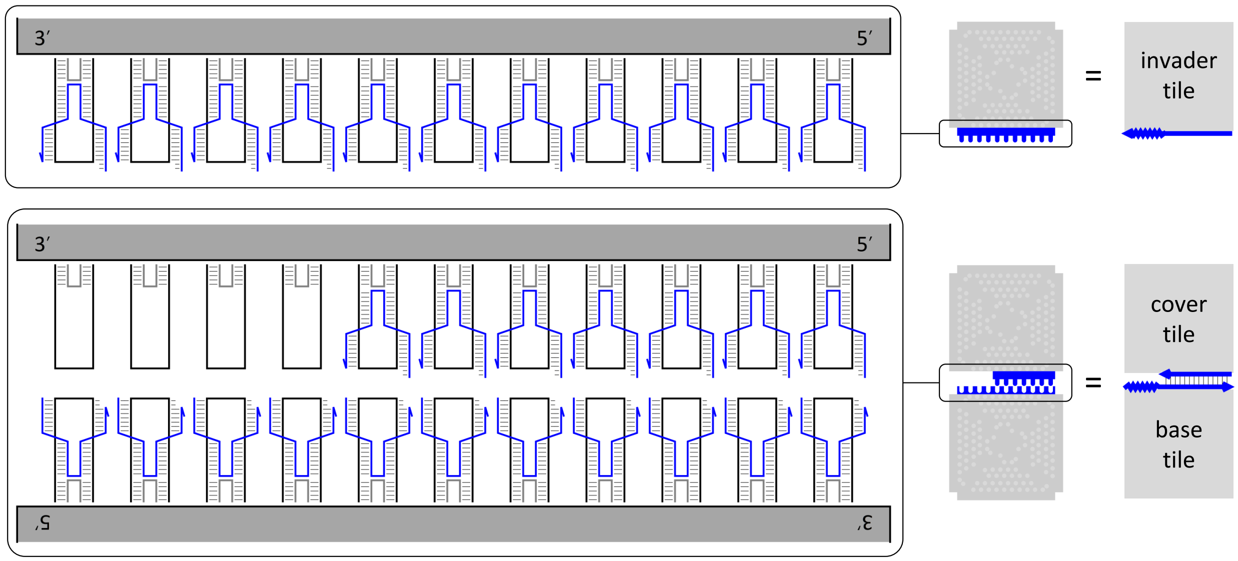

Figure 2: Edge staples composing the toehold and branch migration domains of a tile displacement reaction.

- Any staple in a giving or receiving edge will have a 2-nt extension or truncation, respectively.
- All inert edges will have 5 edge staples with double hairpins interleaved with 6 scaffold loops.

- Use your pattern layout file from part 1 to apply it to one or more tiles that carrying that pattern.
- Save the full layout as a .txt file, and make a screenshot of your design.

3 Design and analysis of invaders

3.1 A snake tail invader (30 min)

- Four unique types of tiles are shown to create the invader structure in Fig. 1c. Can fewer types of tiles self-assemble into the same shape? If so, revise the design to use a minimum number of unique tiles.
- How many unique structures will be created when the revised set of tiles are mixed together?
- Use the second Mathematica notebook (Lab12_polymer_simulation) provided with this lab to simulate the growth of a snake tail modeled as a polymer. An example polymer system is given in the notebook, which is not the system of a snake tail. Use the example as a starting point to understand how to enumerate and simulate a polymer

chemical reaction network (CRN), and then model your revised tile set above as a polymer CRN.

  - Explore how the ratio of tile types affect the population of polymers. What changes in the tile ratio will result in longer polymers? What changes in the tile ratio will result in a higher fraction of polymers with an invader tile on one end that can displace the blade of the sword that you have designed in part 2?
  - Is it possible to create a population of polymers whose concentration increases with length? Provide an intuitive explanation for your observation.
  - Based on the above observations, how will you choose the concentration of each tile type to grow a snake tail with desired length and yield?
    Note: DNA origami tiles will be annealed at 50 nM, which means the total concentration of all types of tiles that are mixed together to create any array structure cannot exceed 50 nM.

- Implement your design in DTD Designer, save the full layout as a .txt file, and make a screenshot of your design.

3.2 A snake head invader (homework)

- Two unique types of tiles are shown to create the invader structure in Fig. 1d. How many unique 2 by 2 arrays will be created when the two types of tiles are mixed together, taking rotational symmetry into consideration?

- Revise the tile design so that all 2 by 2 arrays will have the same structure as shown in Fig. 1d, with one out of the four tiles being an invader tile that can displace the handle of the sword that you have designed in part 2.

- Implement your design in DTD Designer, save the full layout as a .txt file, and make a screenshot of your design.