

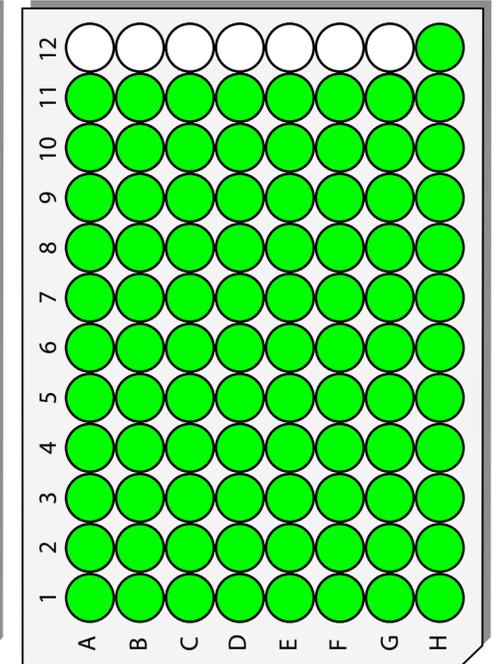
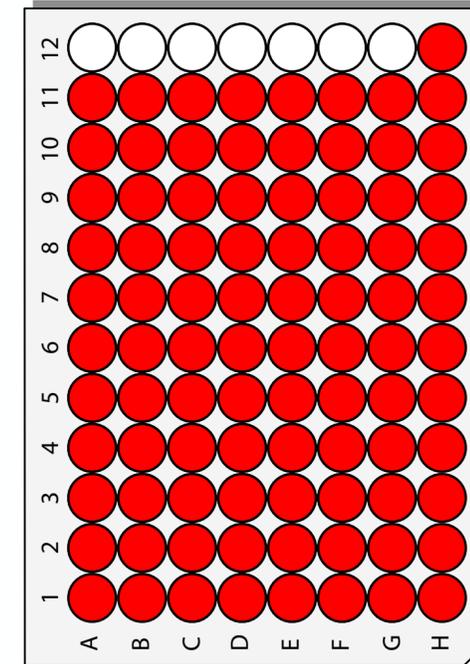
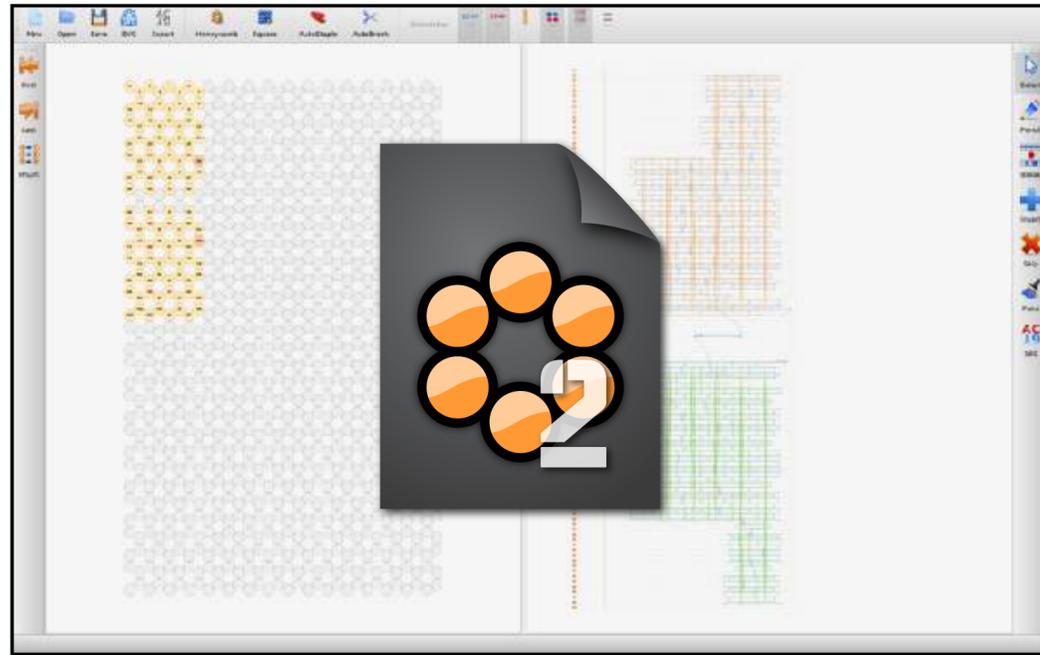
DNA origami design with CaDNAAno ToolKit (CTK)

Tural Aksel

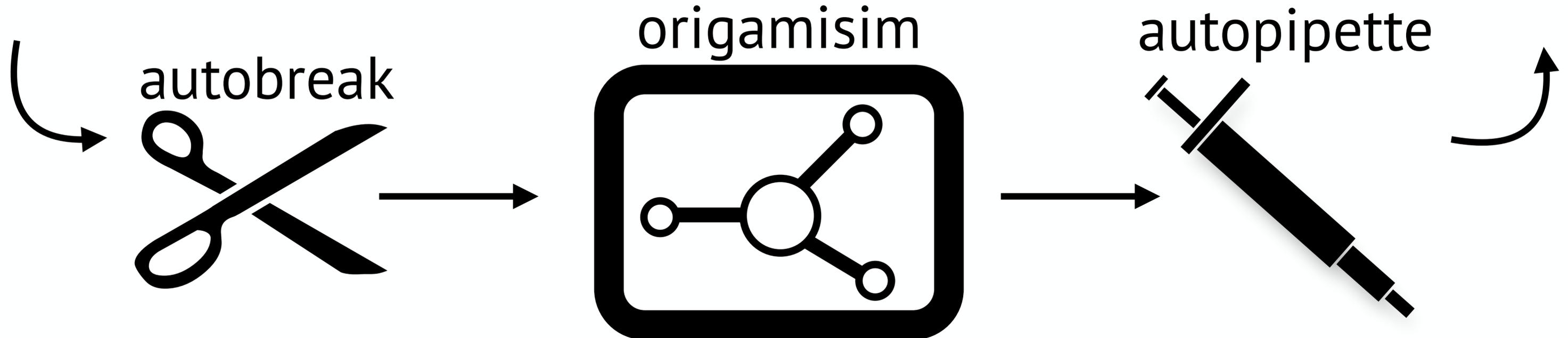
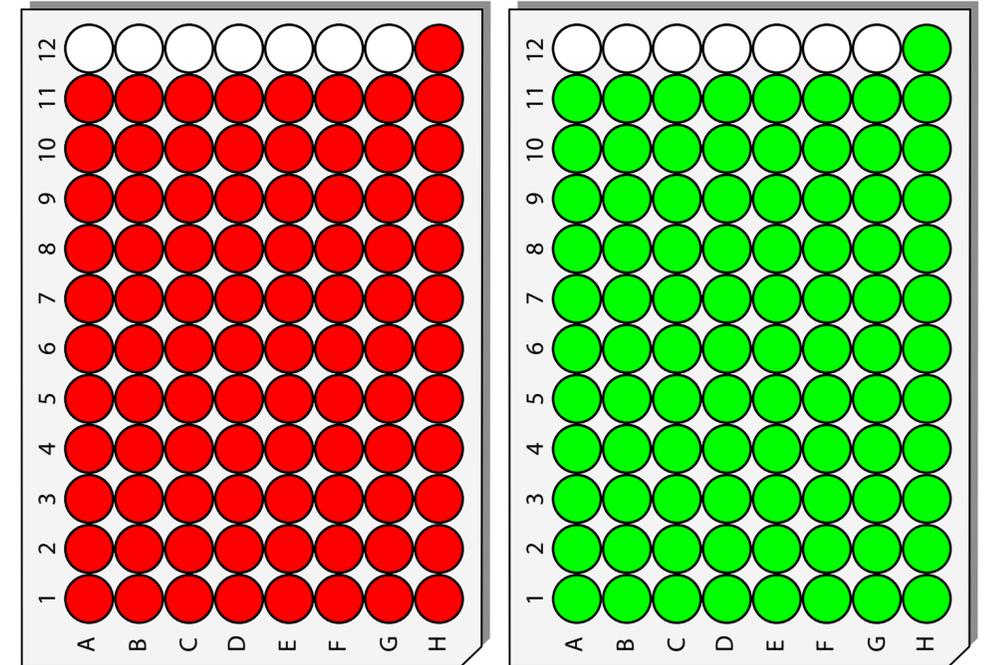
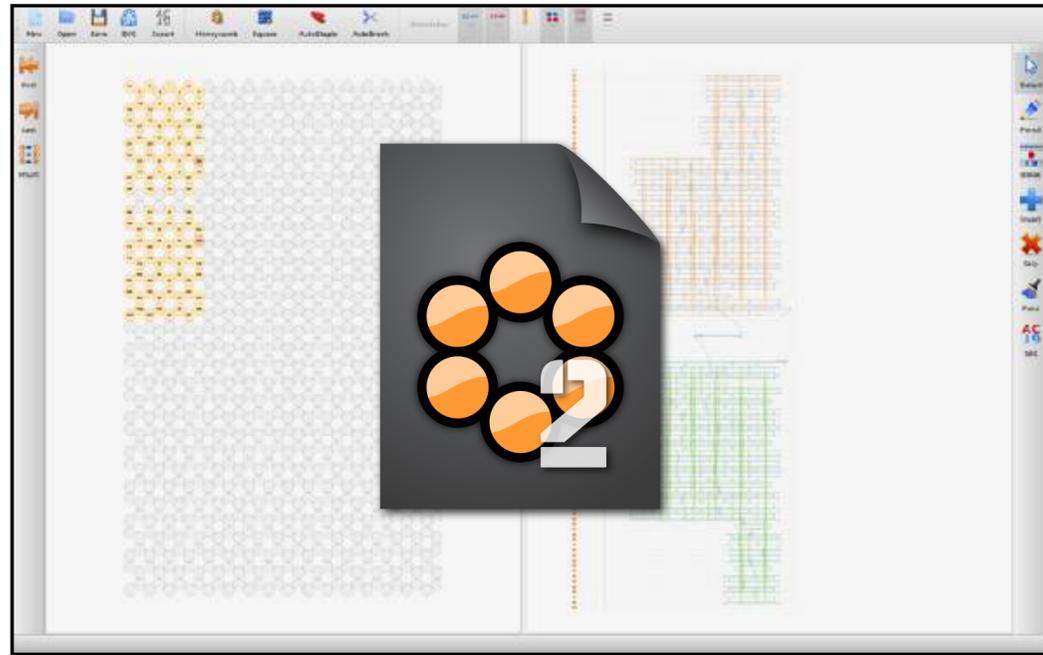
Douglas Lab

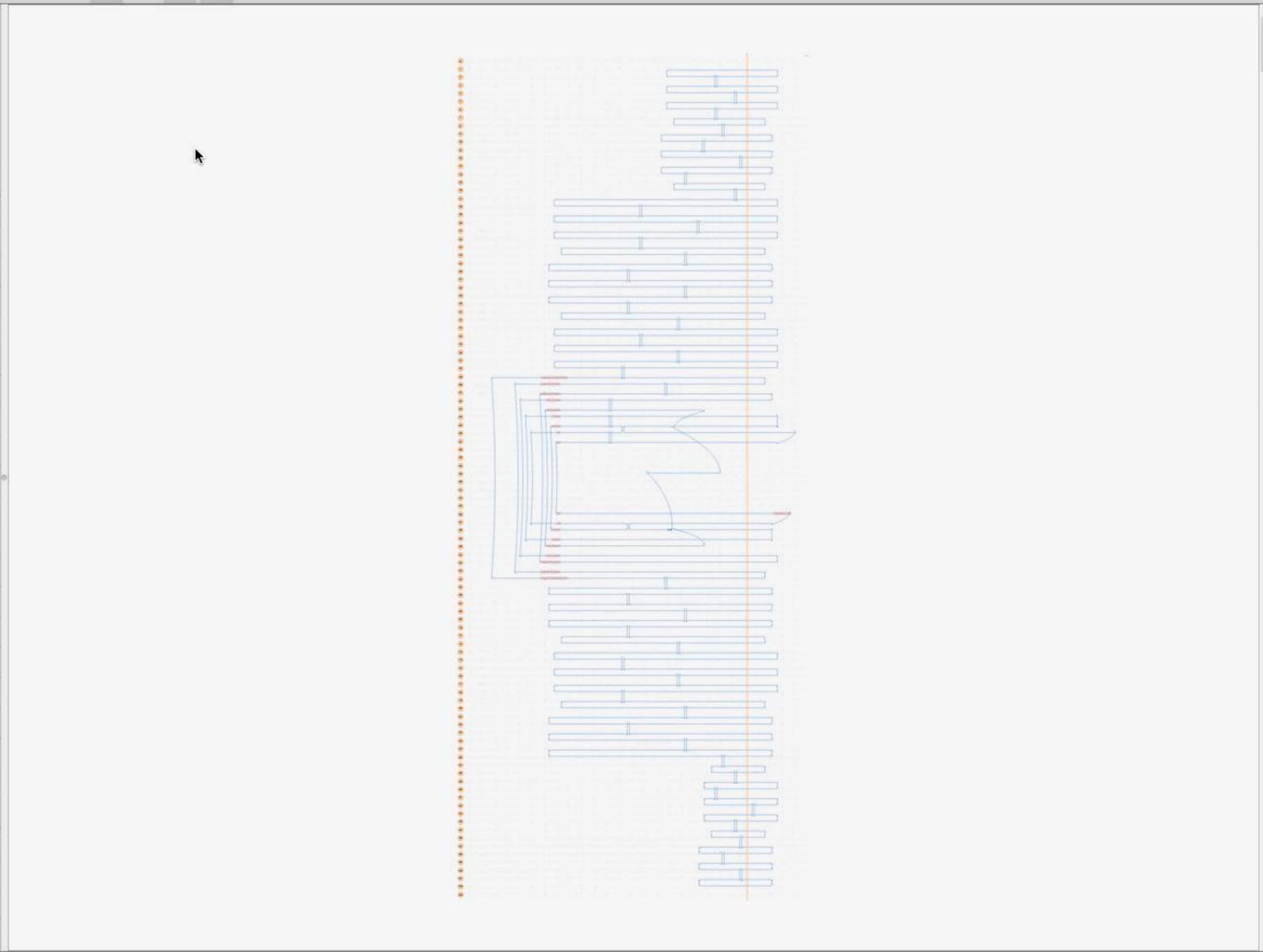
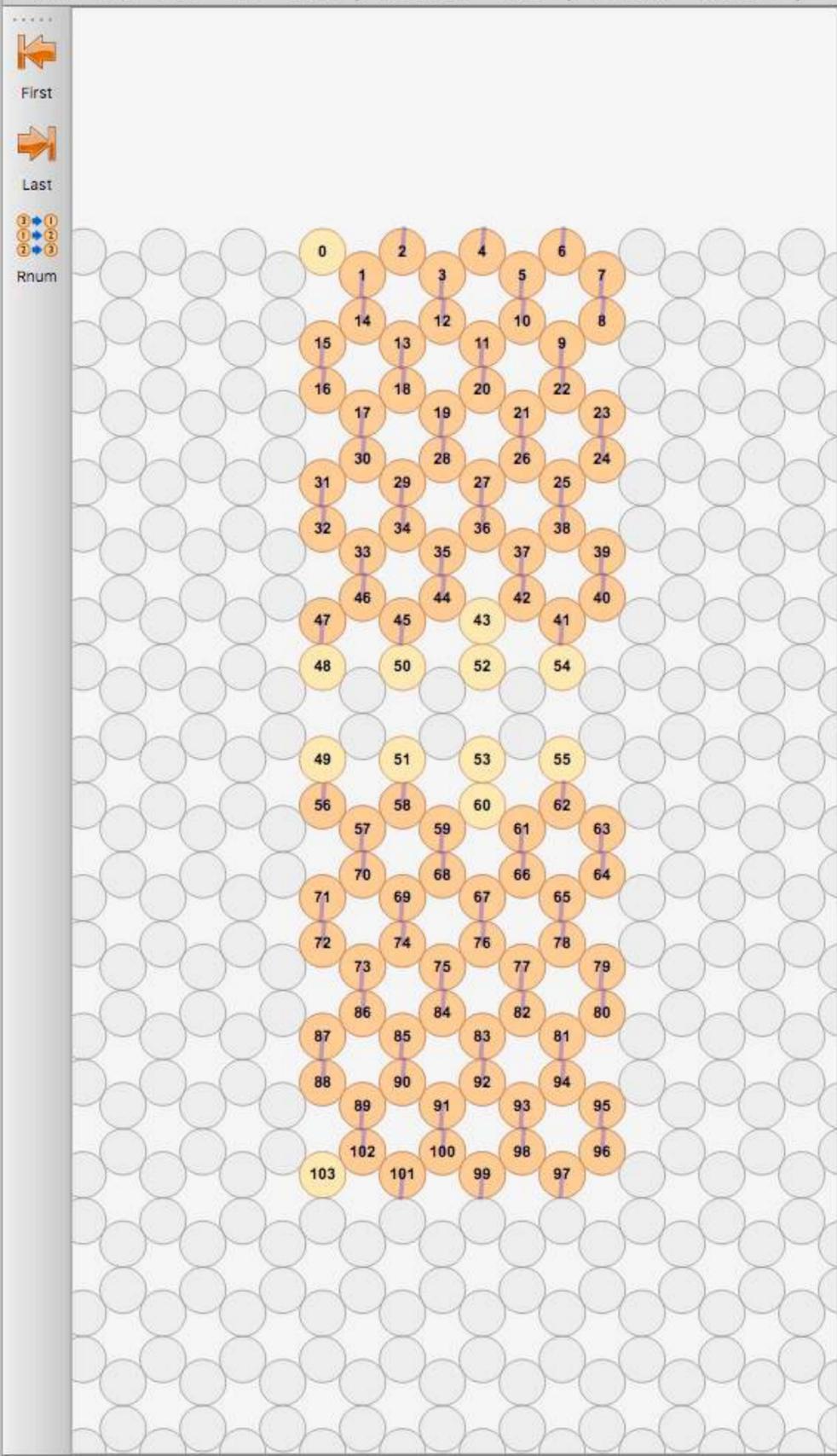
2018-09-25

DNA origami design



DNA origami design with CTK





Navigation and selection tools: First, Last, Rnum (1-5).

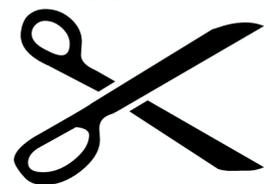
Tool palette: Select, Pencil, Break, Insert, Skip, Paint, AC 19 Seq.

design.json

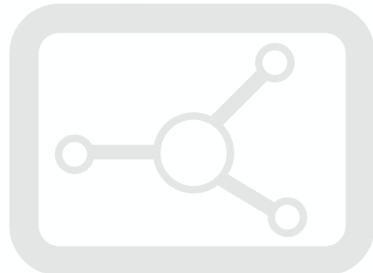
design_**autobreak**.json

CTK

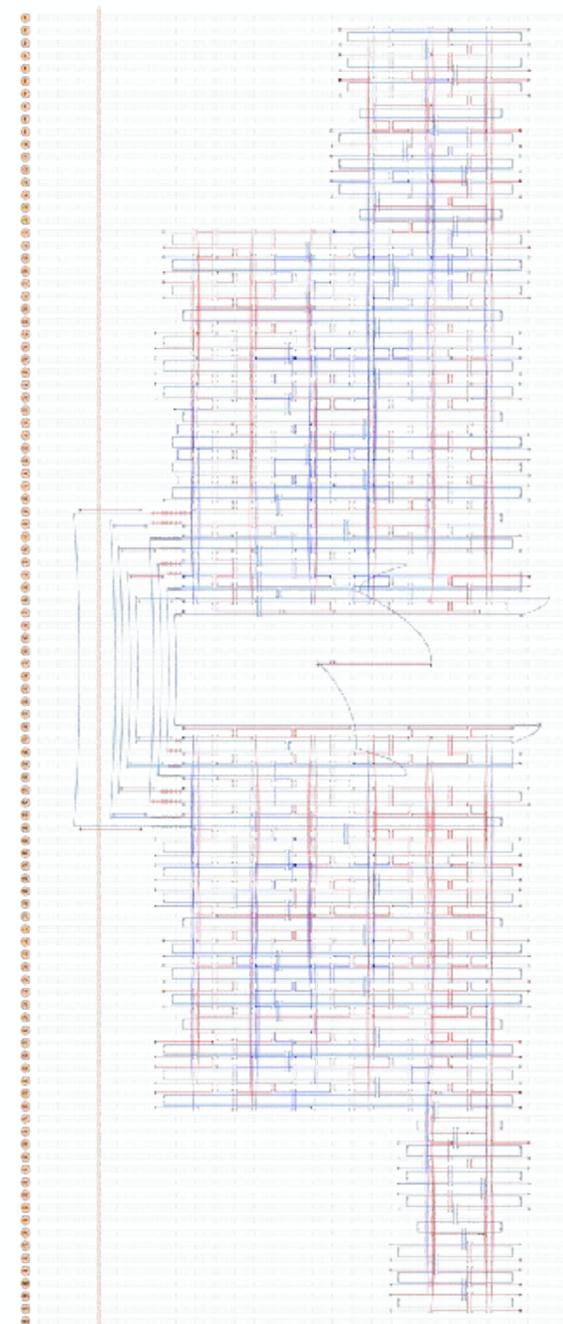
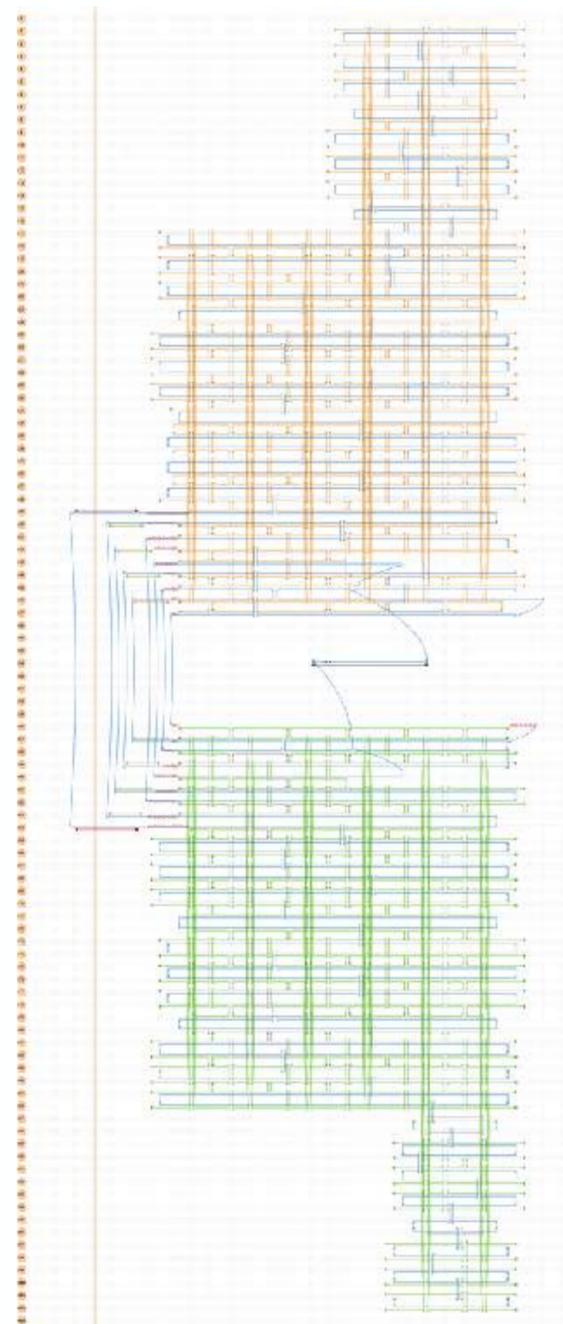
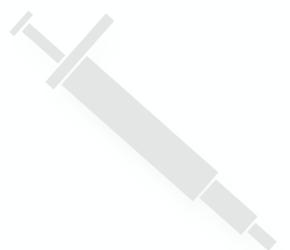
autobreak



origamisim

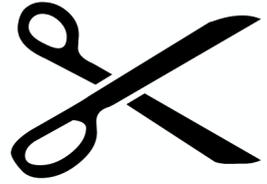


autopipette



CTK

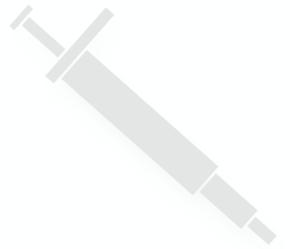
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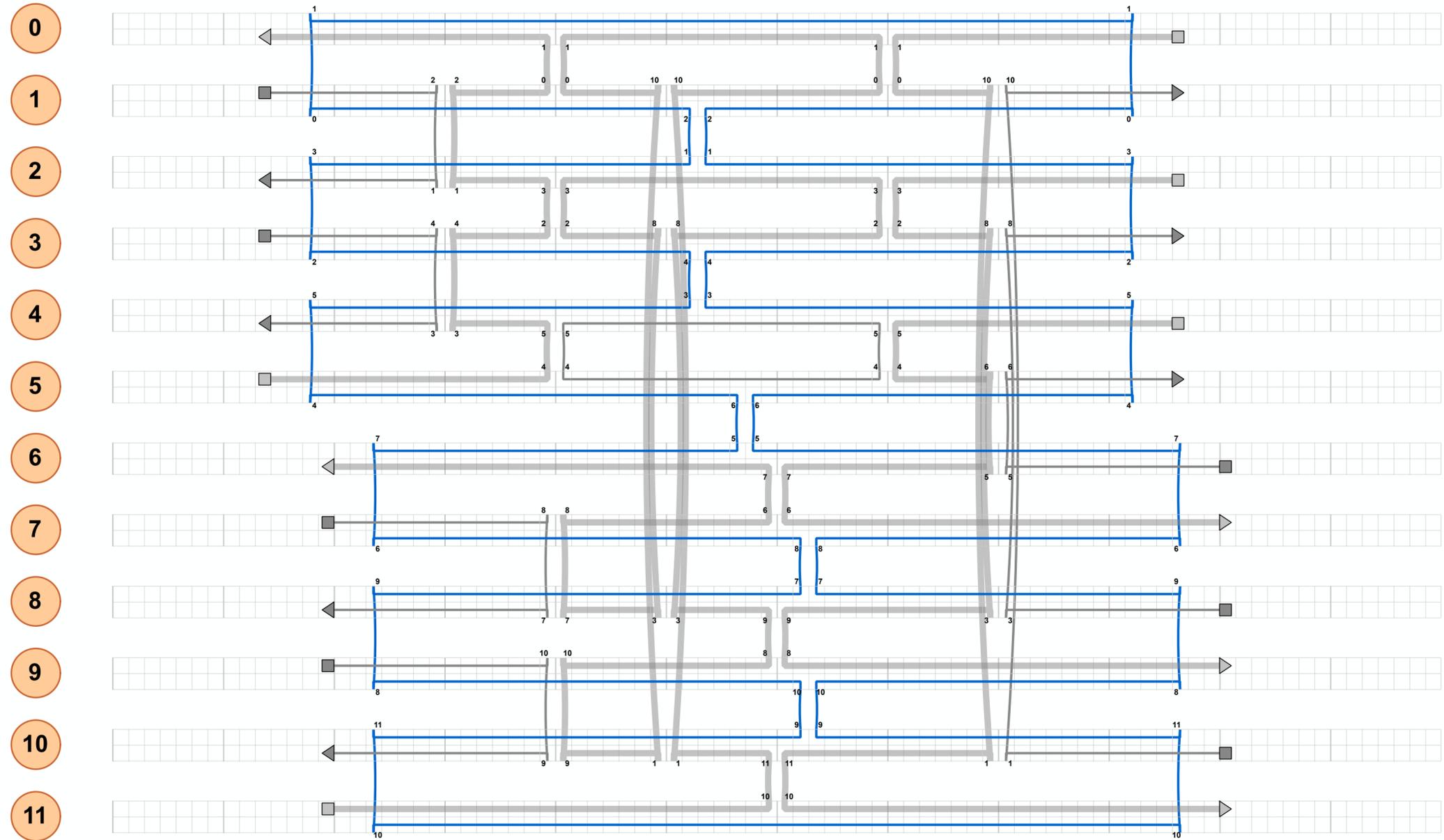
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autopipette



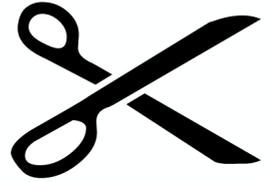
design.json



design.json

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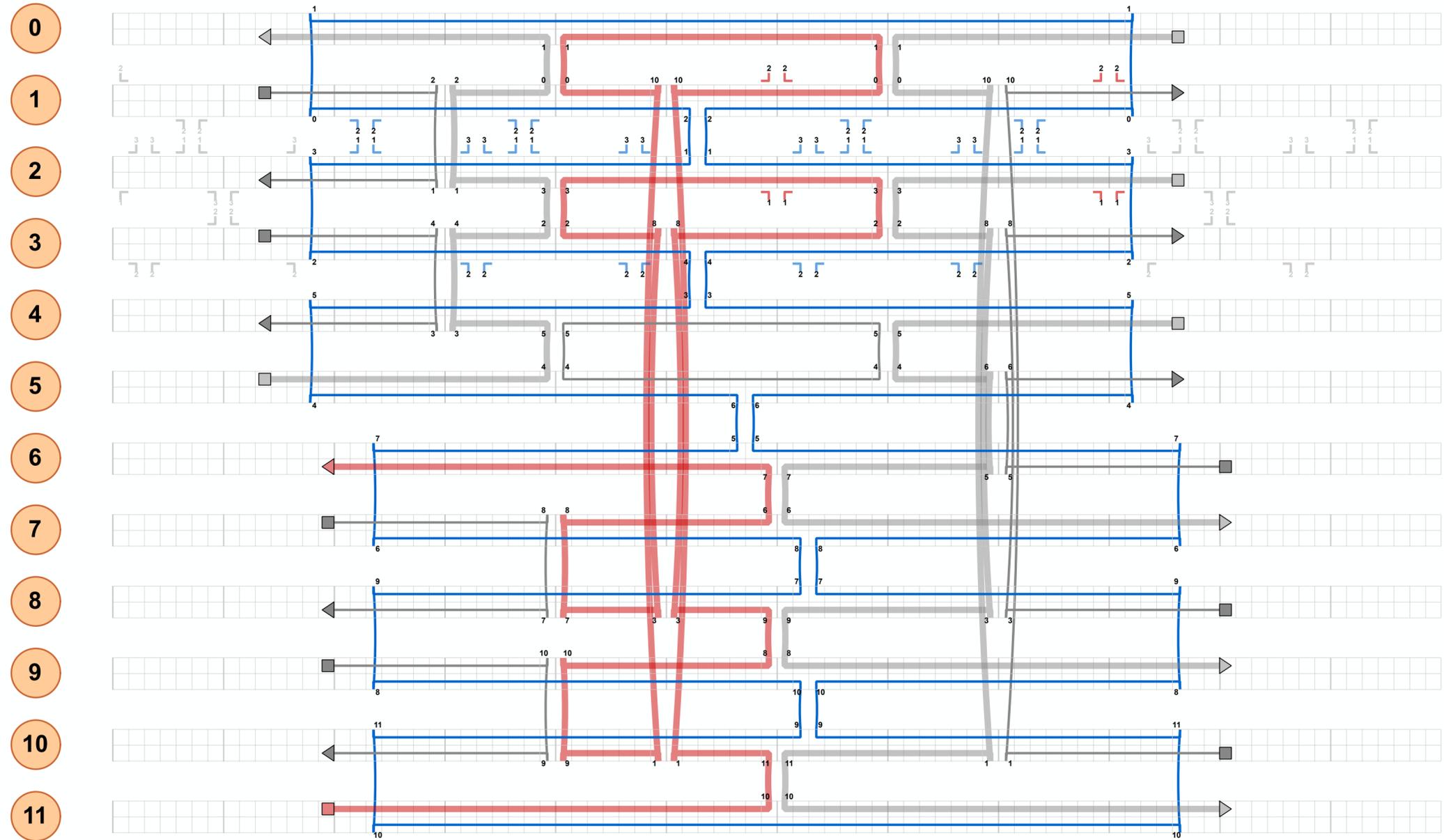
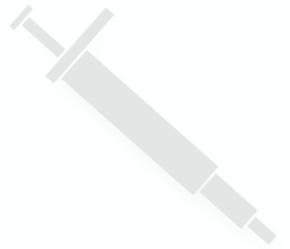
autobreak



origamisim

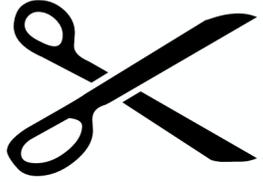


autopipette

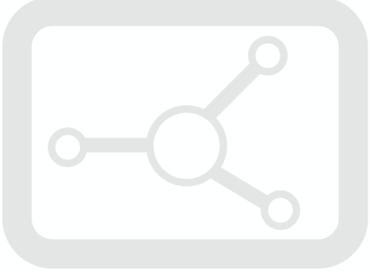


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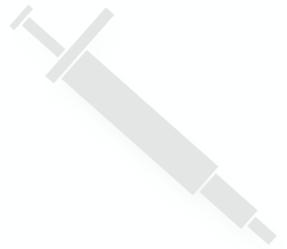
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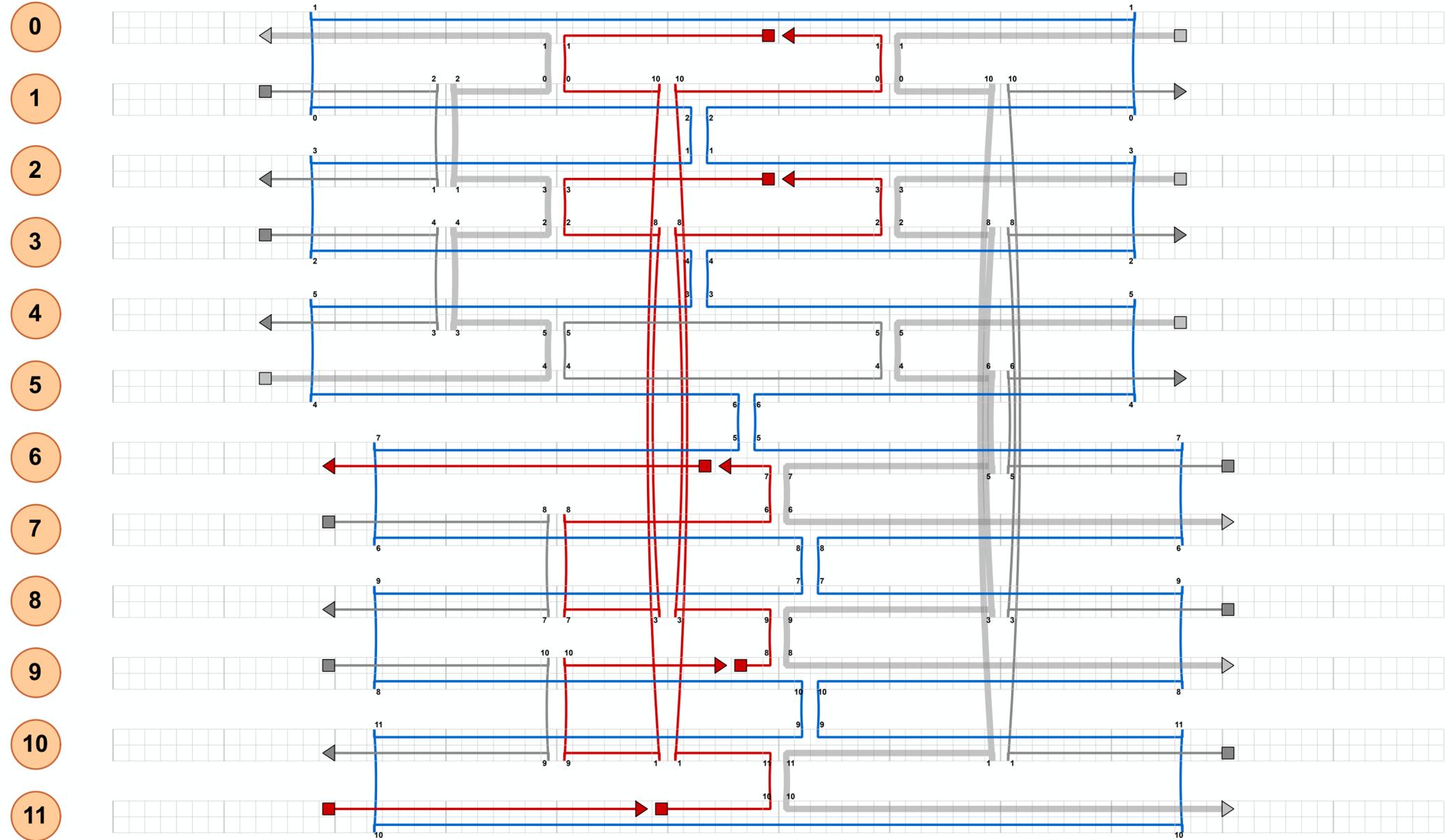
origamisim



autopipette

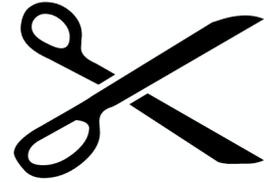


design.json



CTK

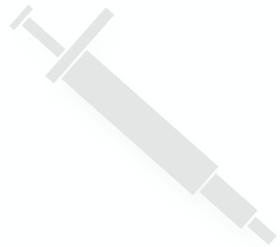
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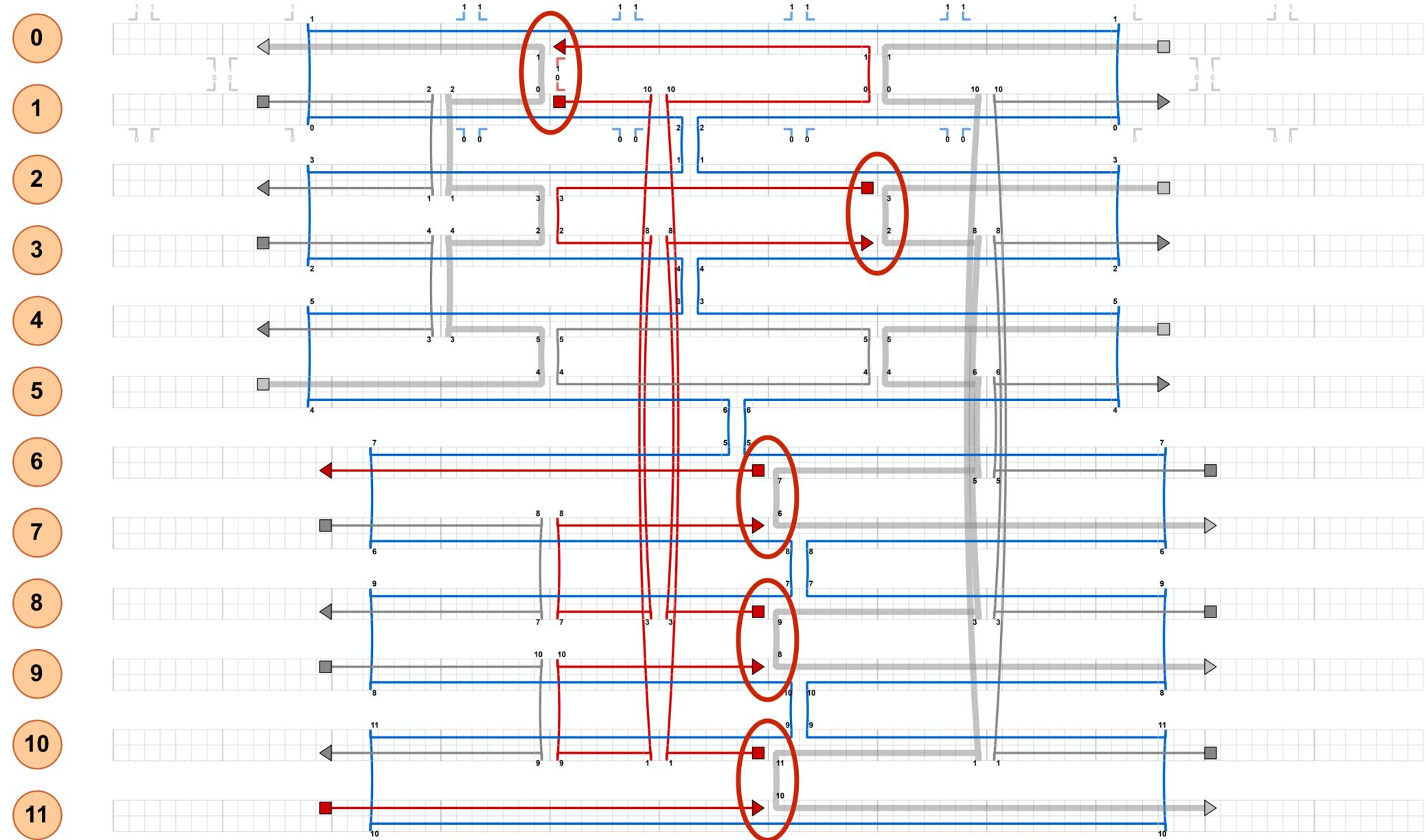
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autopipette



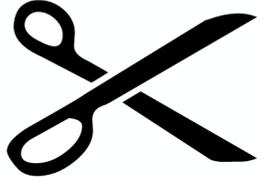
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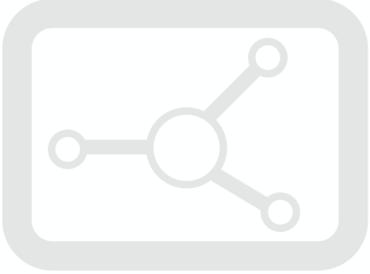
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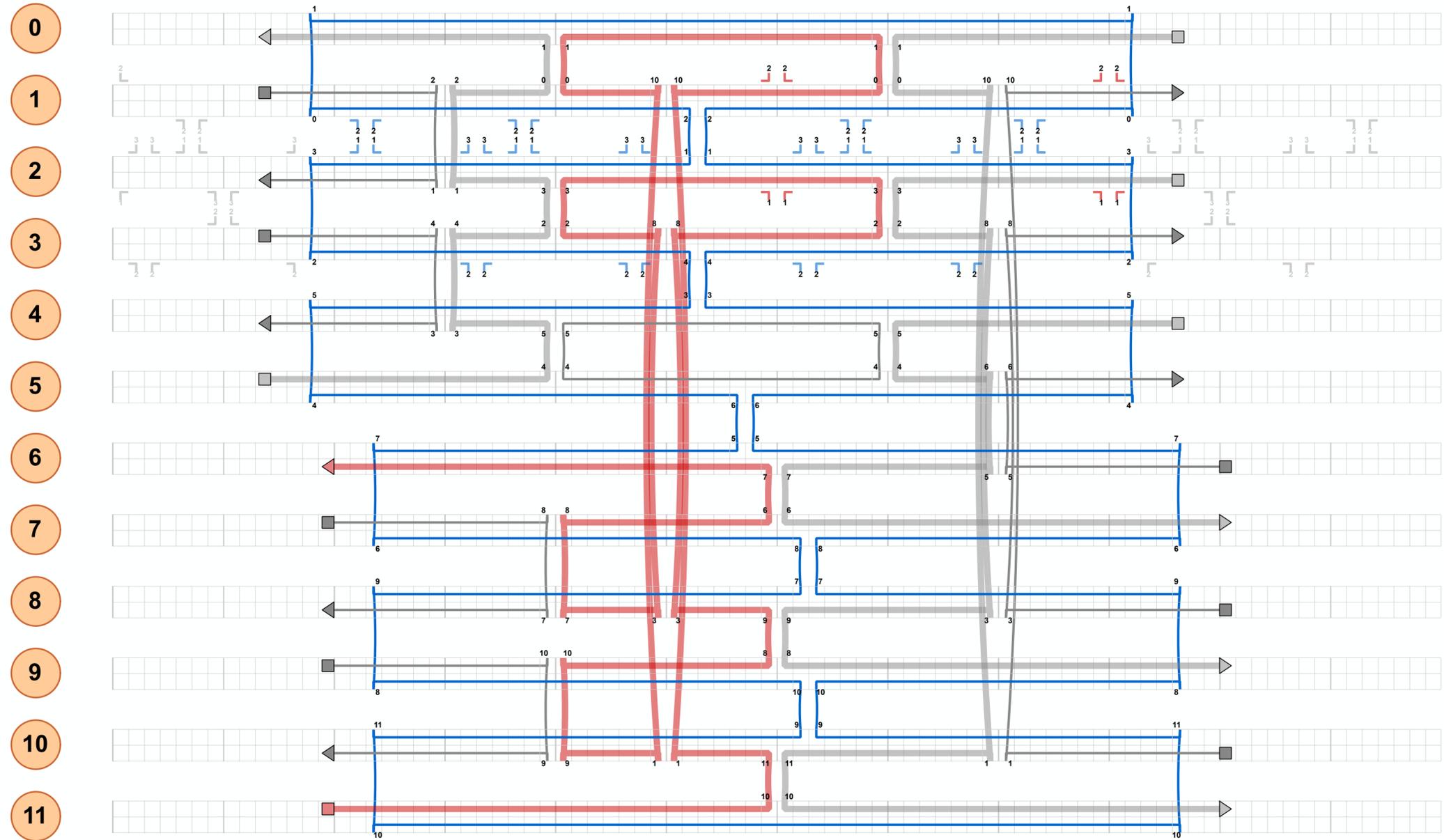
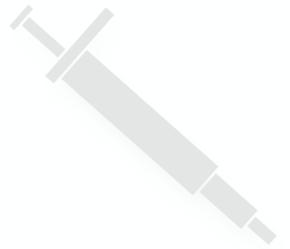
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origamisim



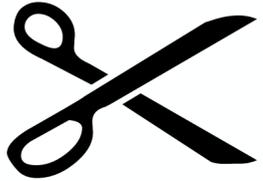
autopipette



design.json

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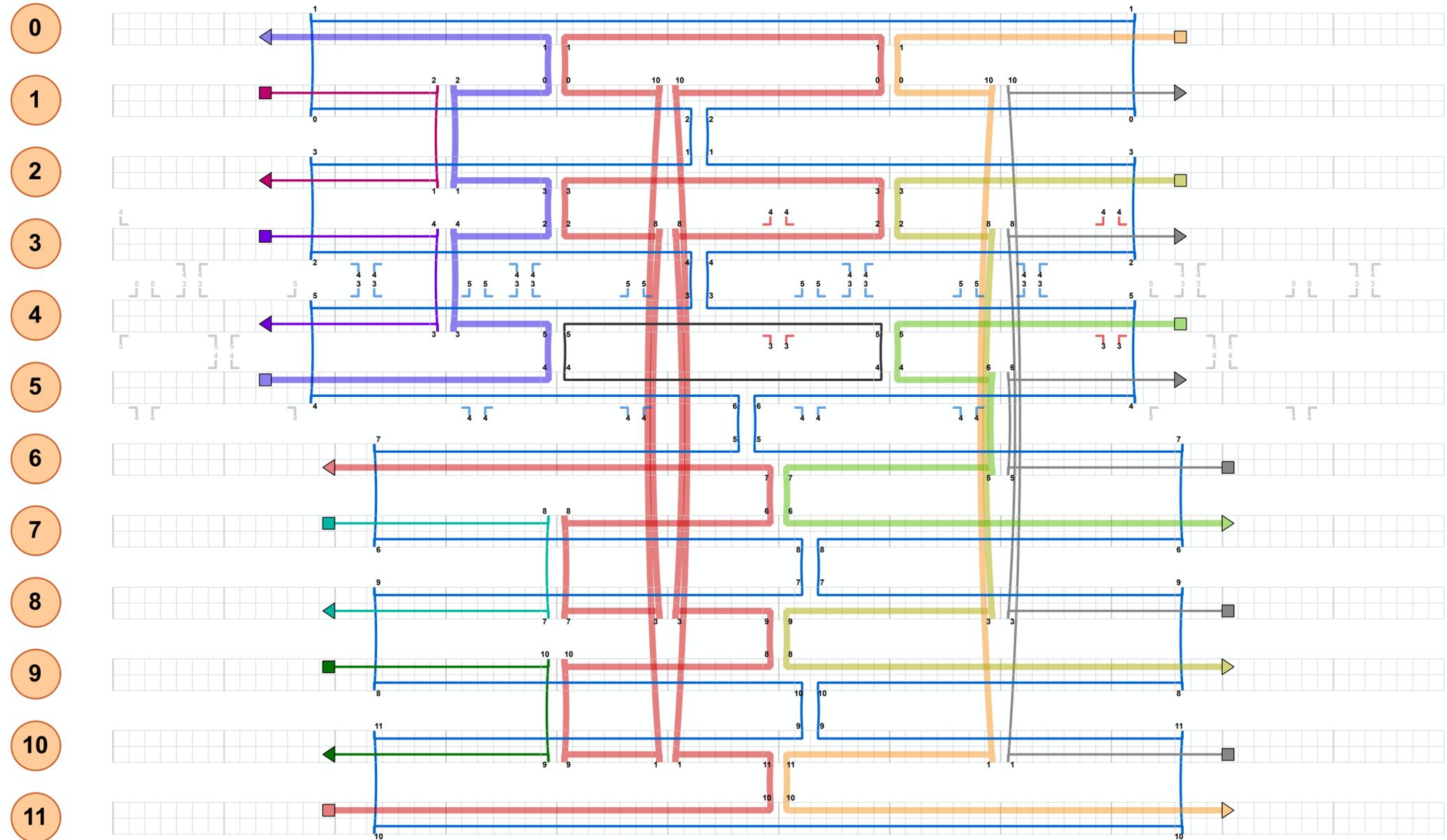
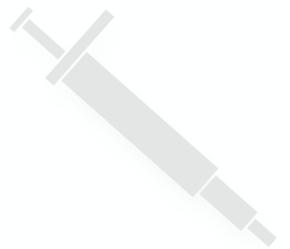
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origamisim



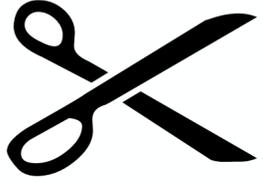
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design.json

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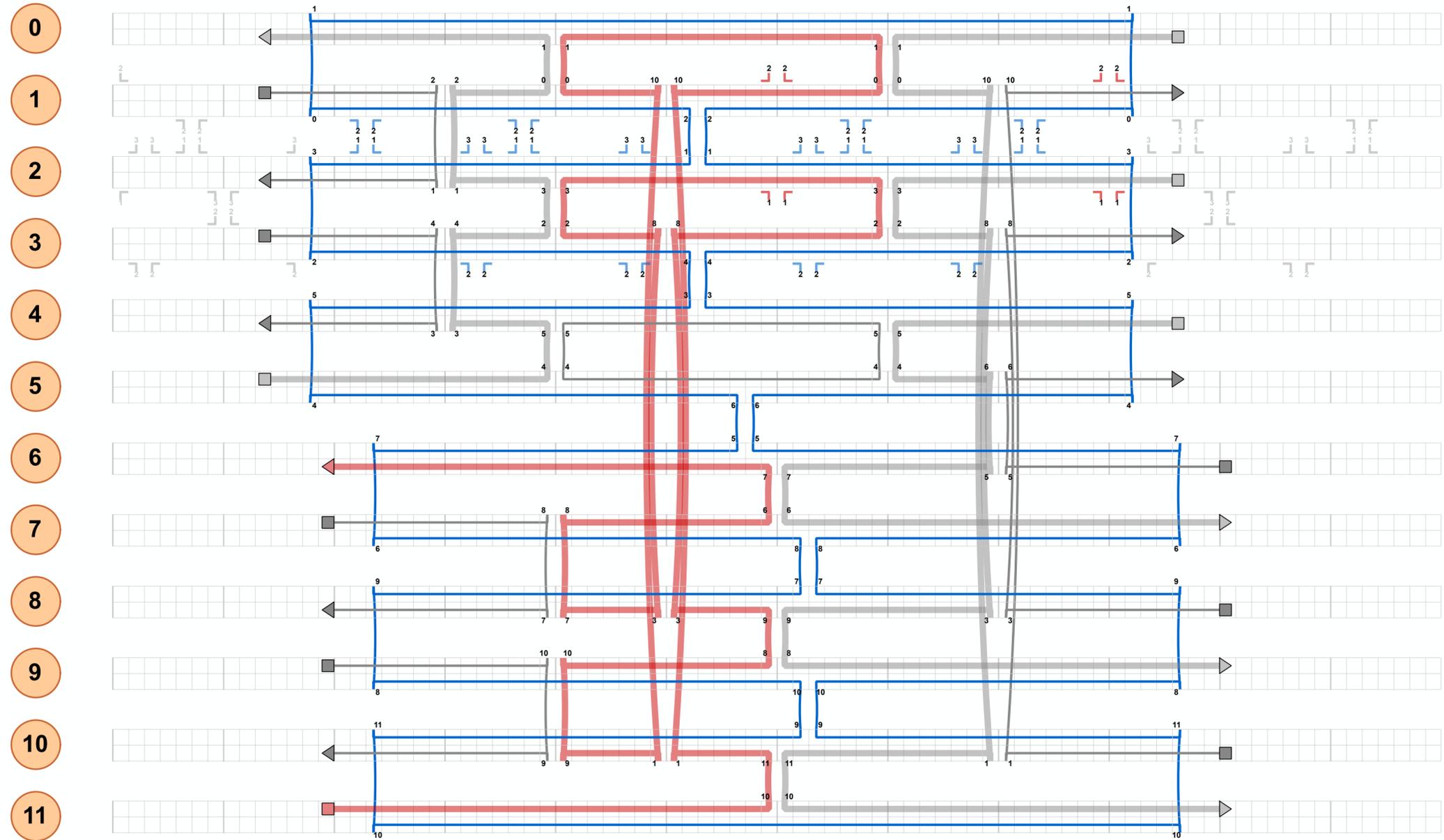
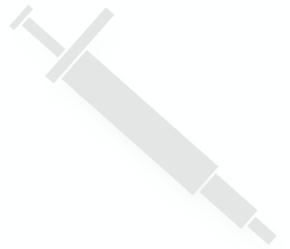
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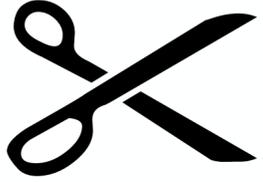
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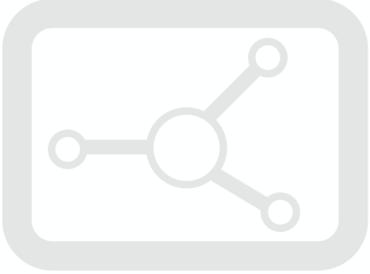
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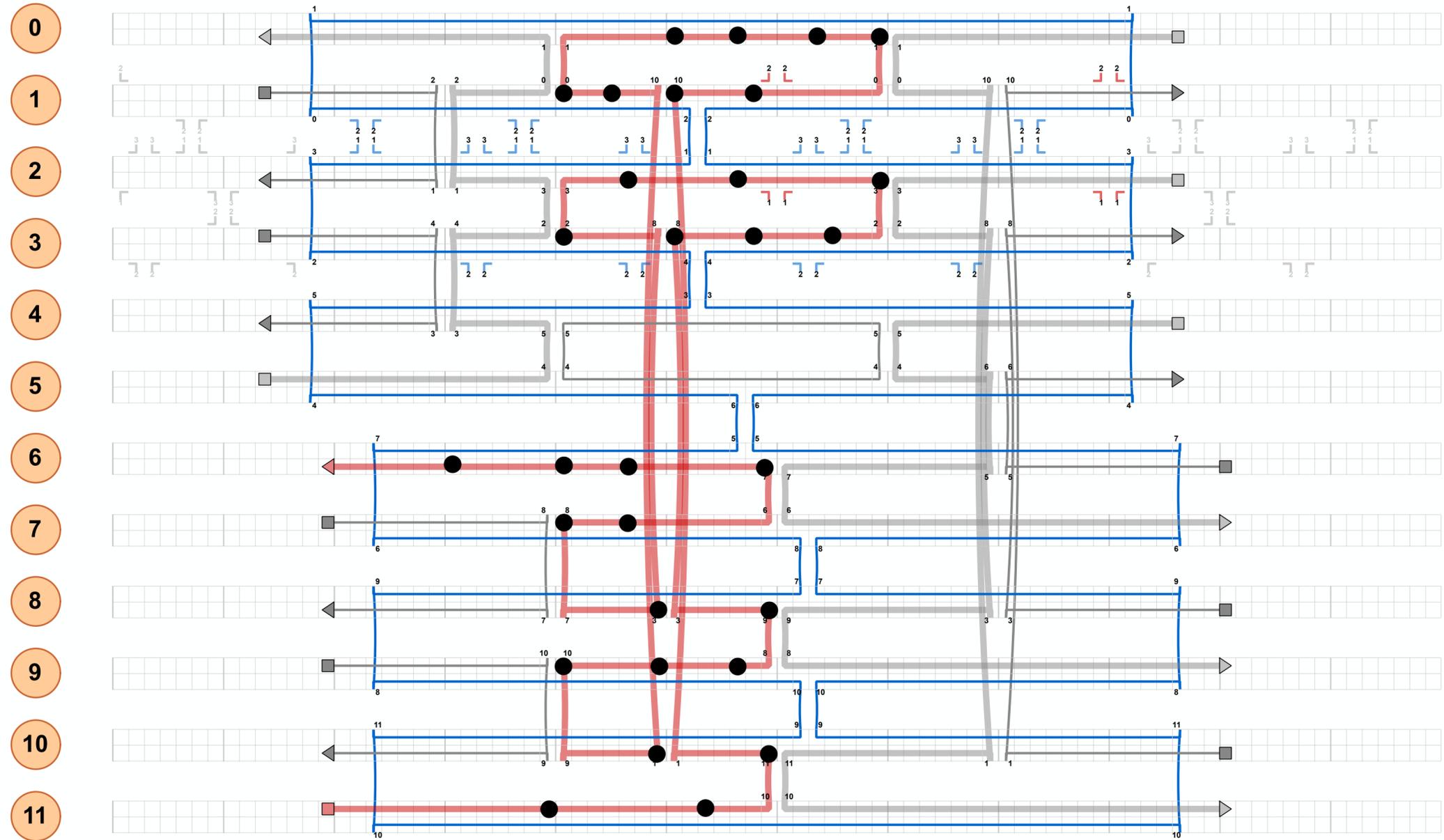
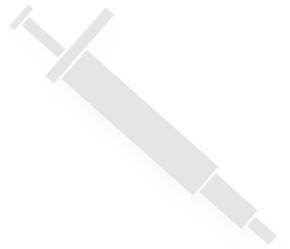
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origamisim

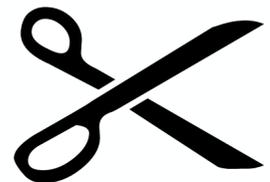


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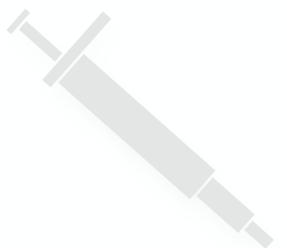
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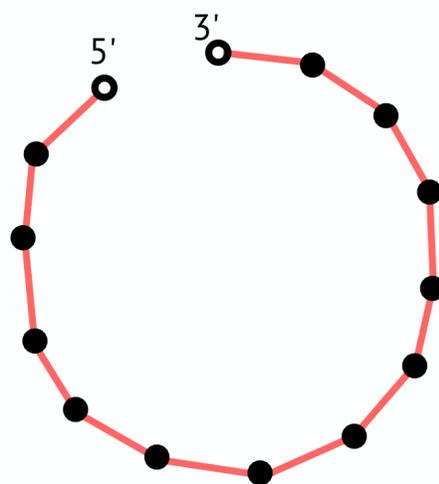
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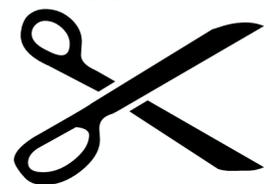


graph representation



CTK

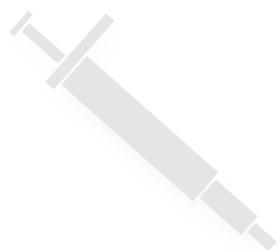
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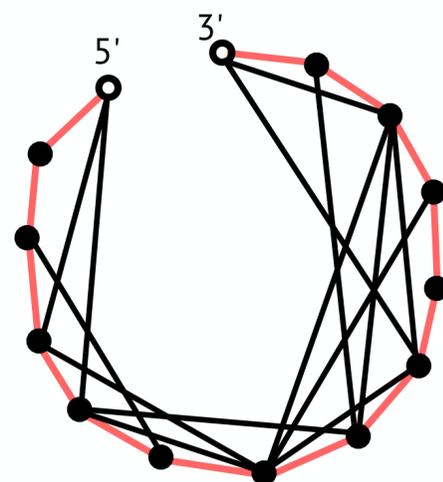
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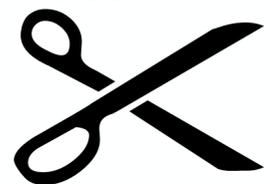


graph representation



CTK

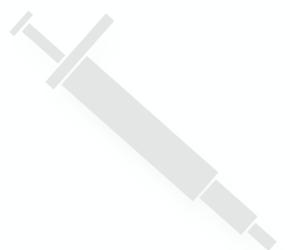
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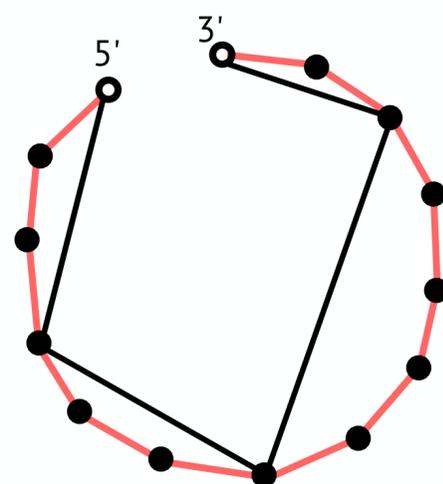
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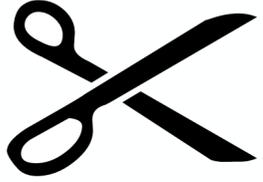


possible solution 1

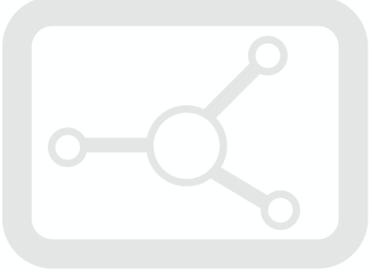


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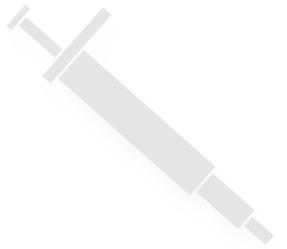
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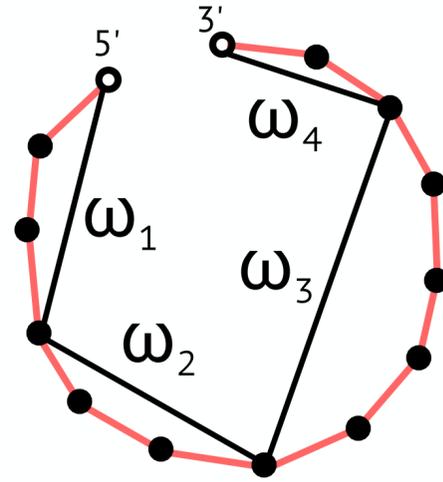
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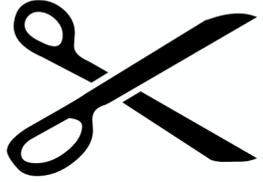


possible solution 1

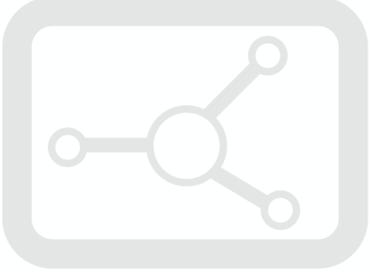


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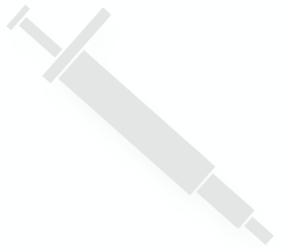
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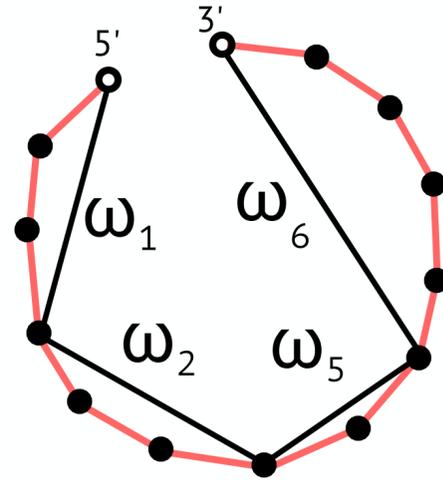
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autopipette

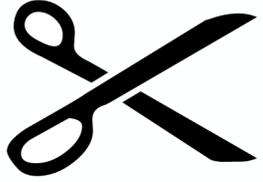


possible solution 2

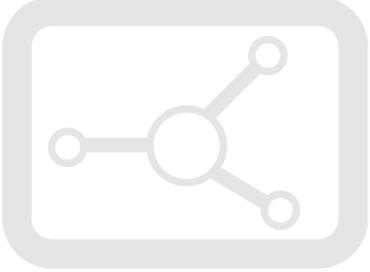


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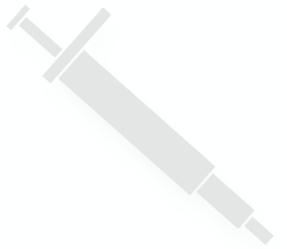
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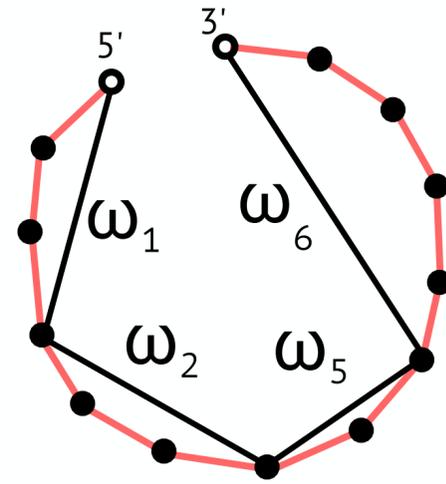
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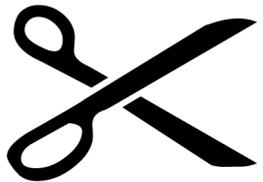
shortest path



$$S = \omega_1 + \omega_2 + \omega_5 + \omega_6$$

CTK

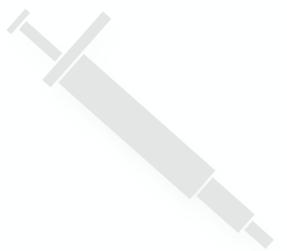
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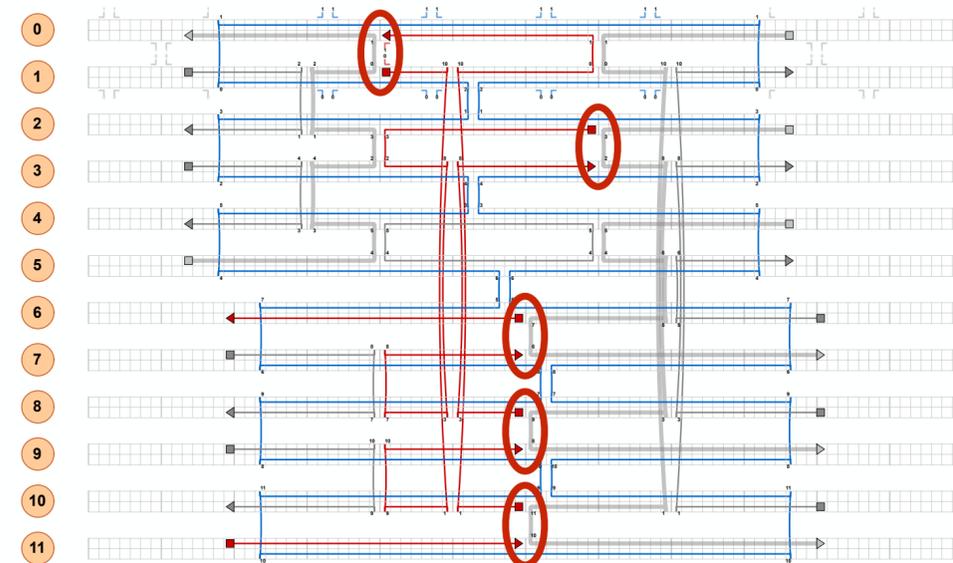
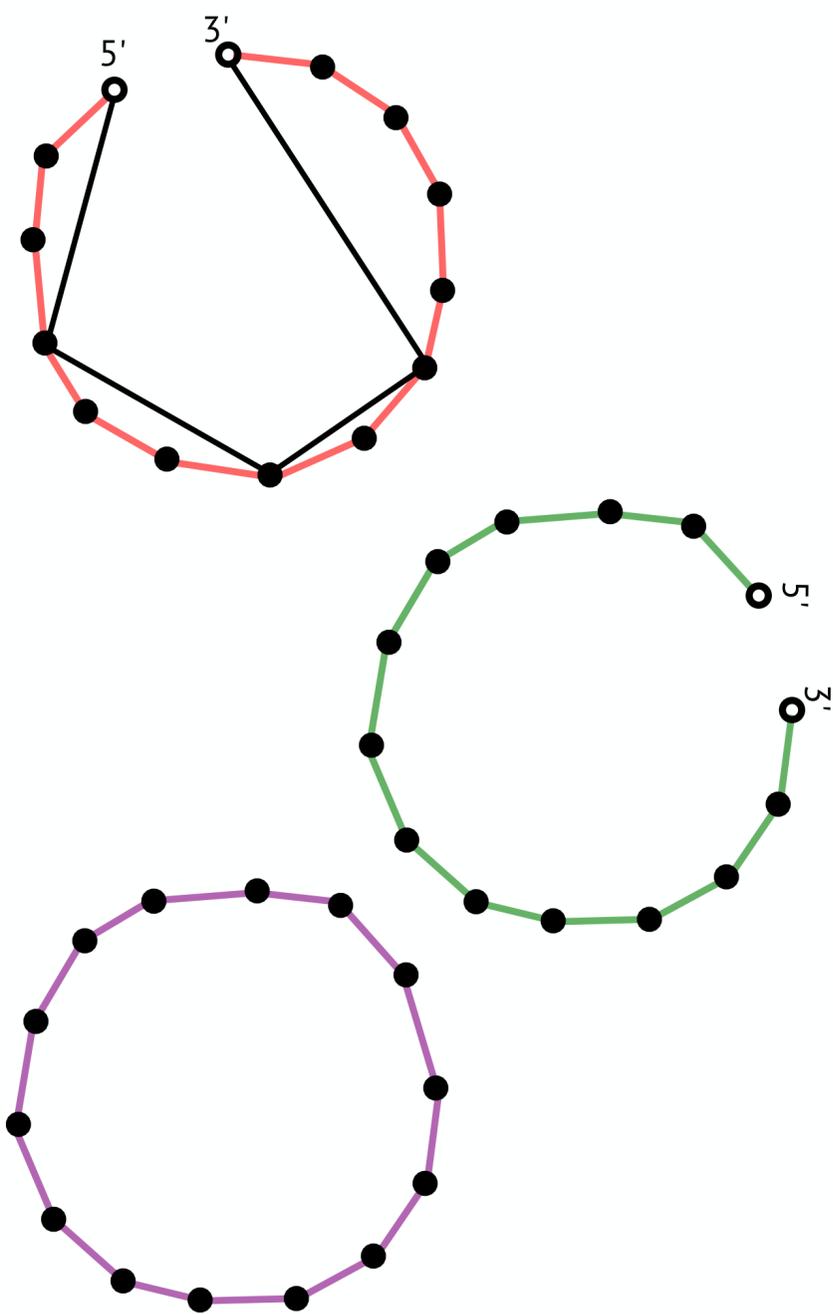
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autopipette

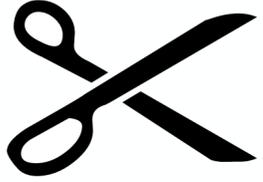


graph representation



CTK

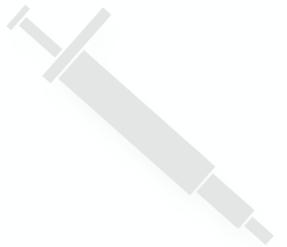
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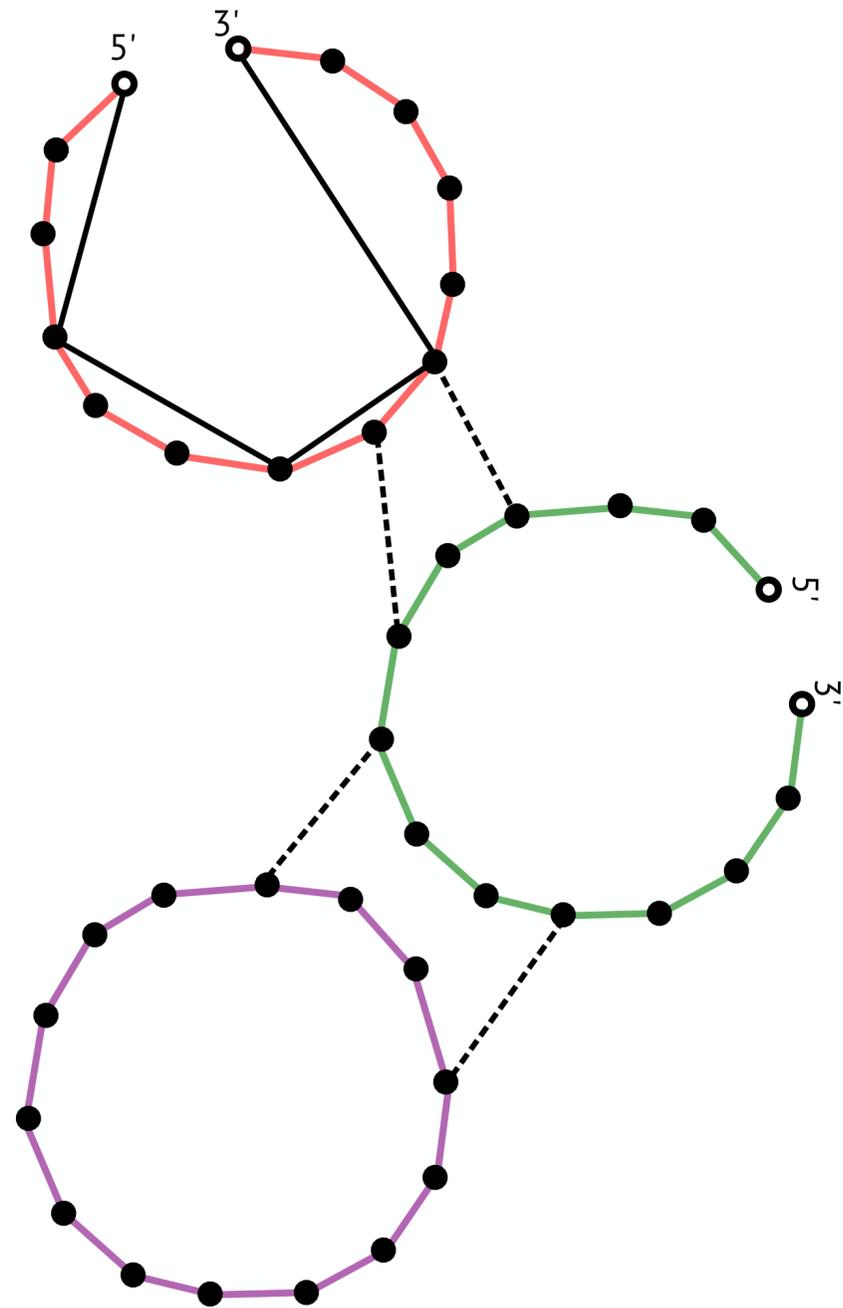
origamisim



autopipette

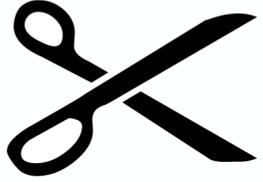


graph representation

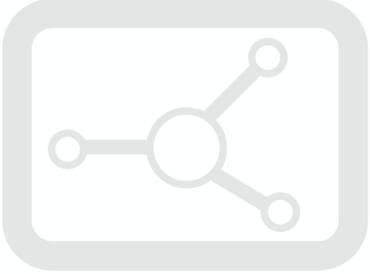


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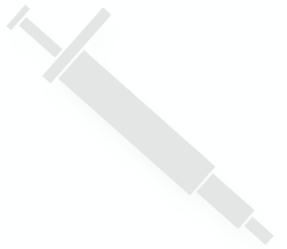
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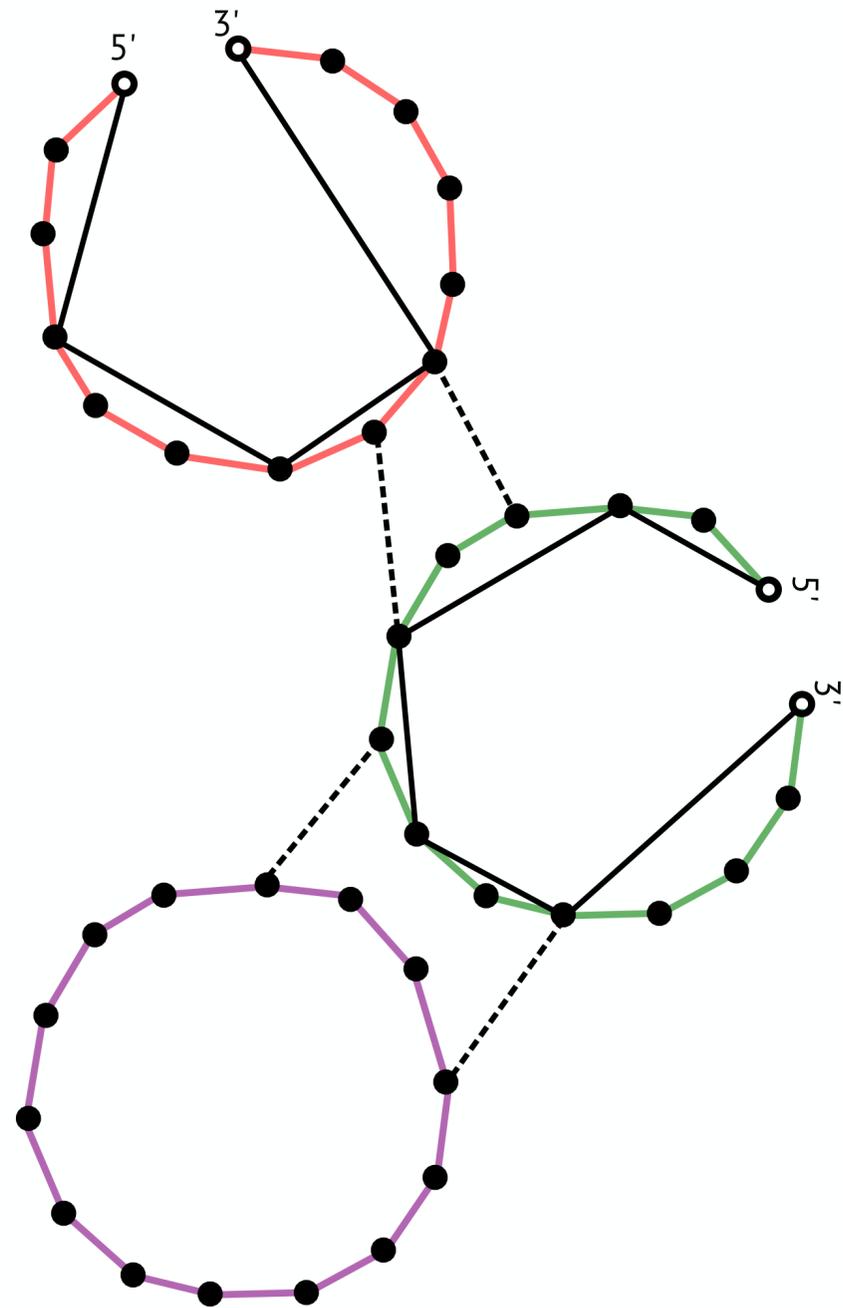
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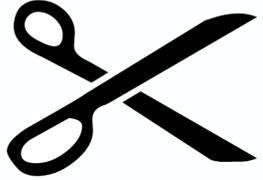


graph representation



CTK

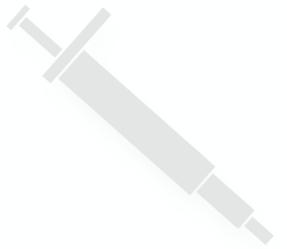
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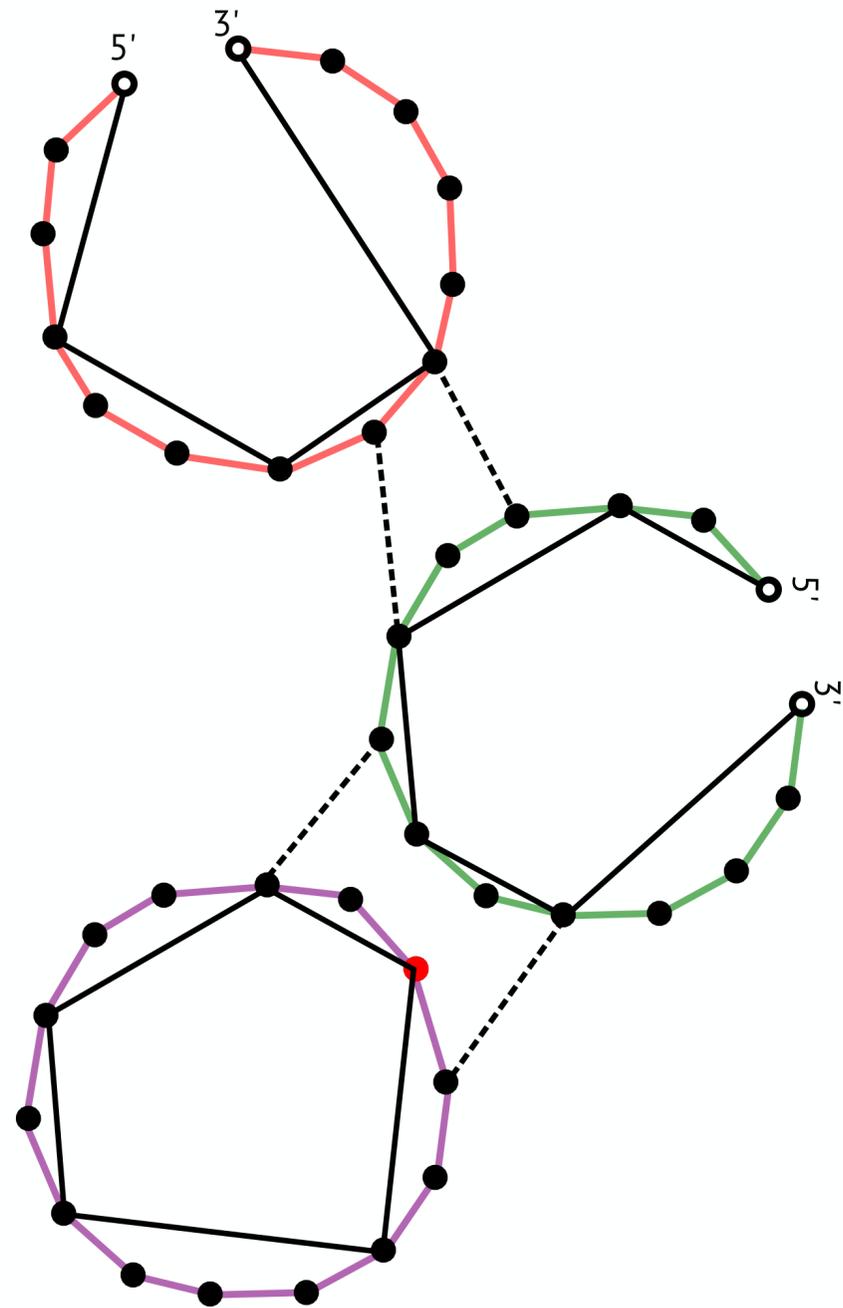
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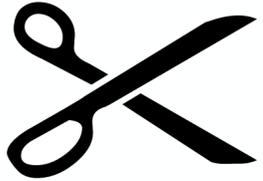


graph representation



CTK

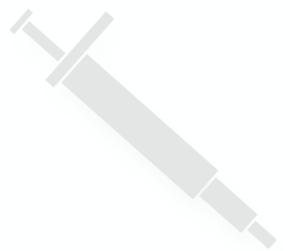
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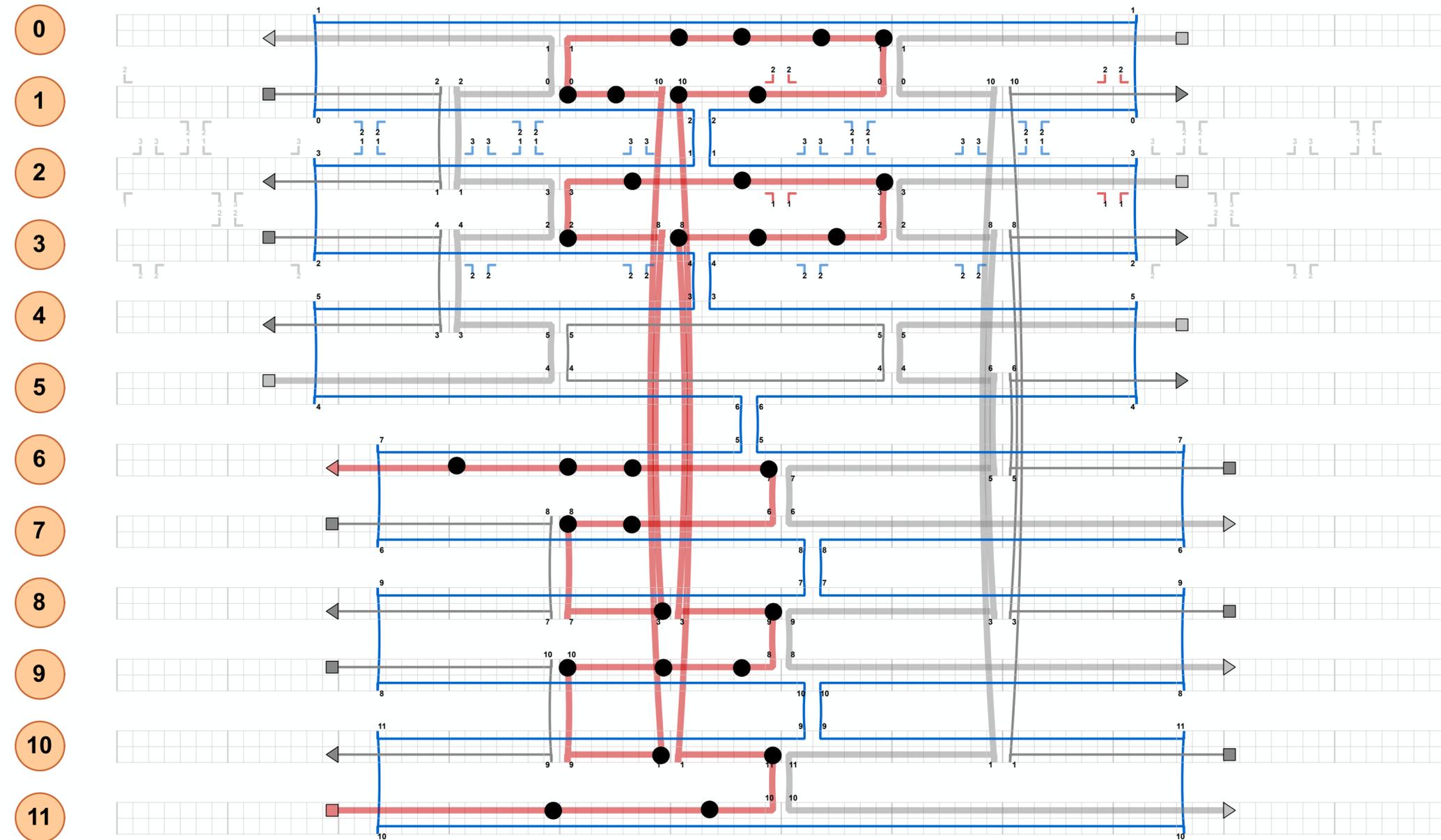
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autopipette

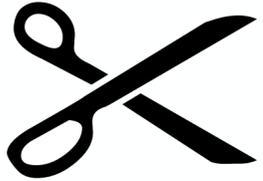


edge weights



CTK

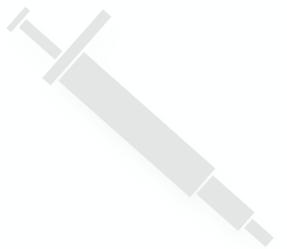
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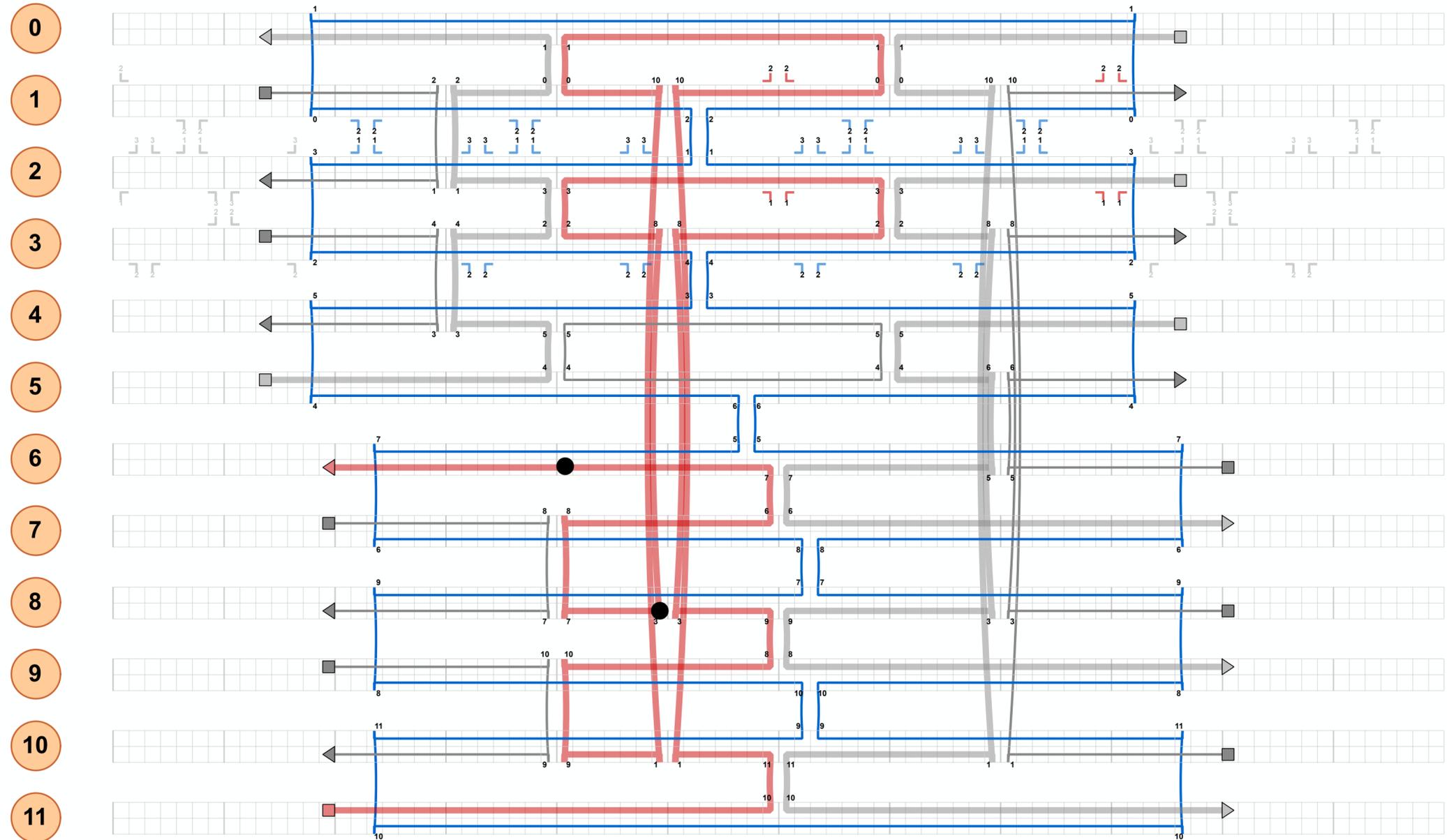
origamisim



autopipette



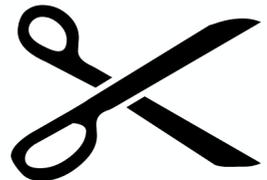
edge weights



hybridization

CTK

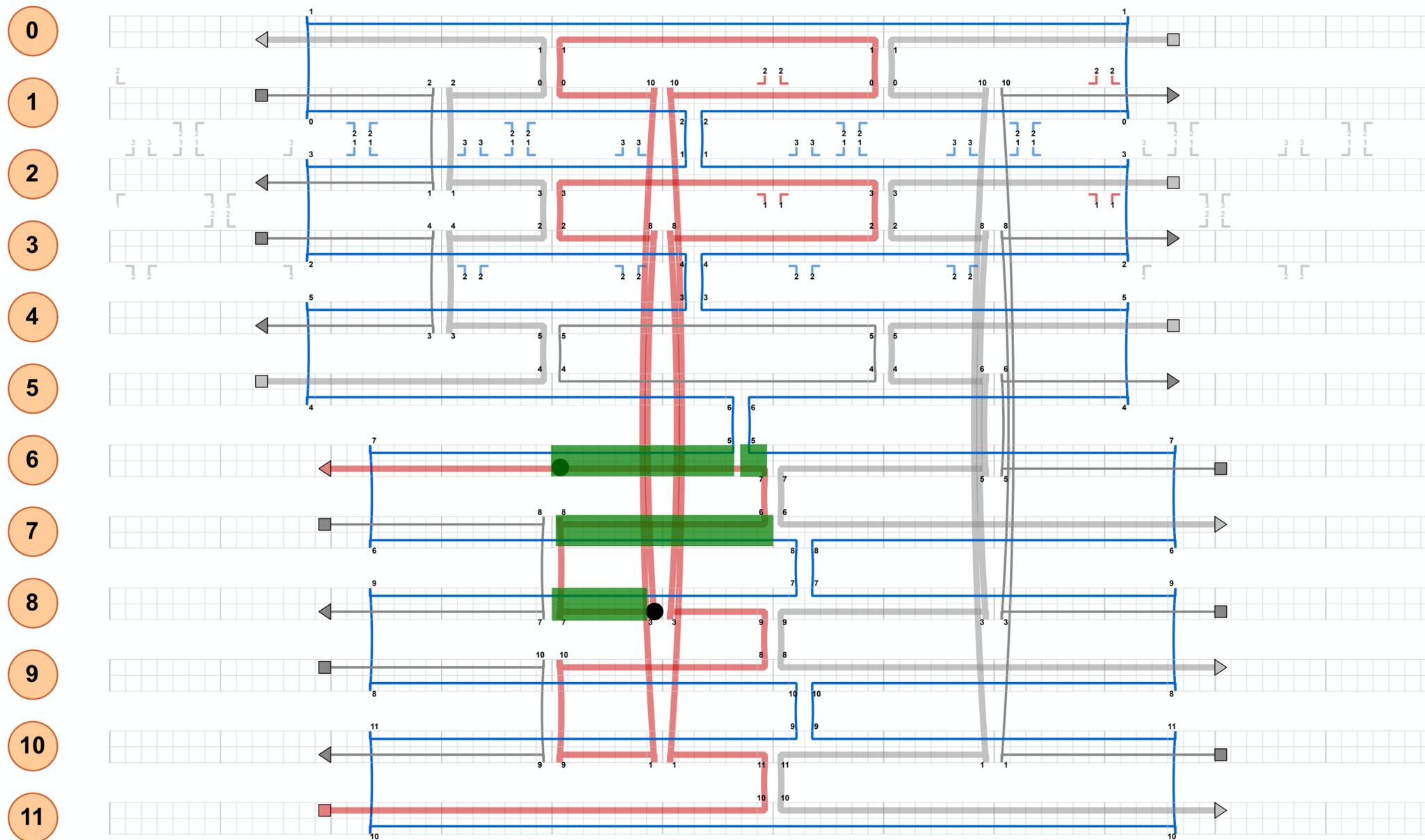
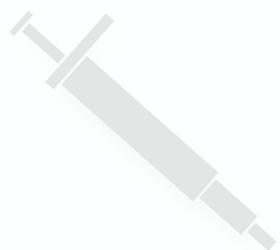
autobreak



origamisim



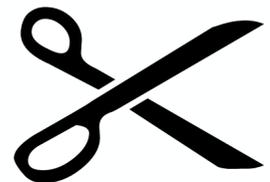
autopipette



hybridization loop closure

CTK

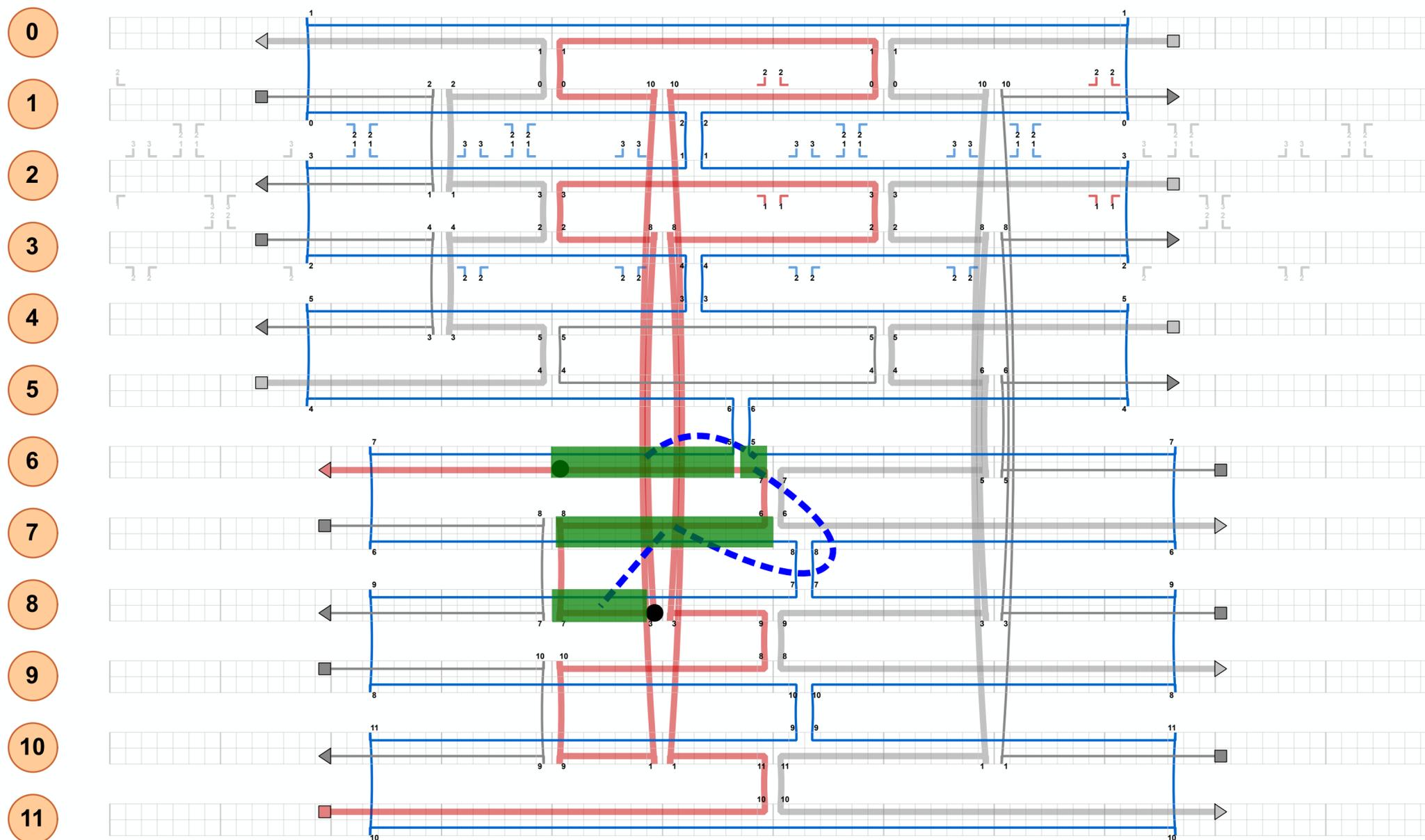
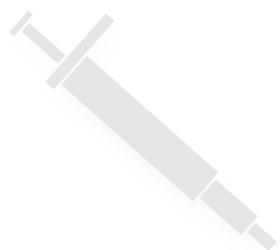
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origamisim



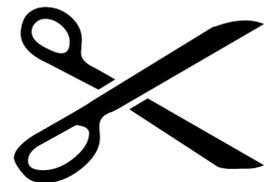
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hybridization loop closure

CTK

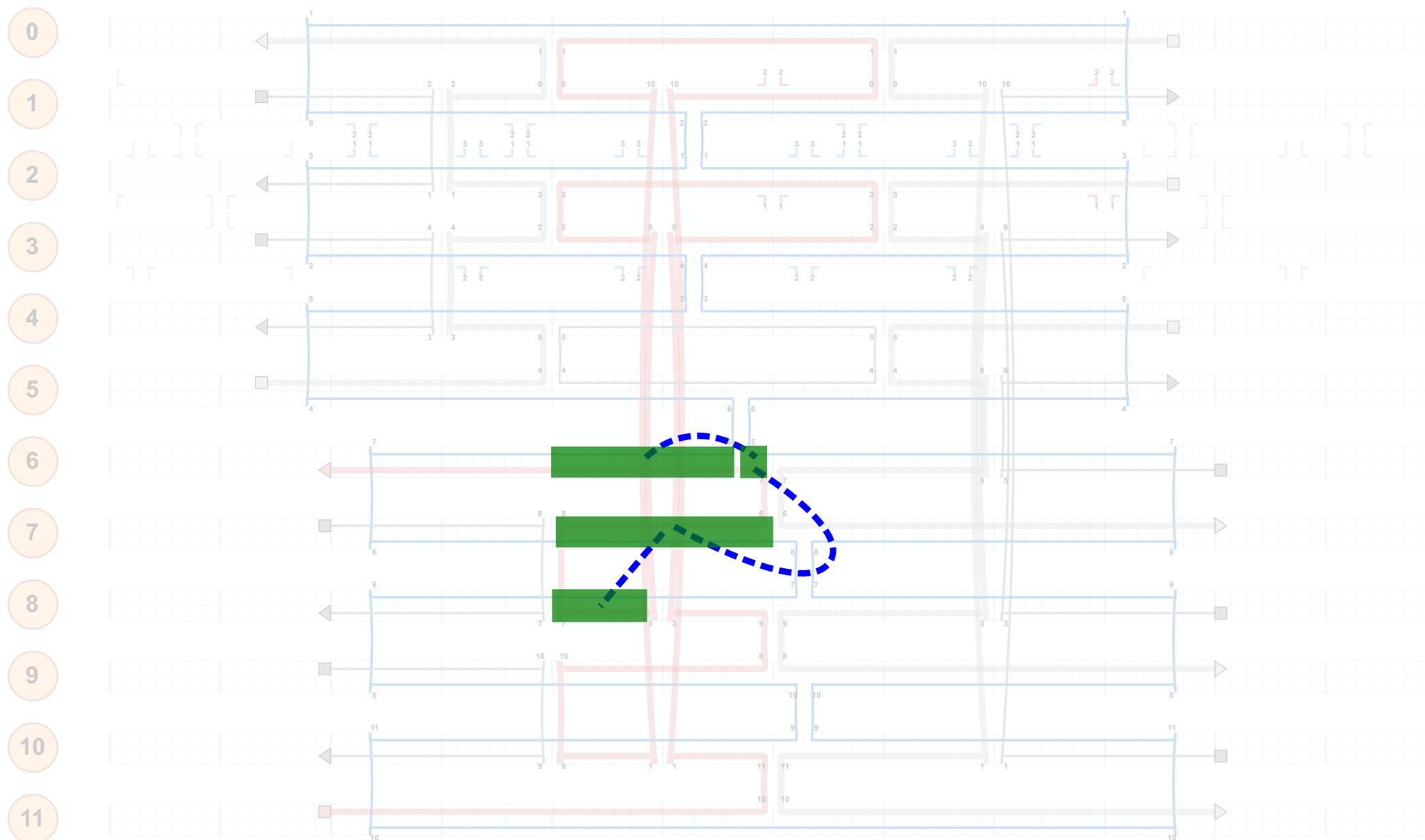
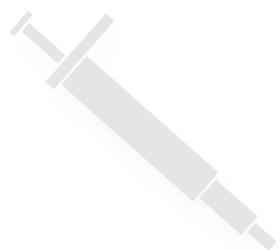
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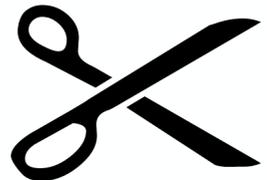
autopipette



hybridization loop closure

CTK

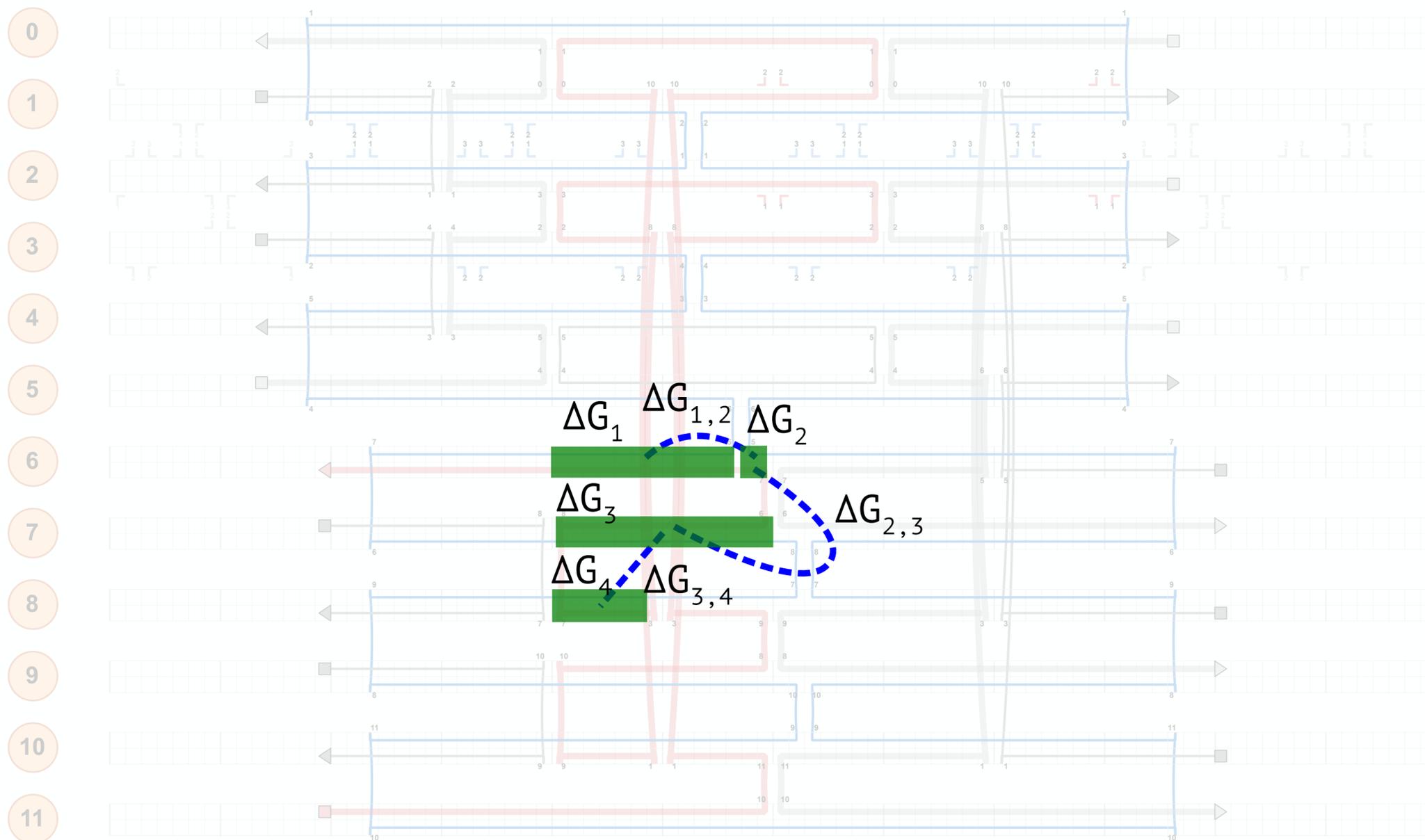
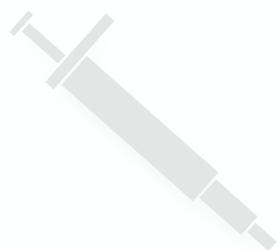
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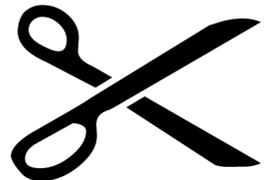
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hybridization loop closure

CTK

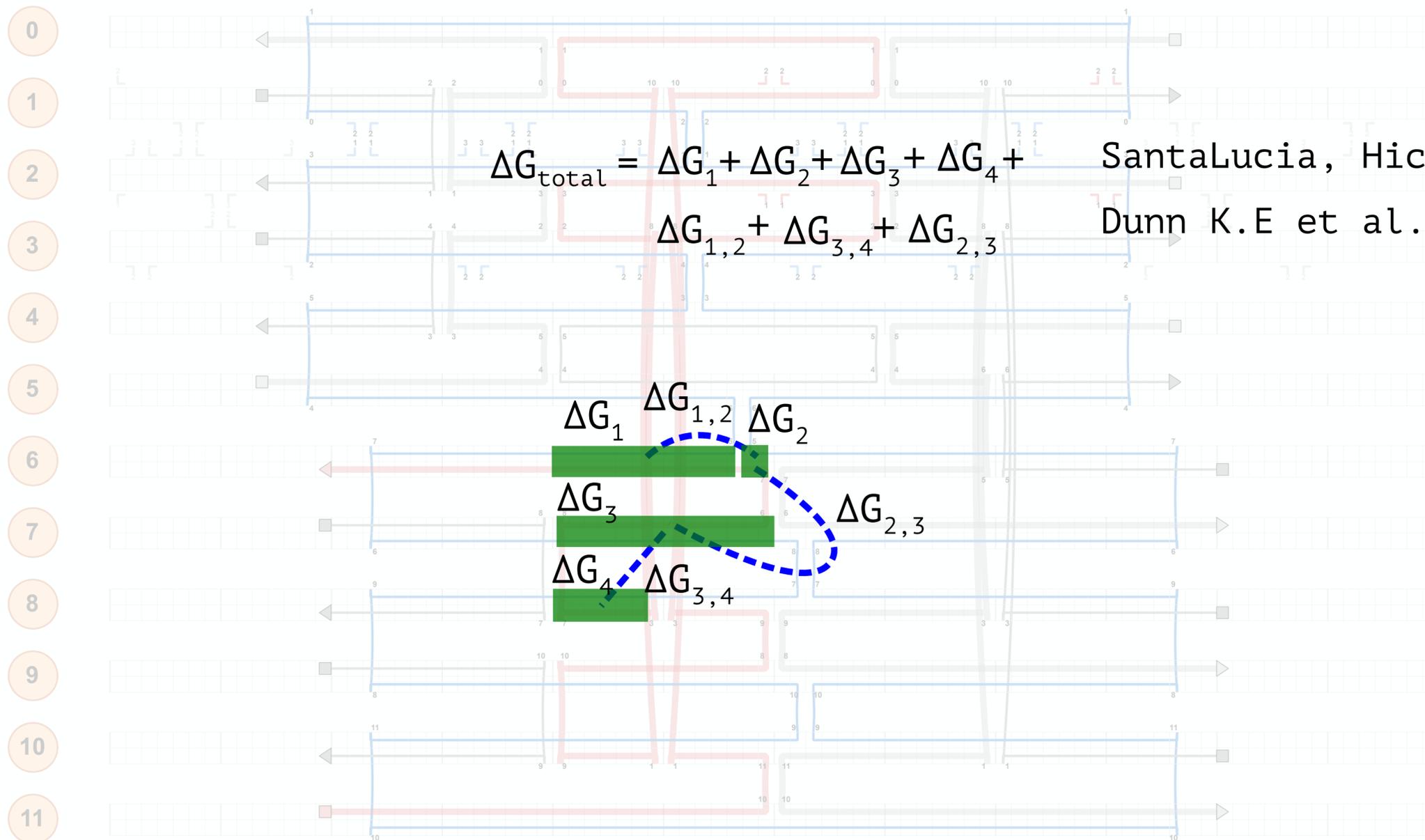
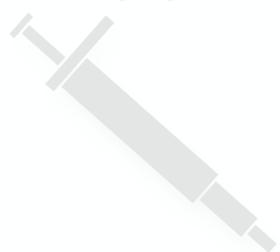
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origamisim



autopipette



SantaLucia, Hicks (2004)

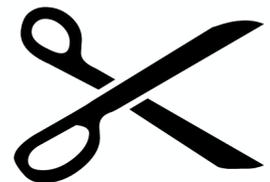
Dunn K.E et al.(2015)

hybridization loop closure

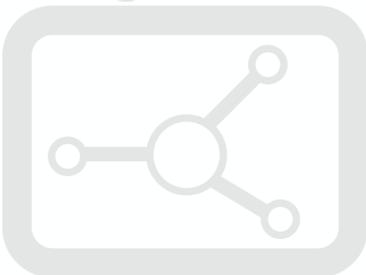
encounter probability

CTK

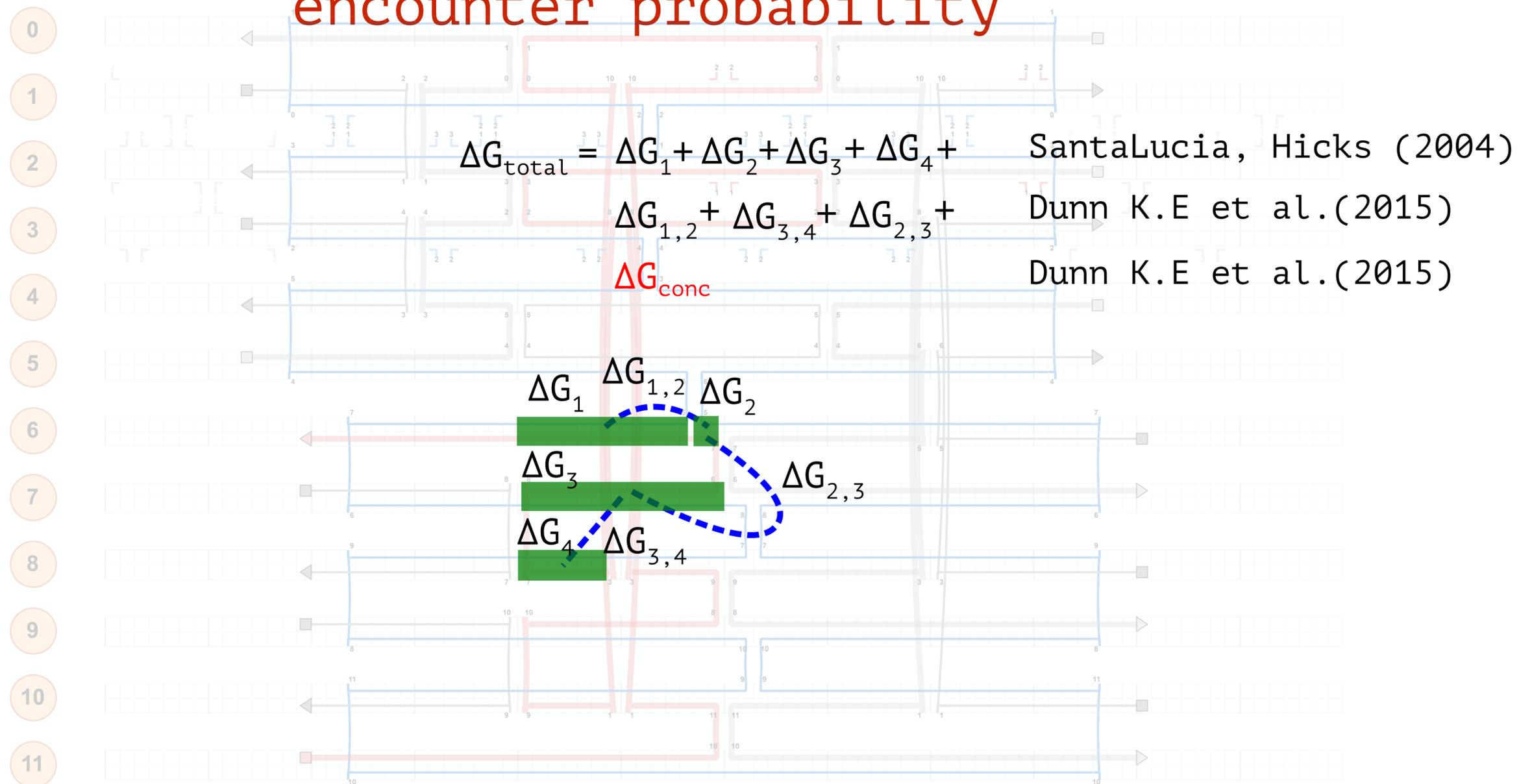
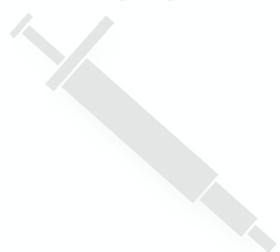
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origamisim



autopipette



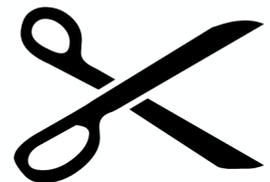
hybridization

loop closure

encounter probability

CTK

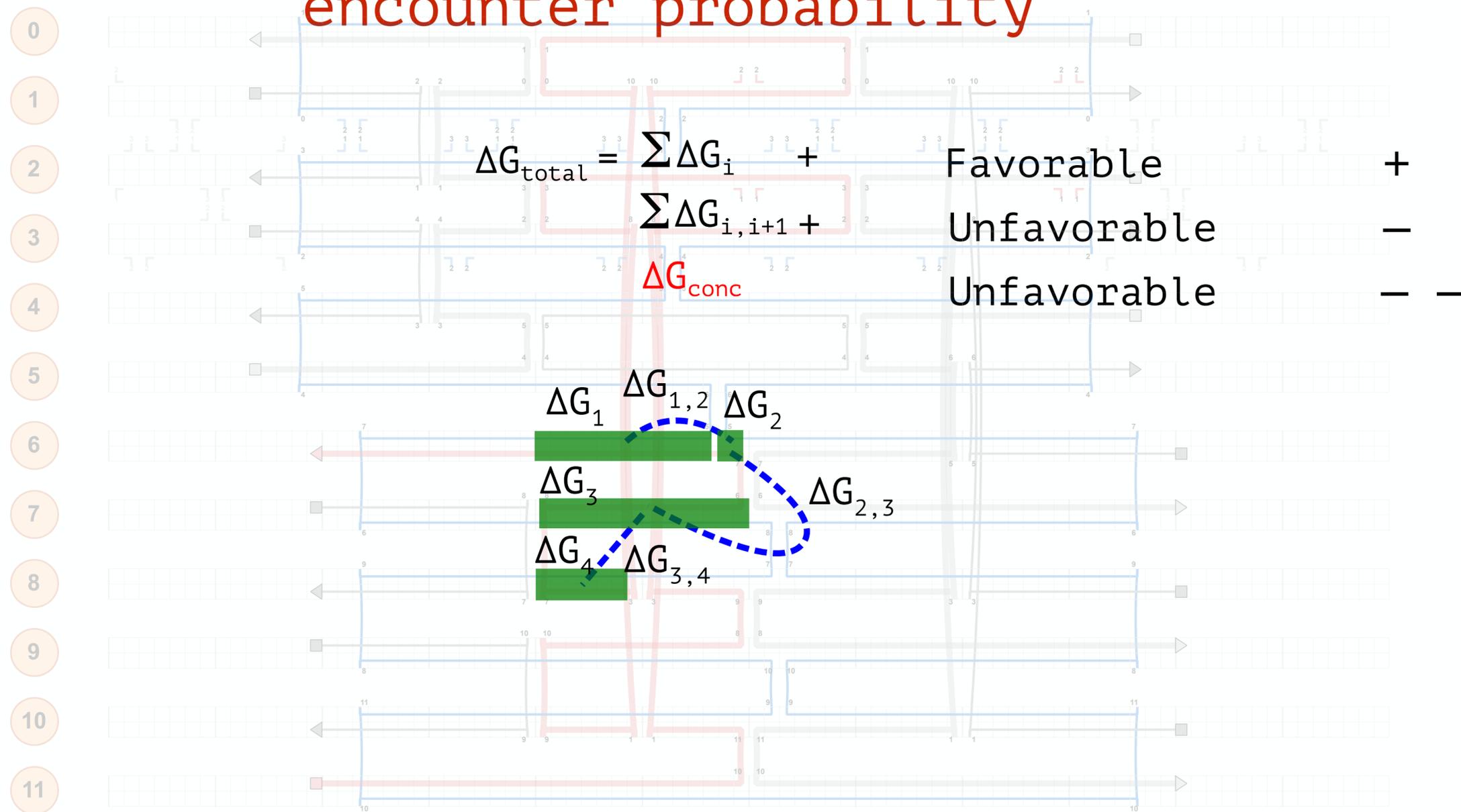
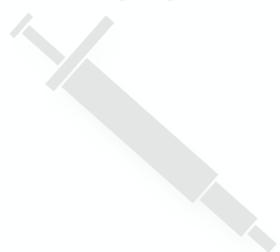
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origamisim



autopipette

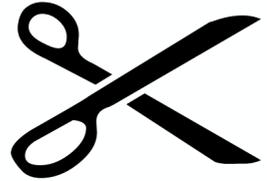


hybridization loop closure

encounter probability

CTK

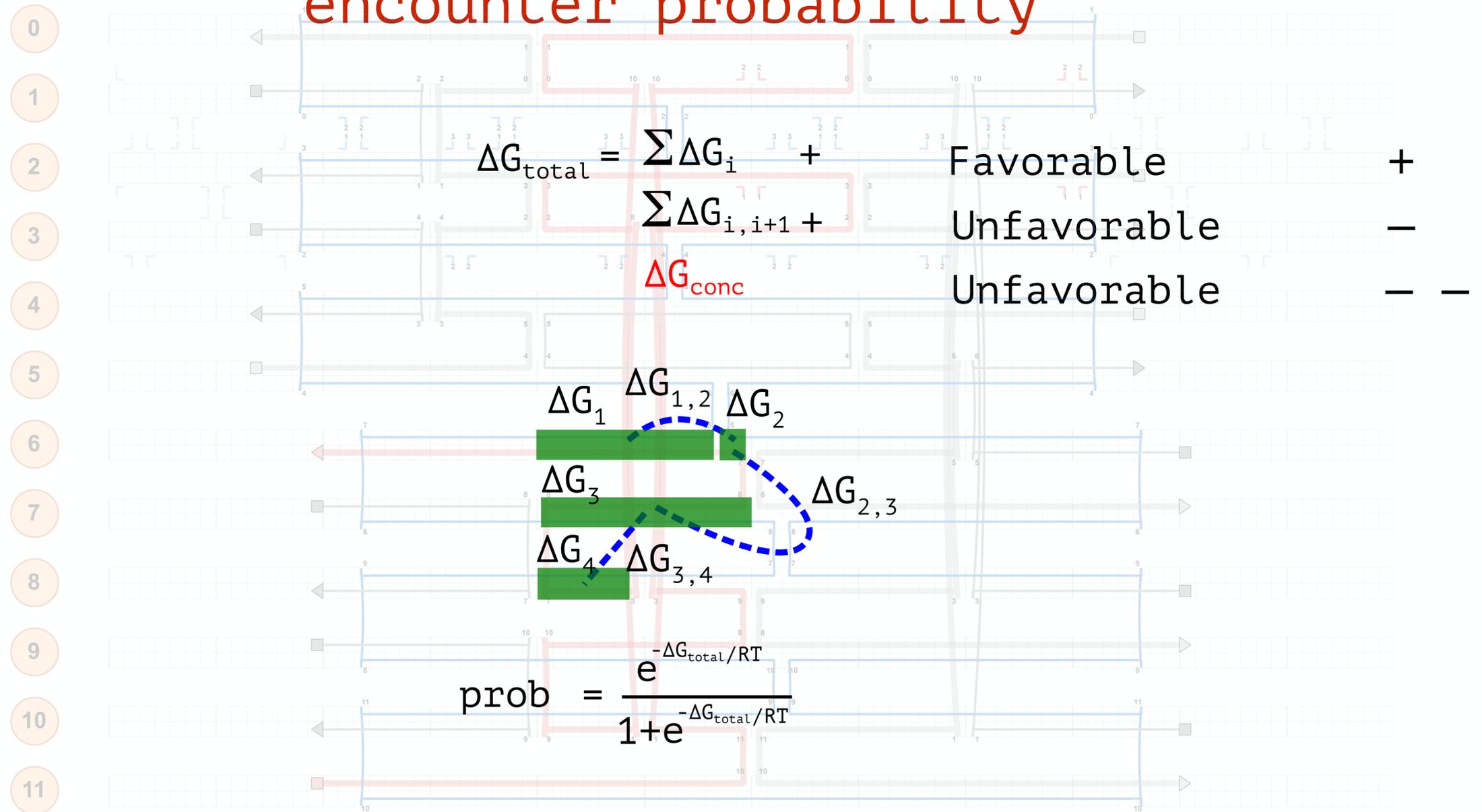
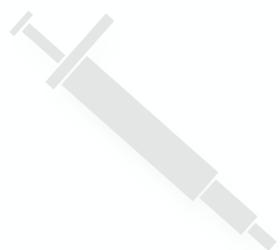
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autopipette

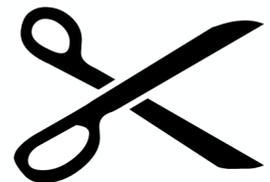


hybridization loop closure

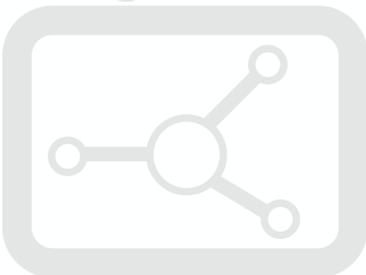
encounter probability

CTK

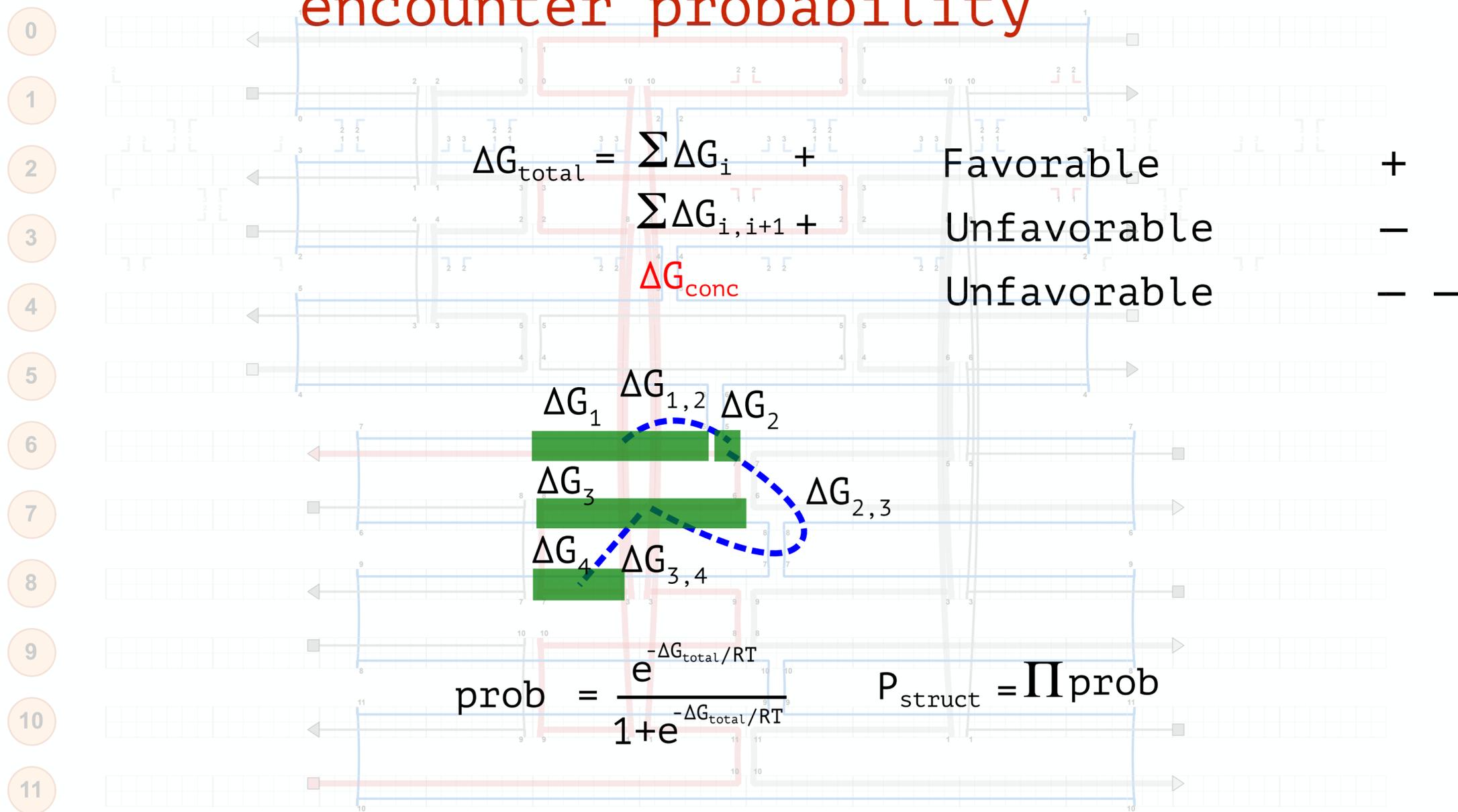
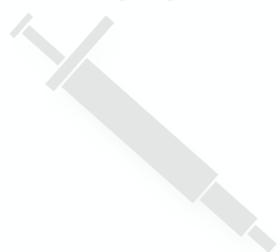
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origamisim



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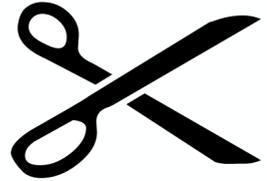


hybridization loop closure

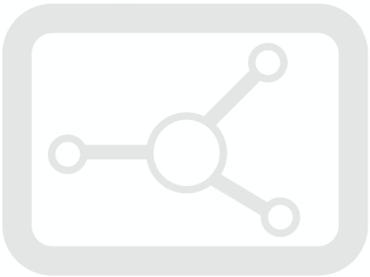
encounter probability

CTK

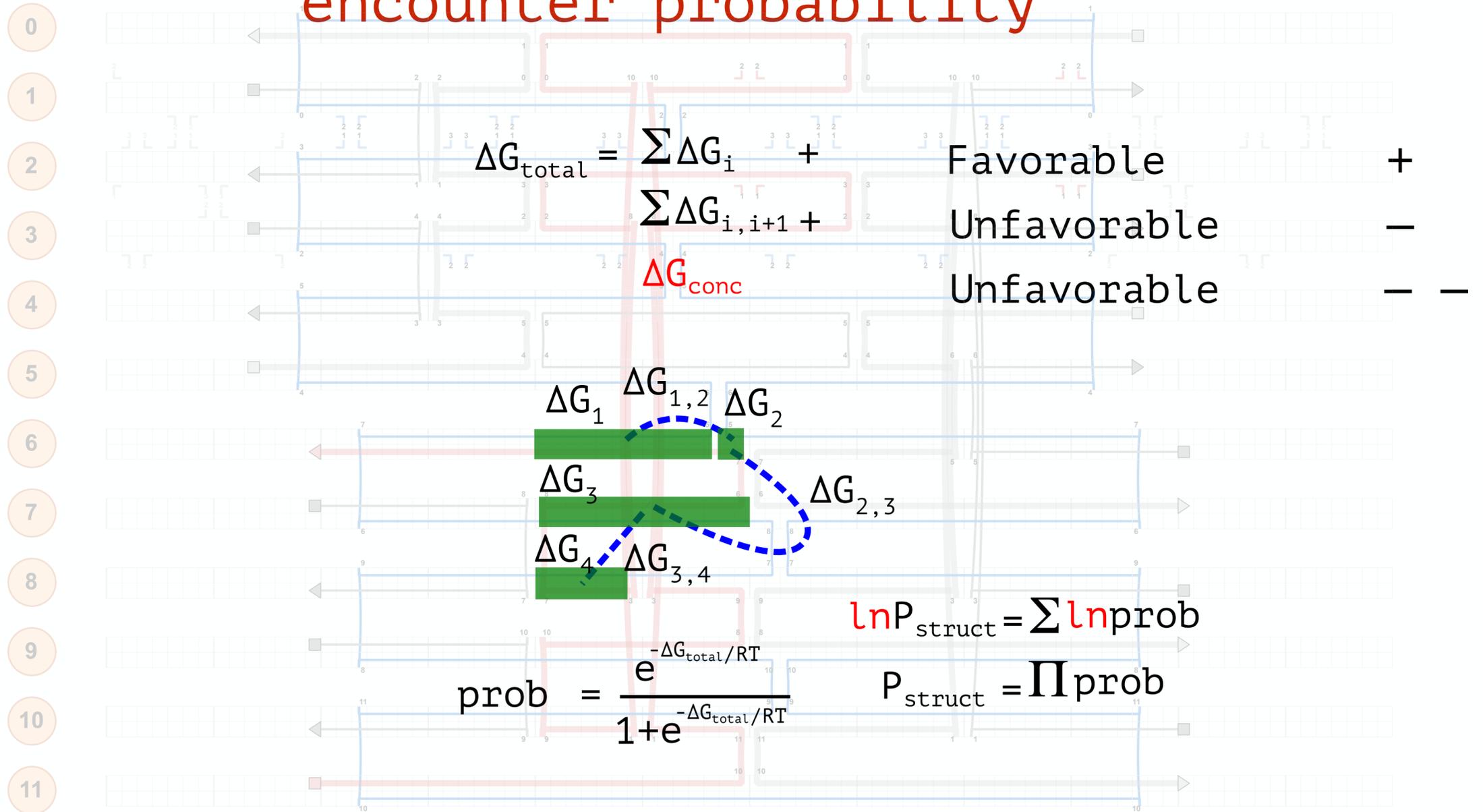
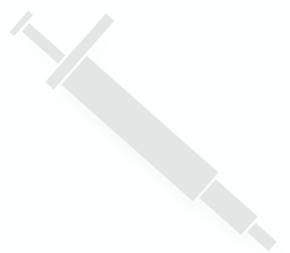
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origamisim

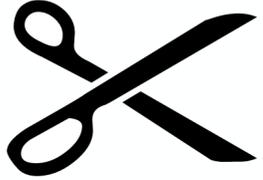


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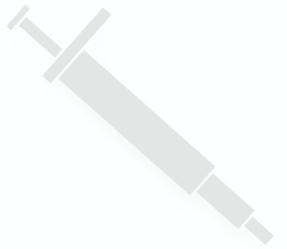
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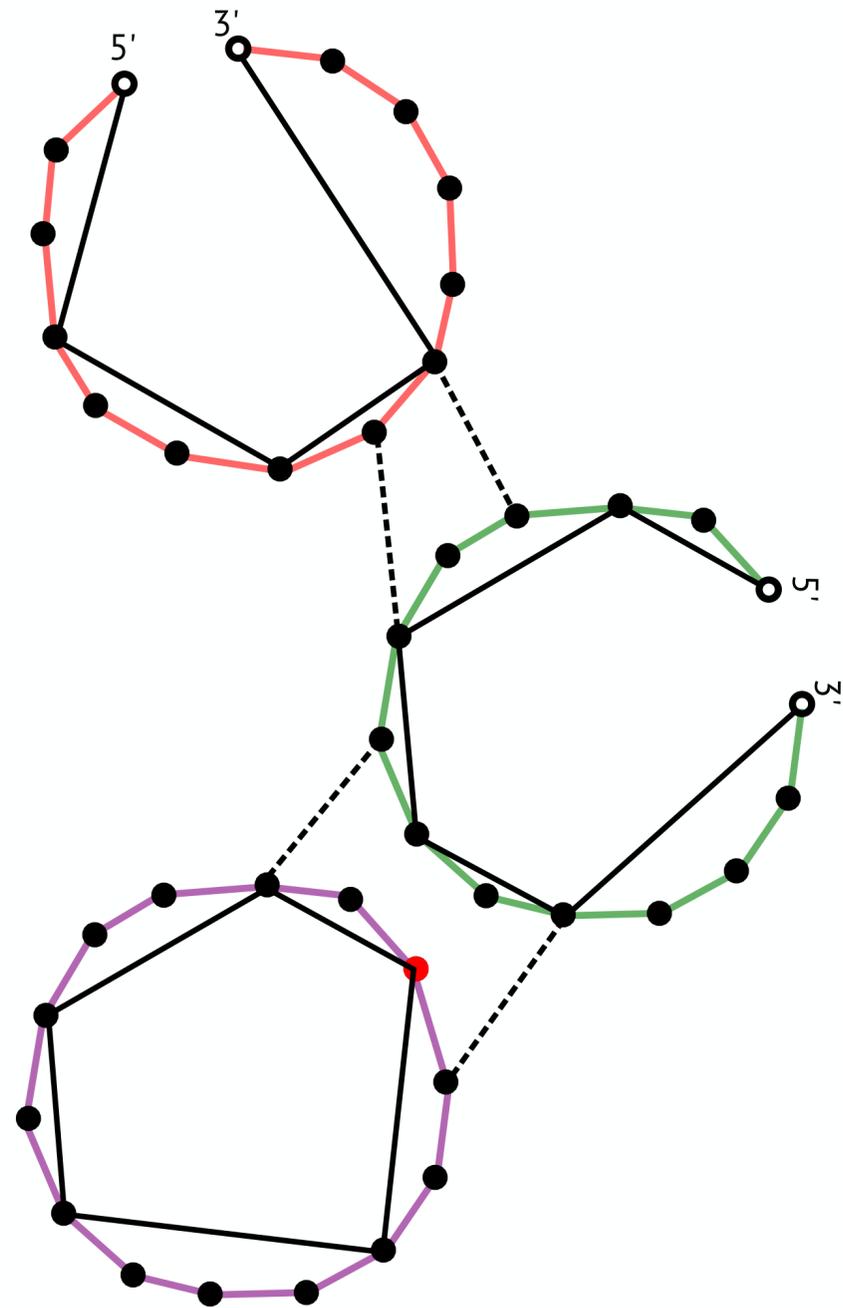
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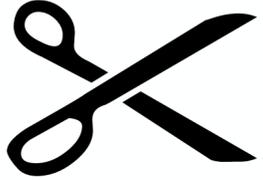


graph representation



CTK

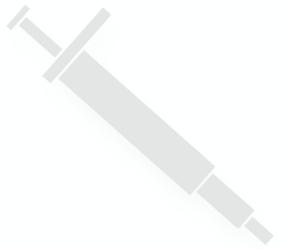
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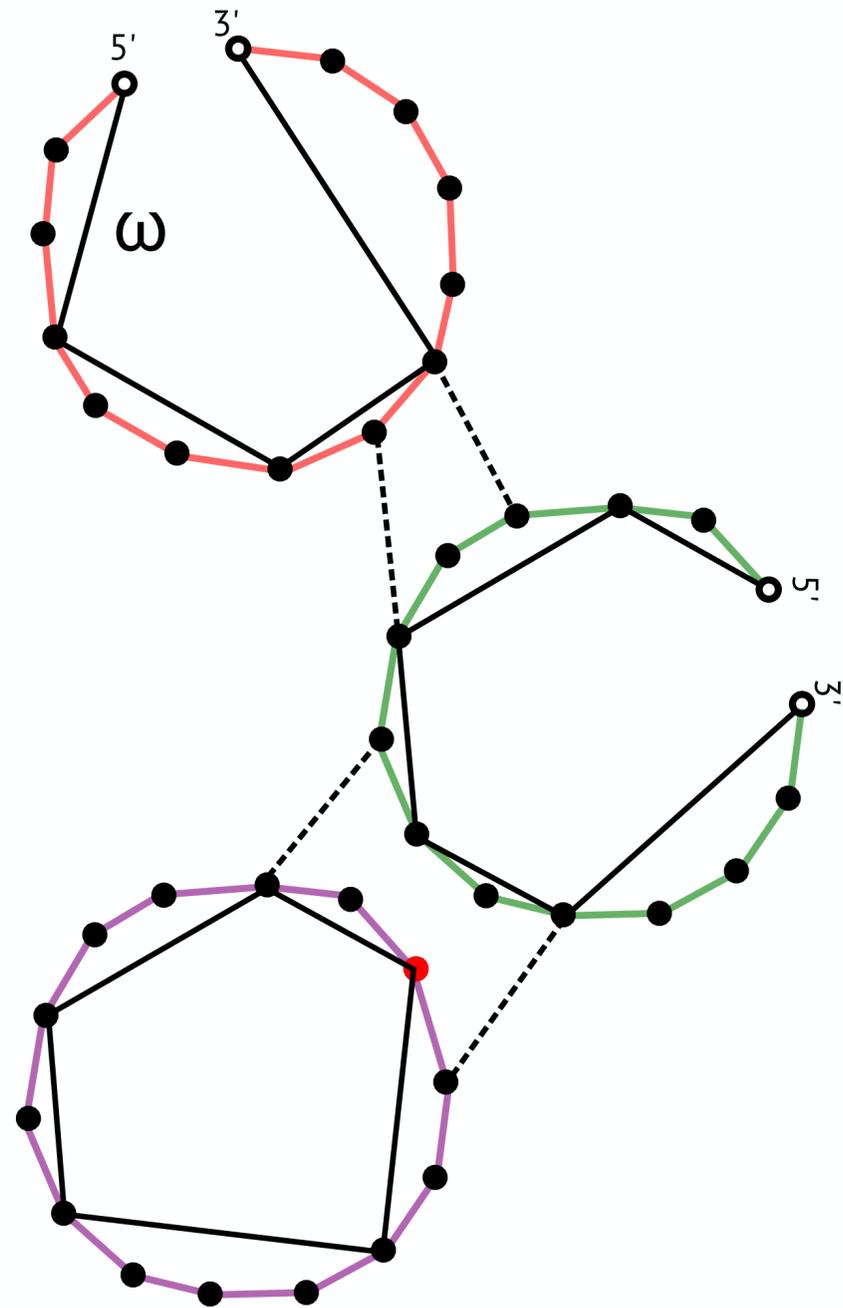
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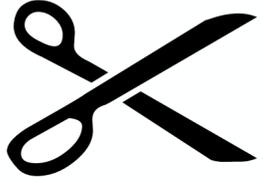


graph representation

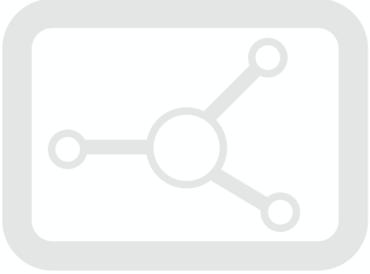


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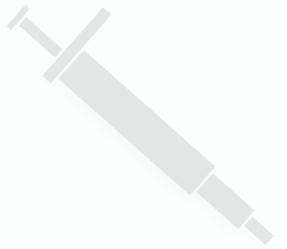
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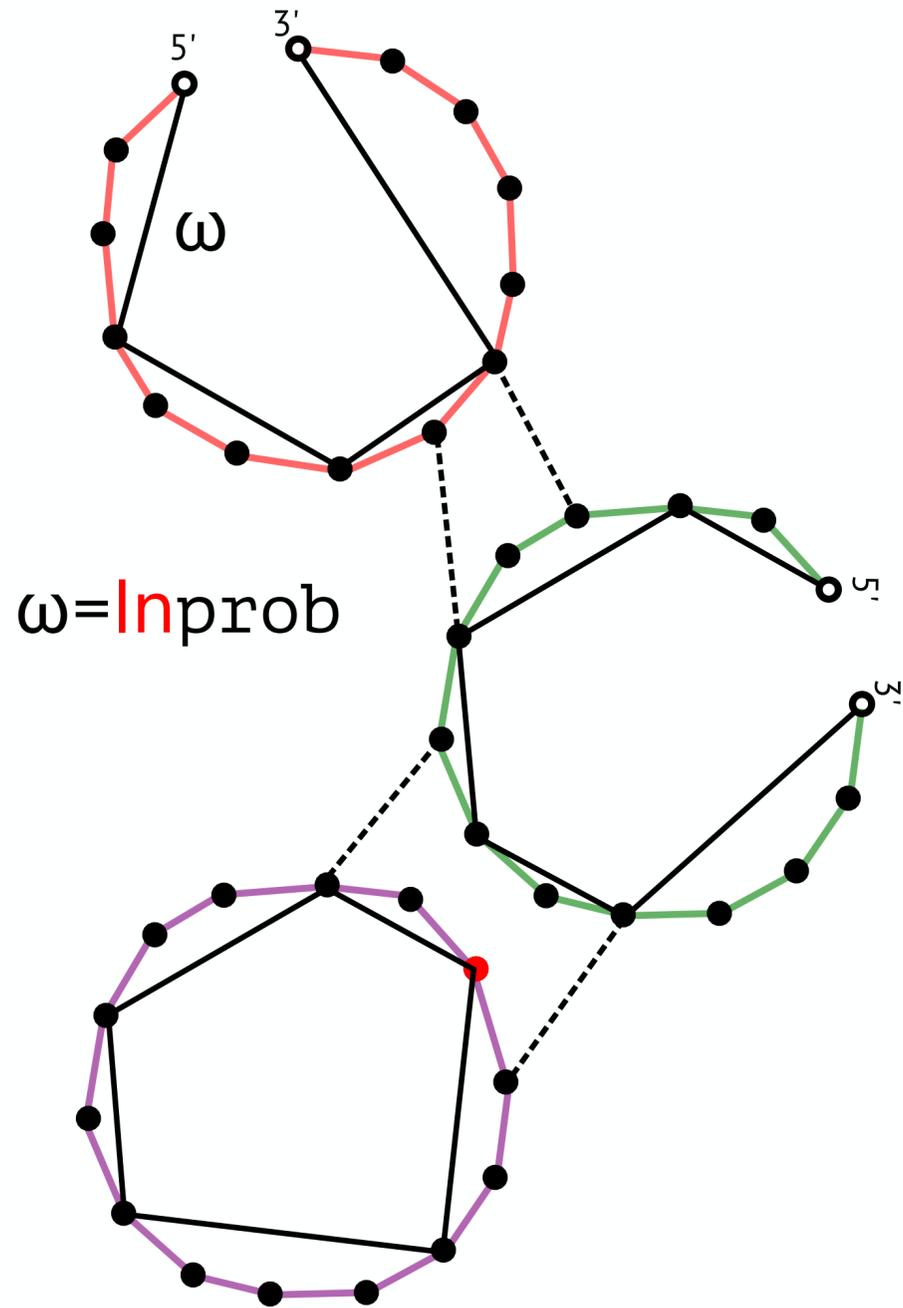
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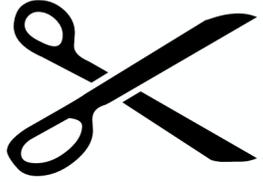
graph representation



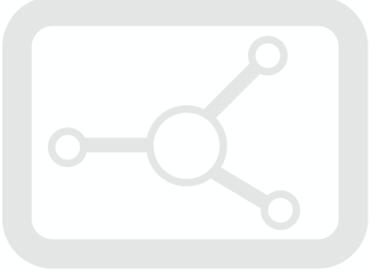
break positions

CTK

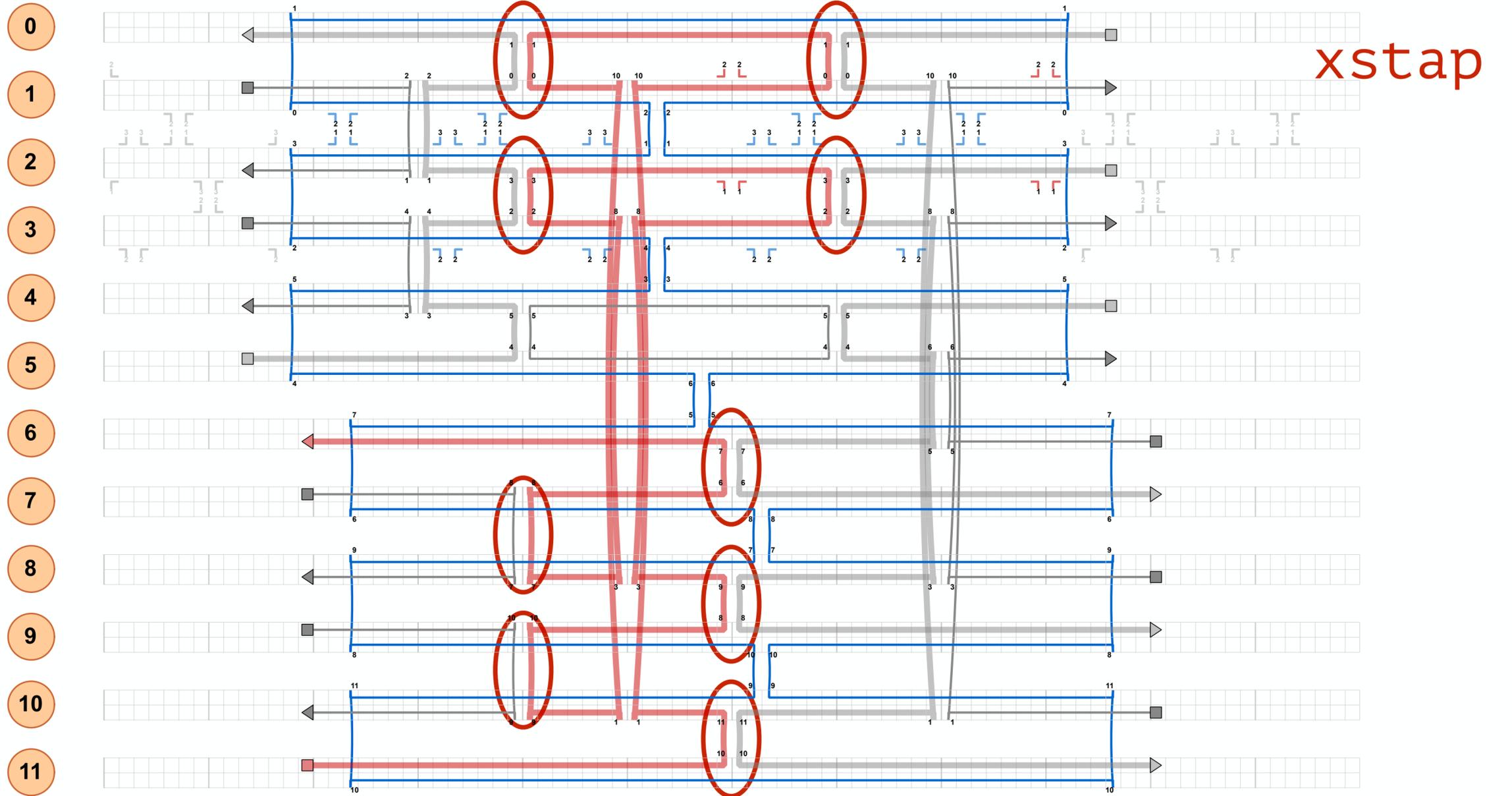
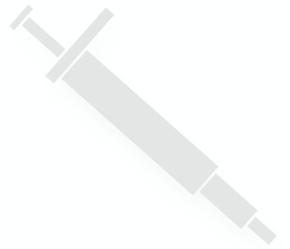
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break positions

CTK

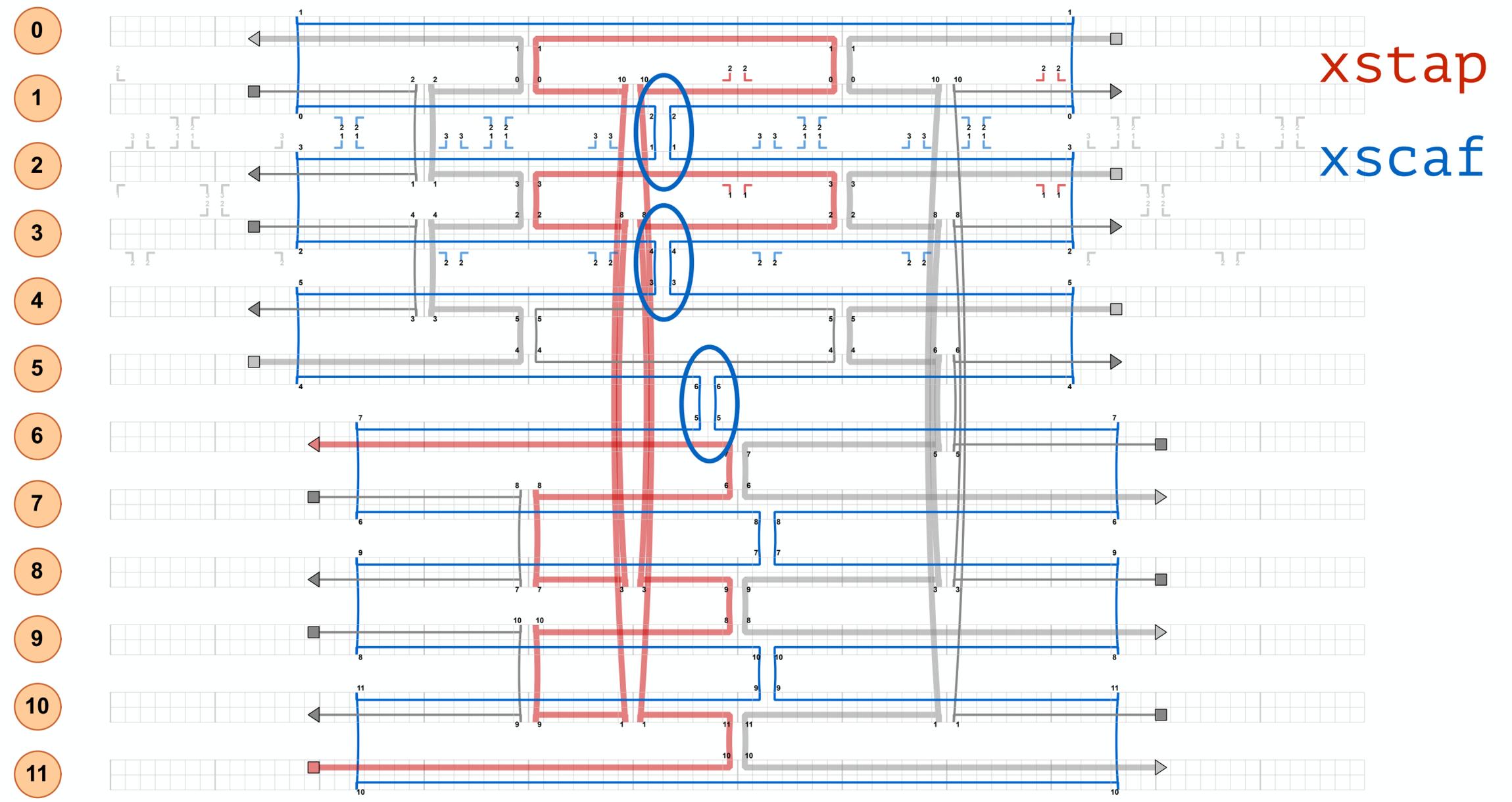
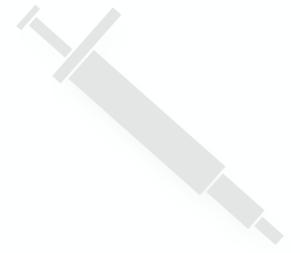
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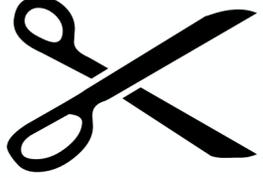
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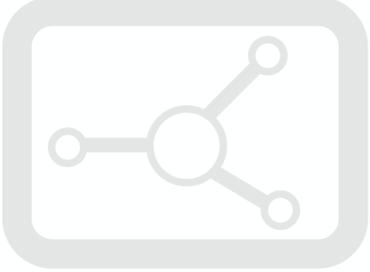
break positions

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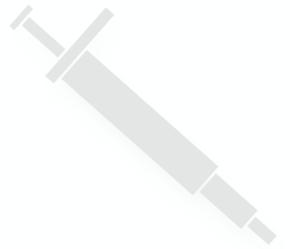
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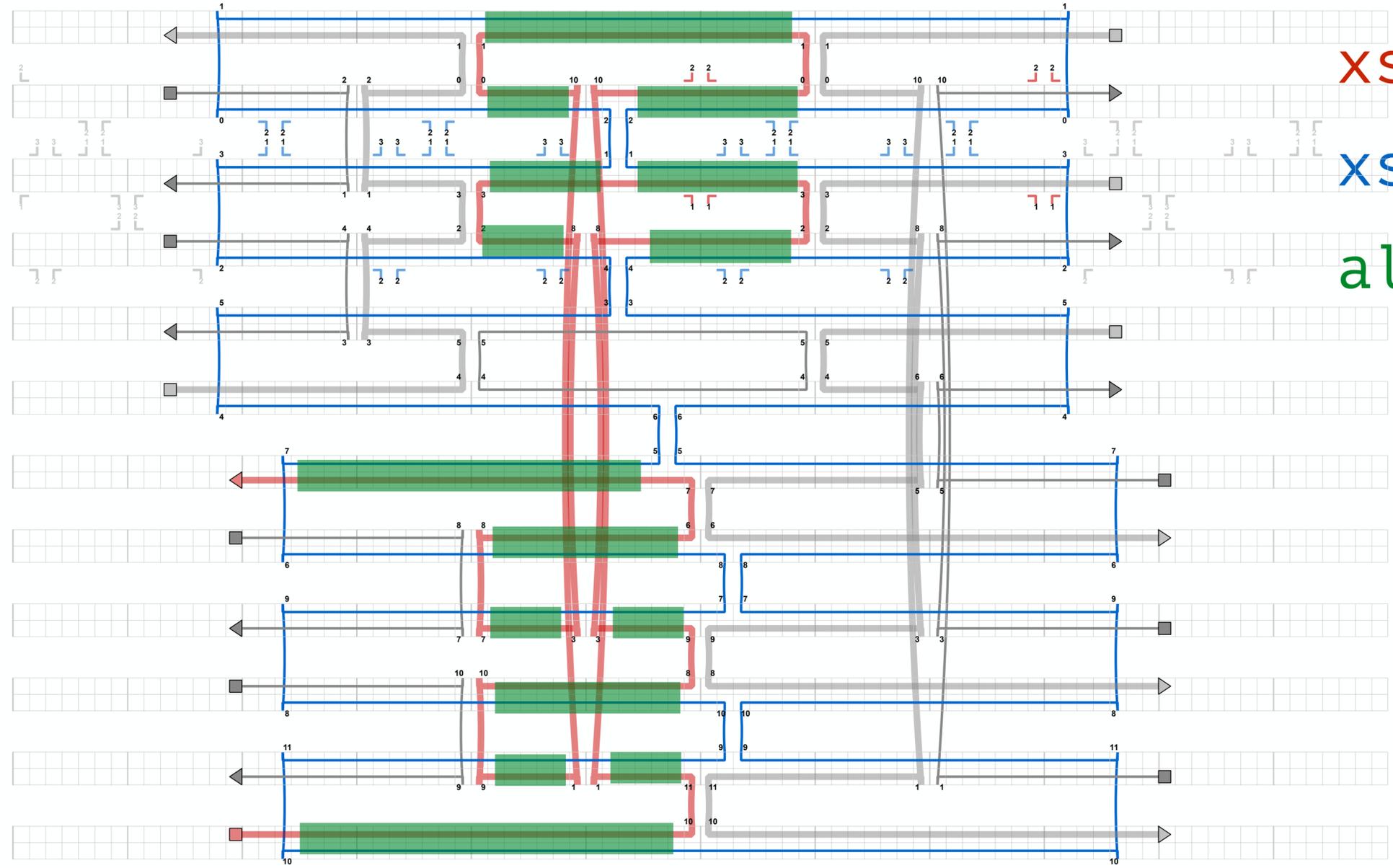
origamisim



autopipette



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- 2
- 3
- 4
- 5
- 6
- 7
- 8
- 9
- 10
- 11



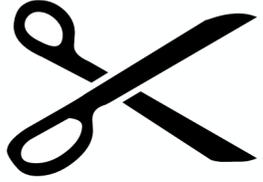
xstap

xscaf

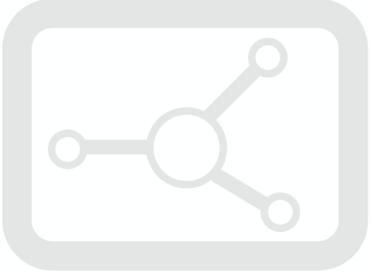
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CTK

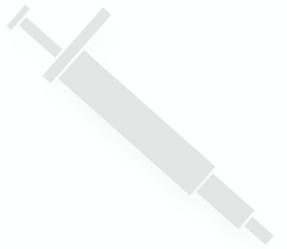
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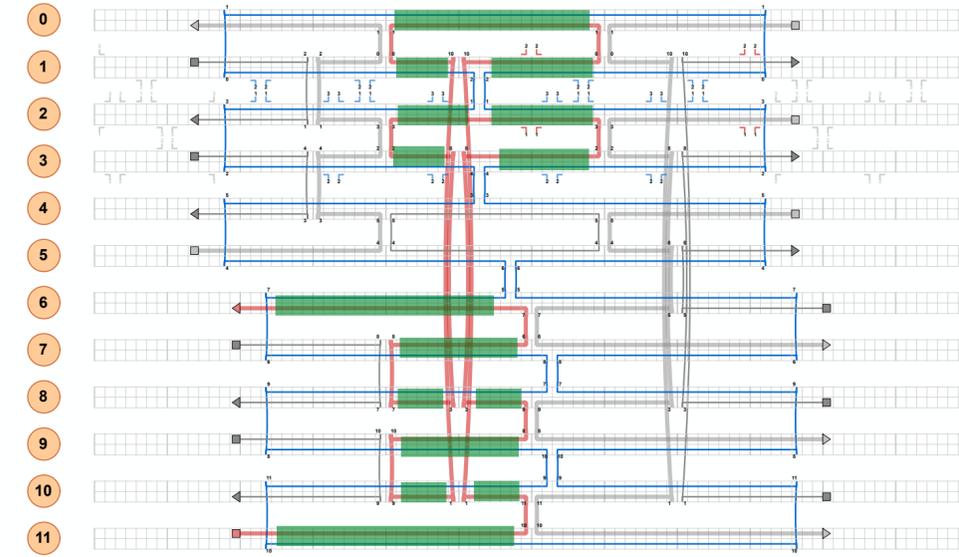
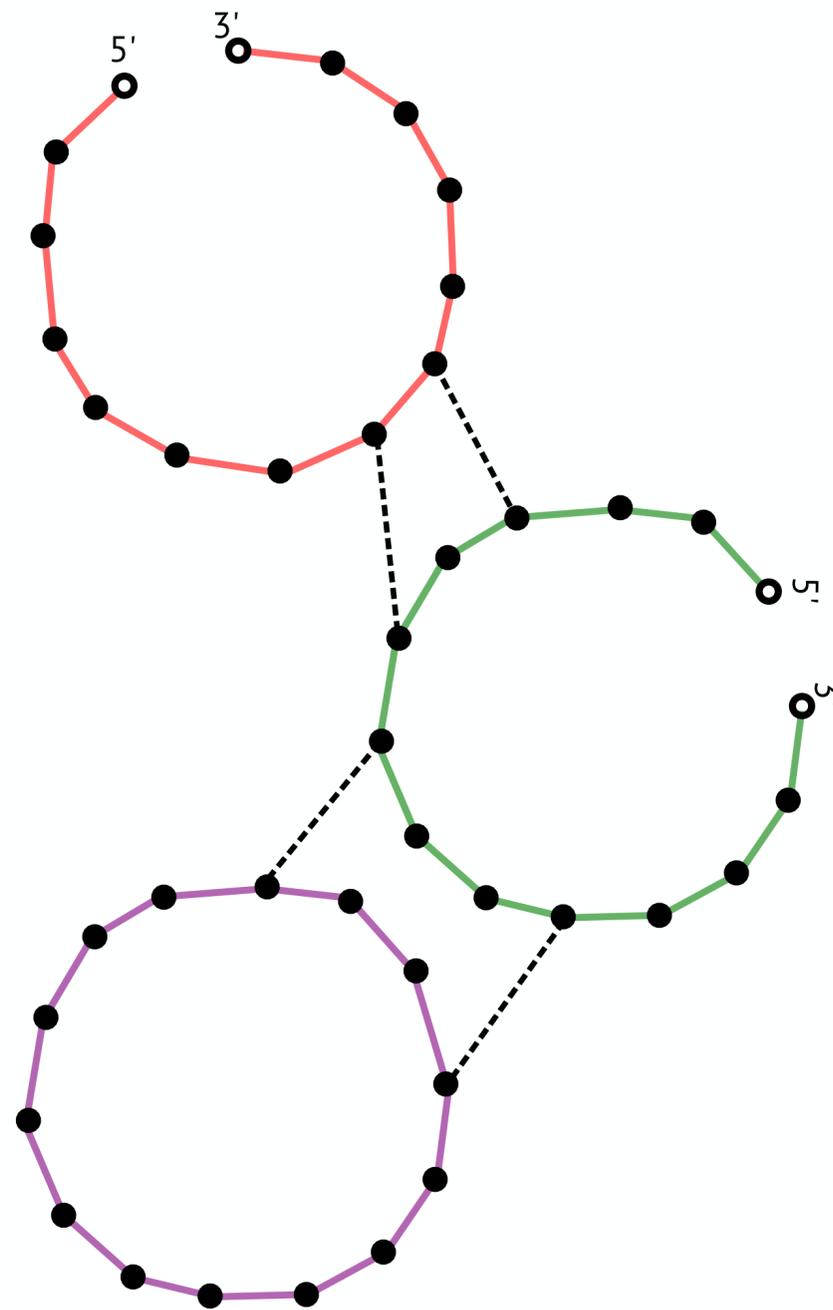
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autopipette



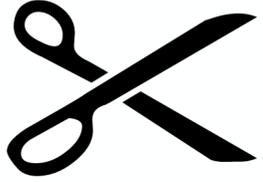
optimization algorithm



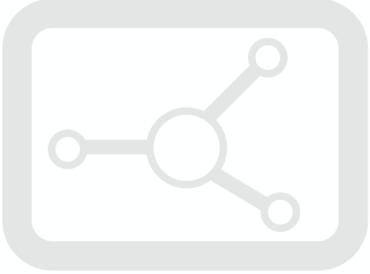
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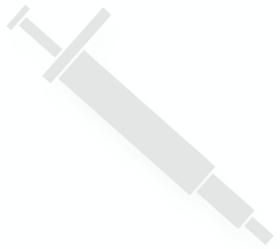
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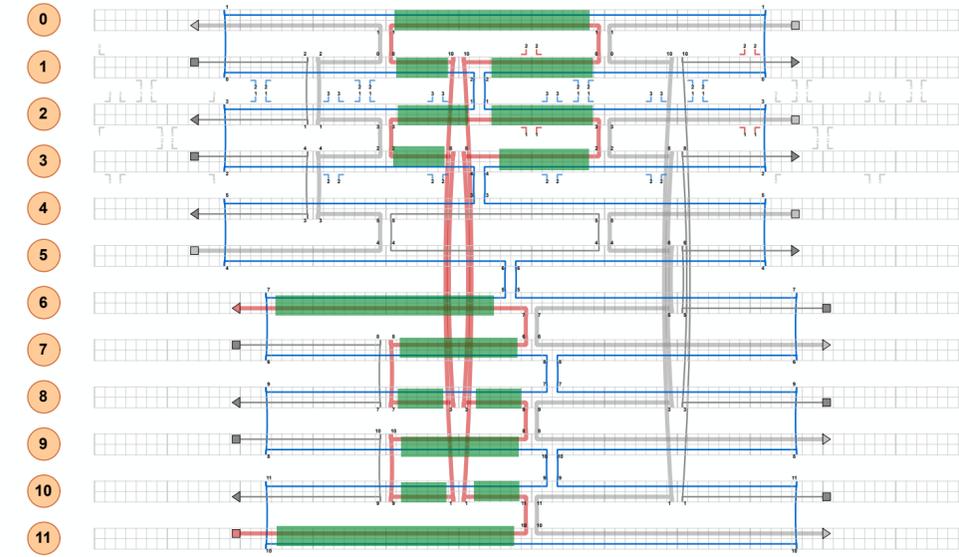
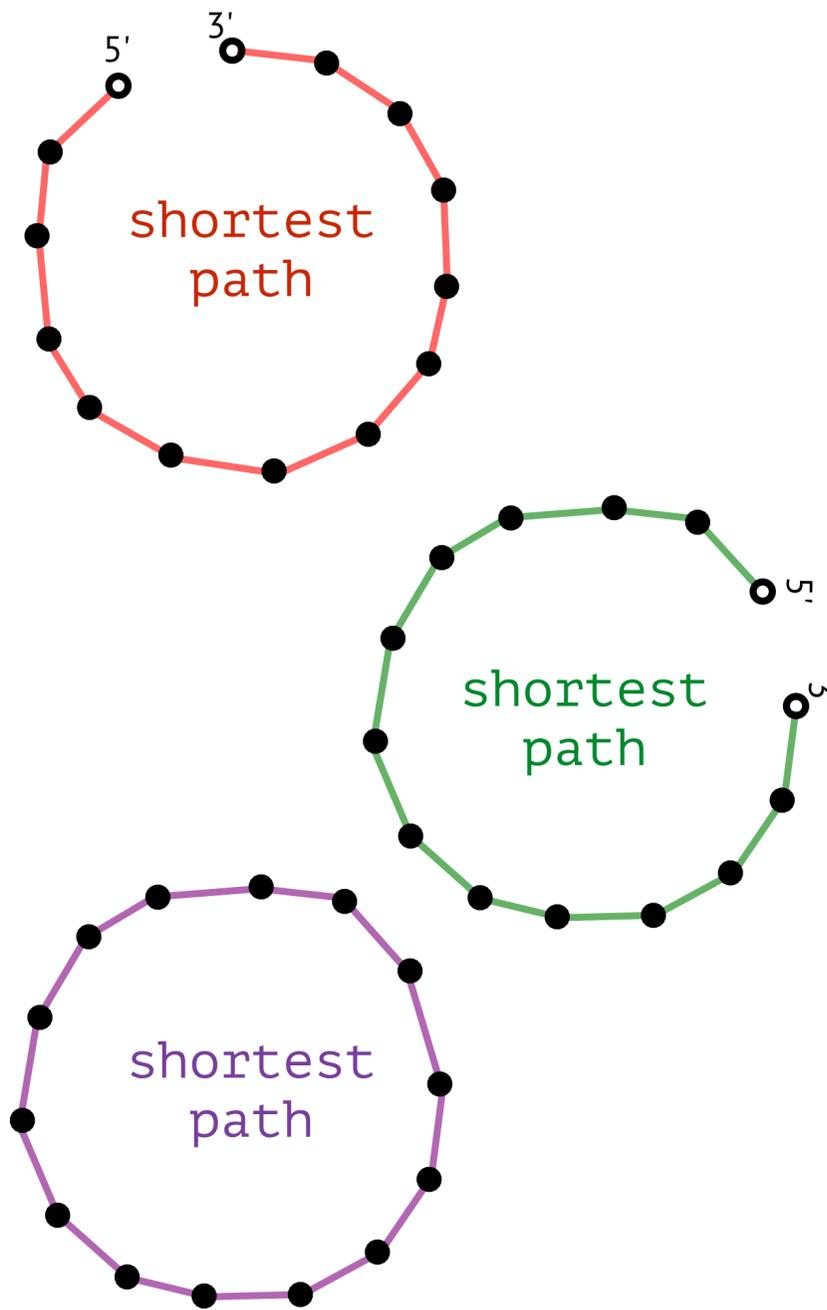
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autopipette



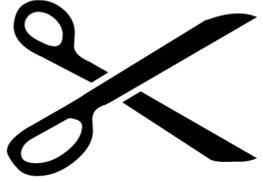
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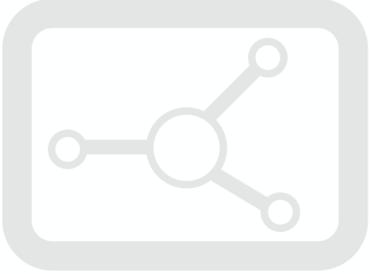
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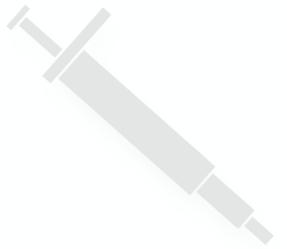
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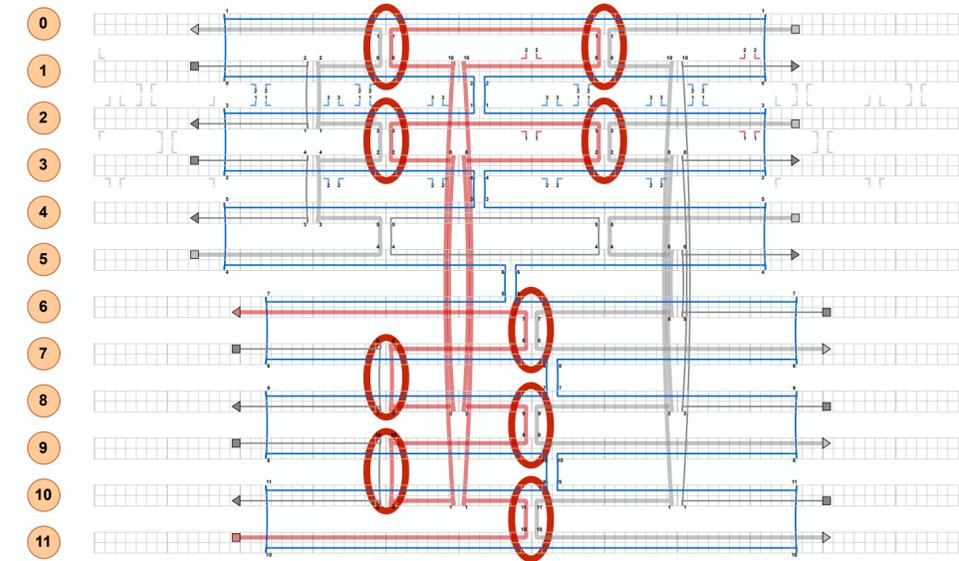
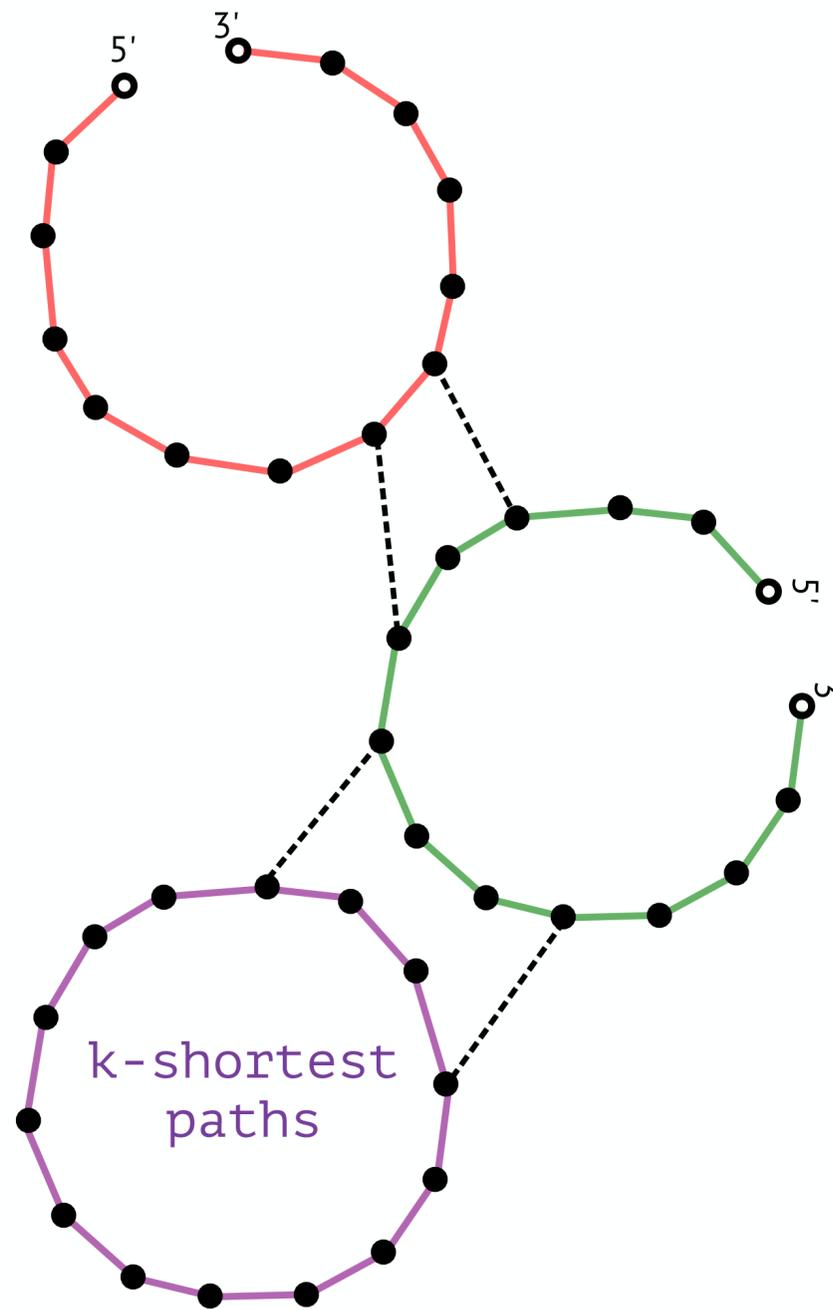
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autopipette



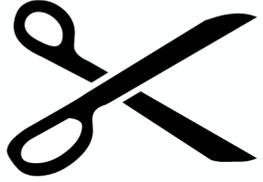
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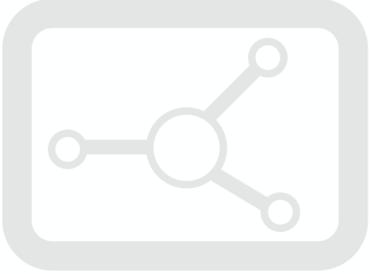
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CTK

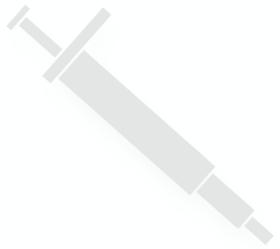
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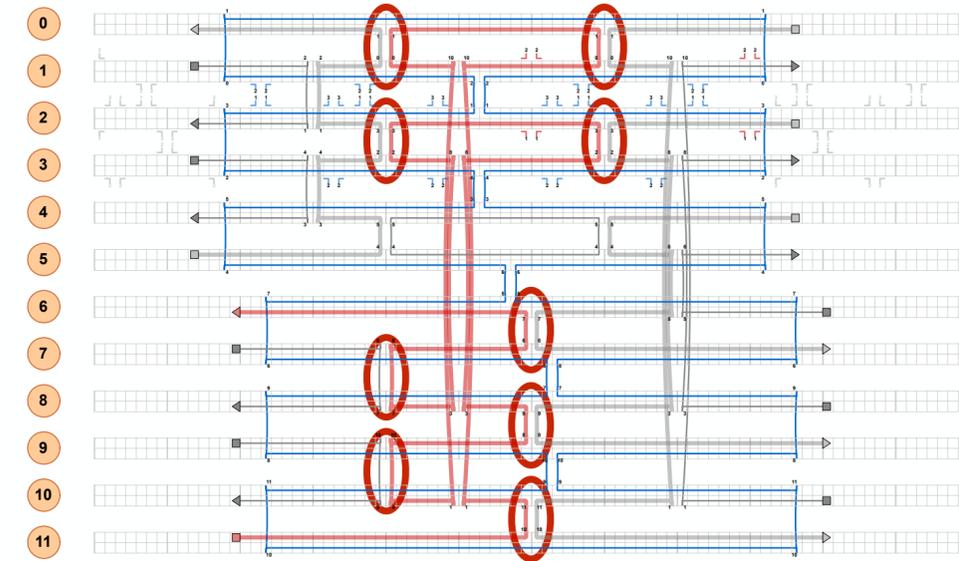
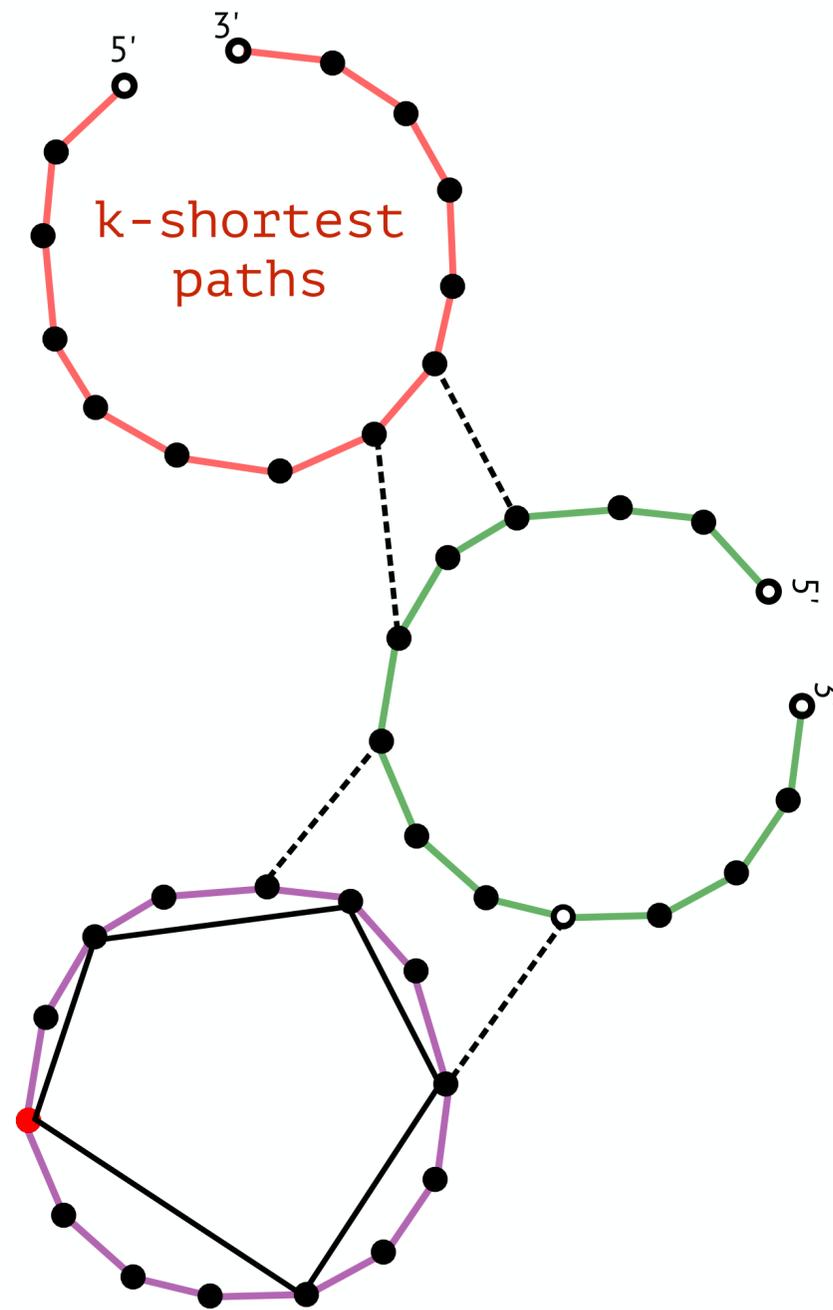
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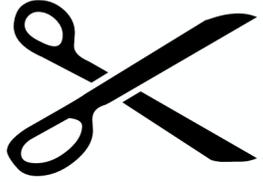
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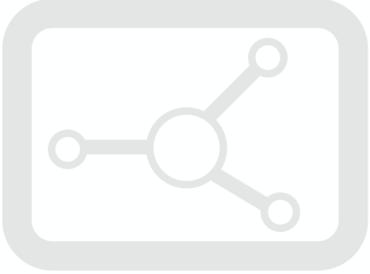
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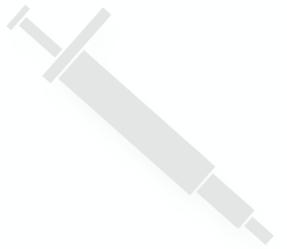
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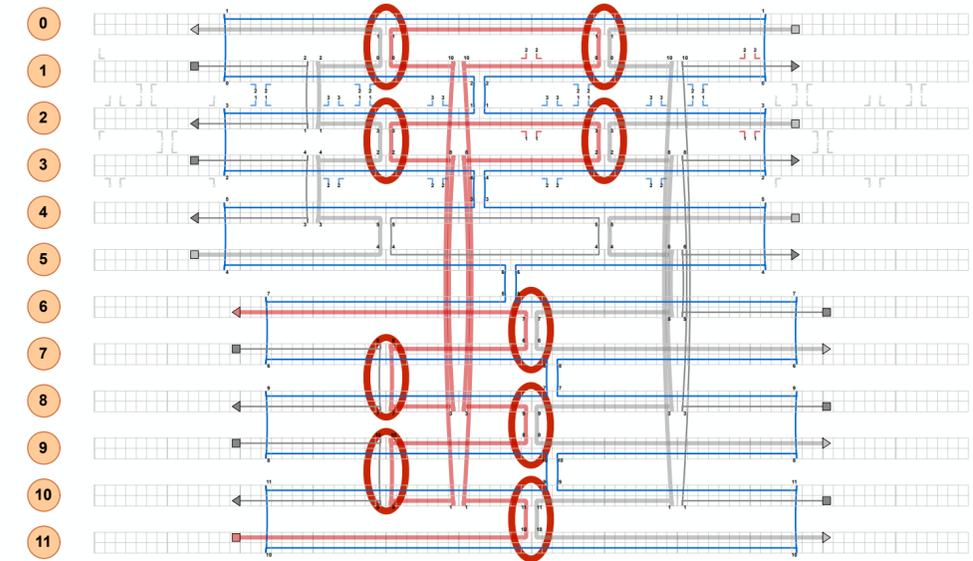
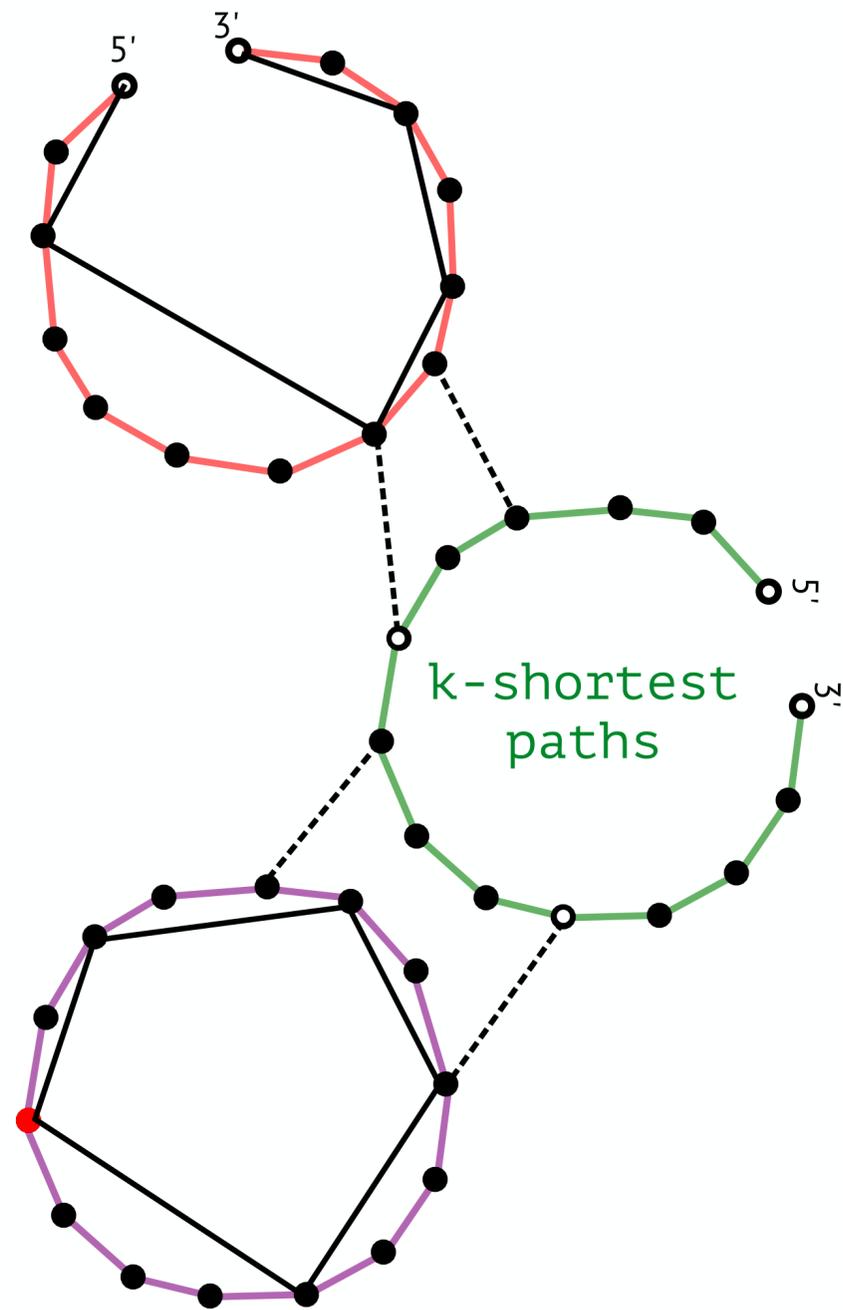
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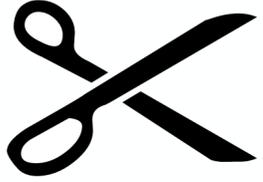


optimization algorithm

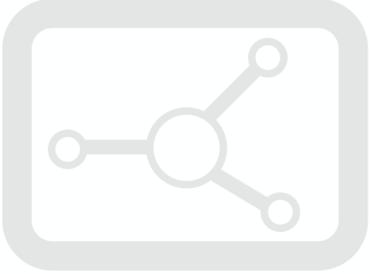


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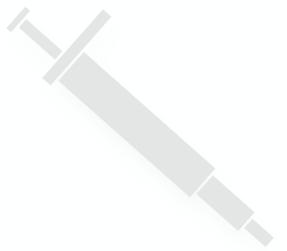
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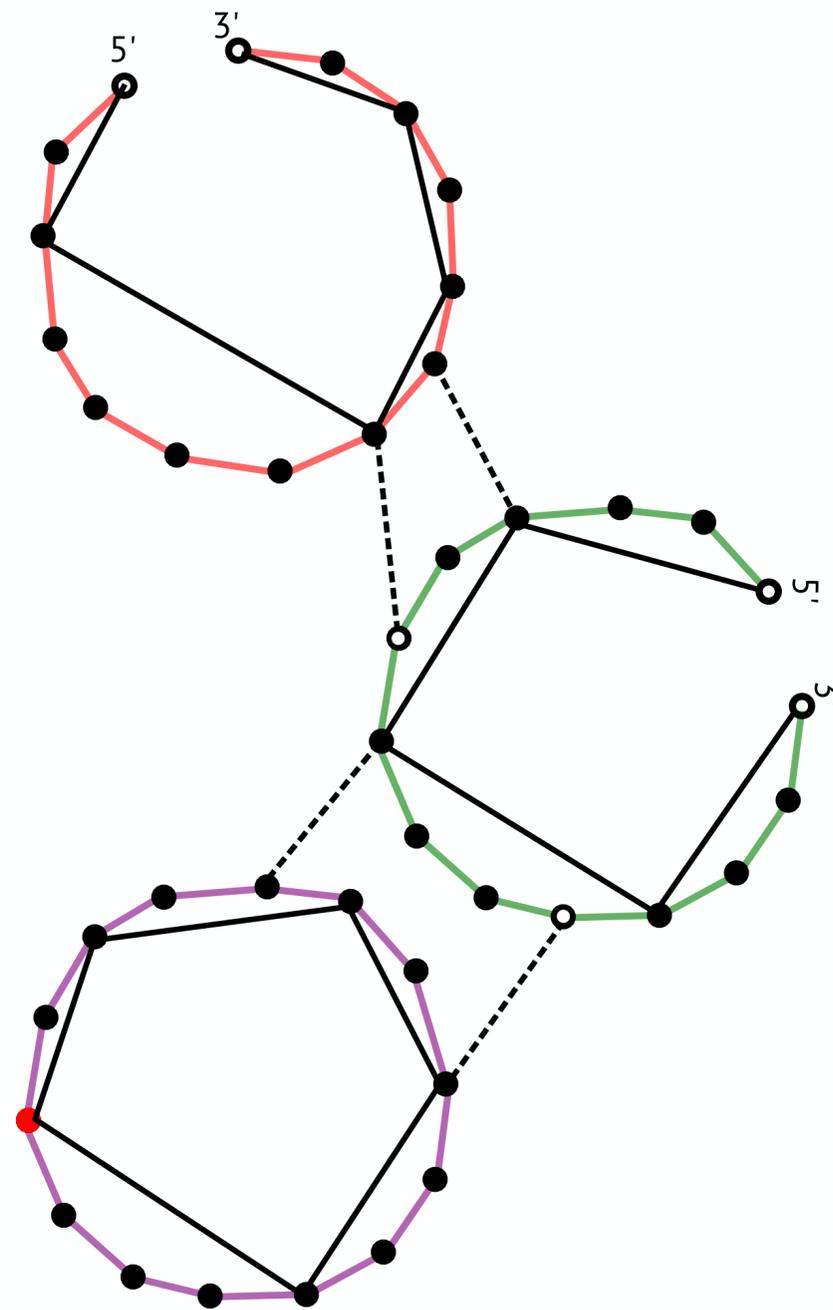
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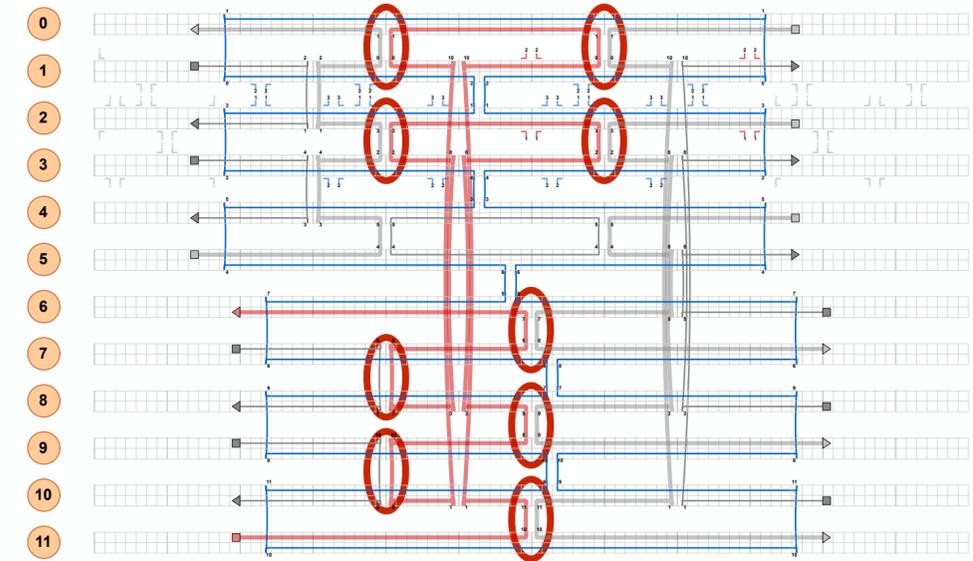
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optimization algorithm



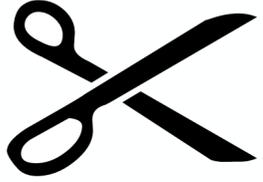
Repeat n times



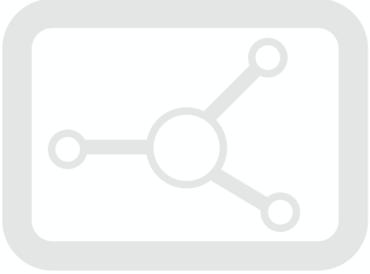
xstap

CTK

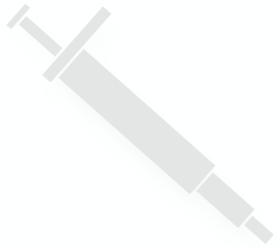
autobreak



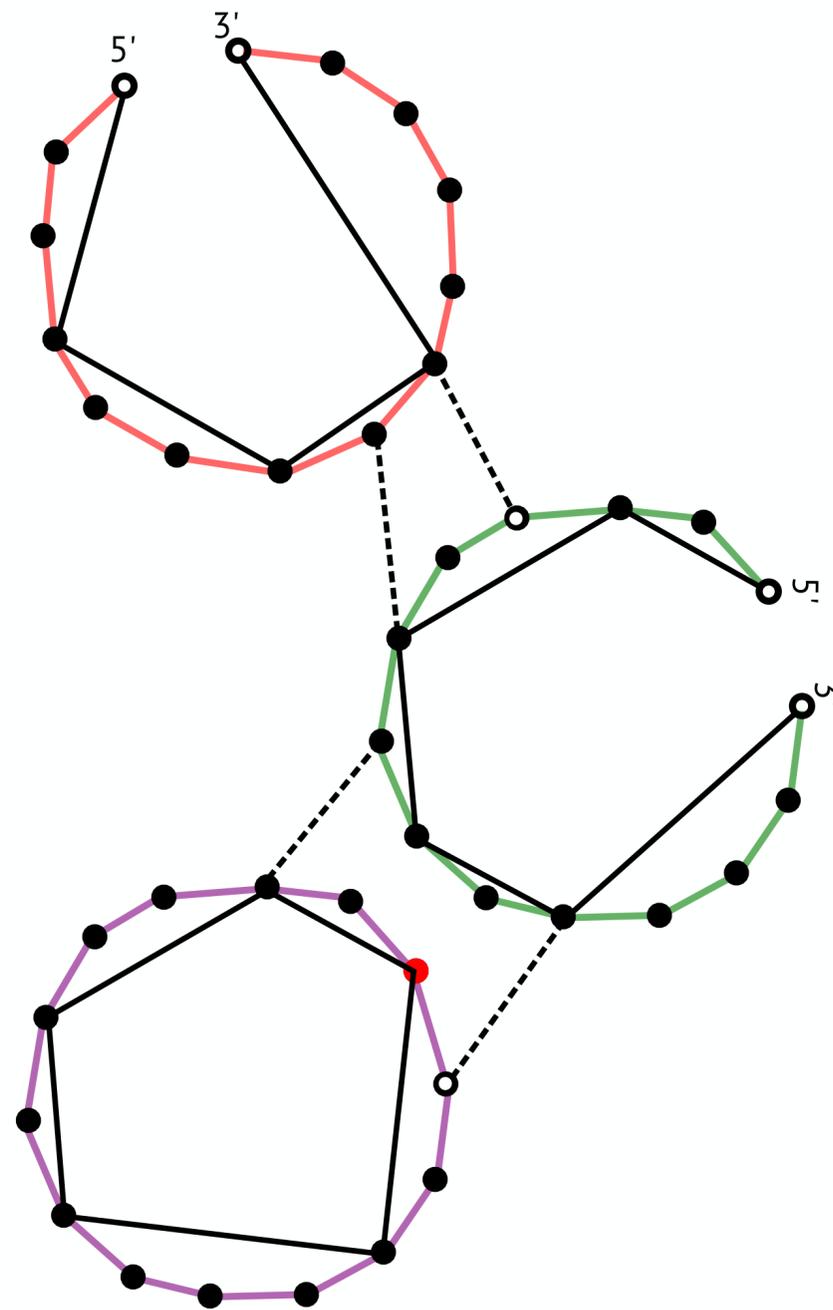
origamisim



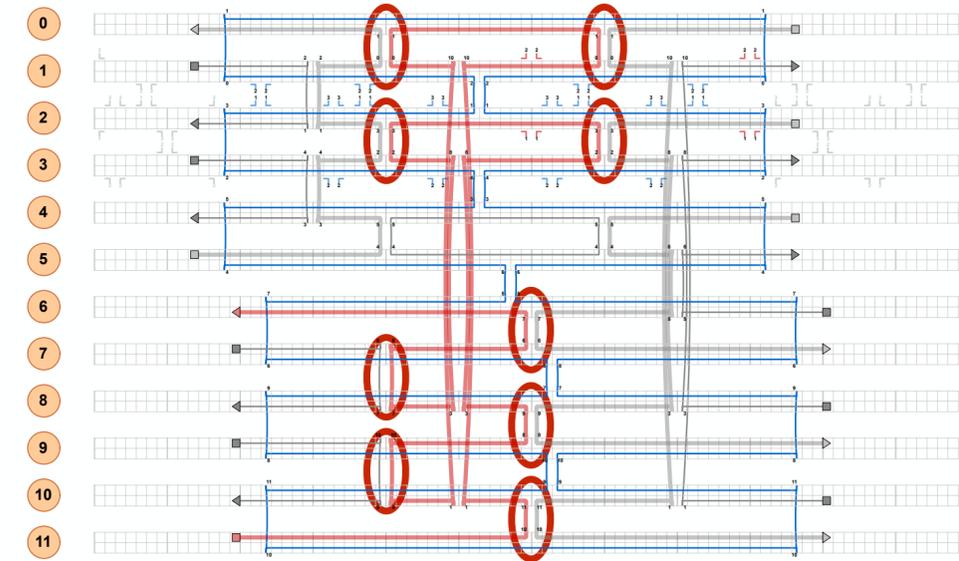
autopipette



optimization
algorithm



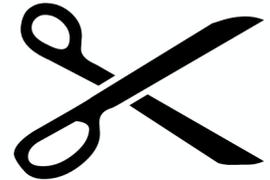
best solution



xstap

CTK

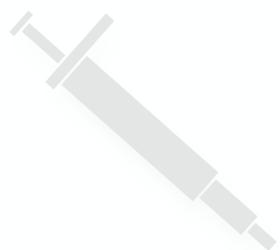
autobreak



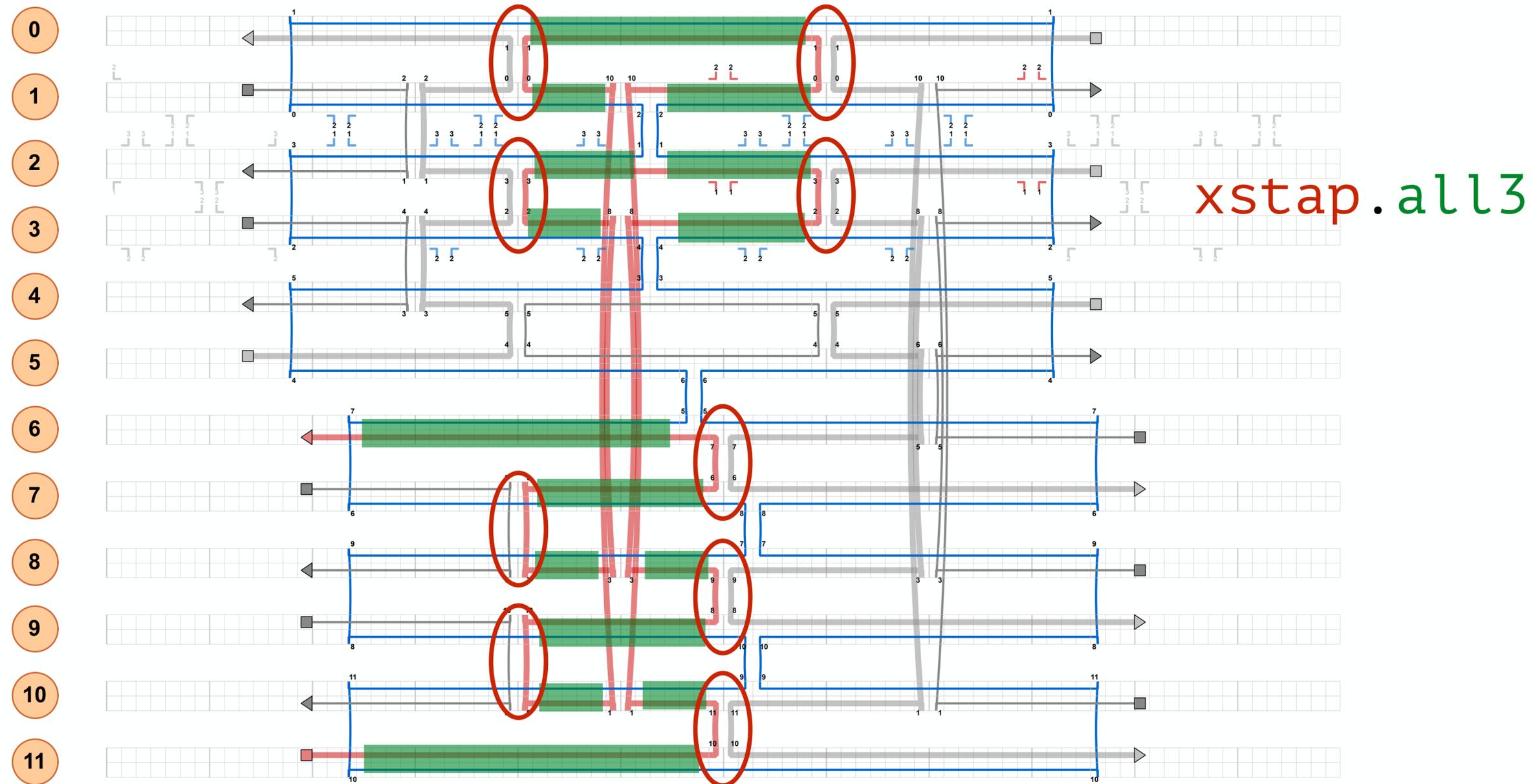
origamisim



autopipette



recommended setting

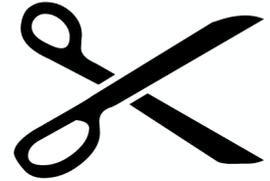


```
autobreak.py -i design.json -rule xstap.all3 -seq p8064
```

extra features

CTK

autobreak



- Sequence permutation
- Read-only option to score previous designs

origamisim



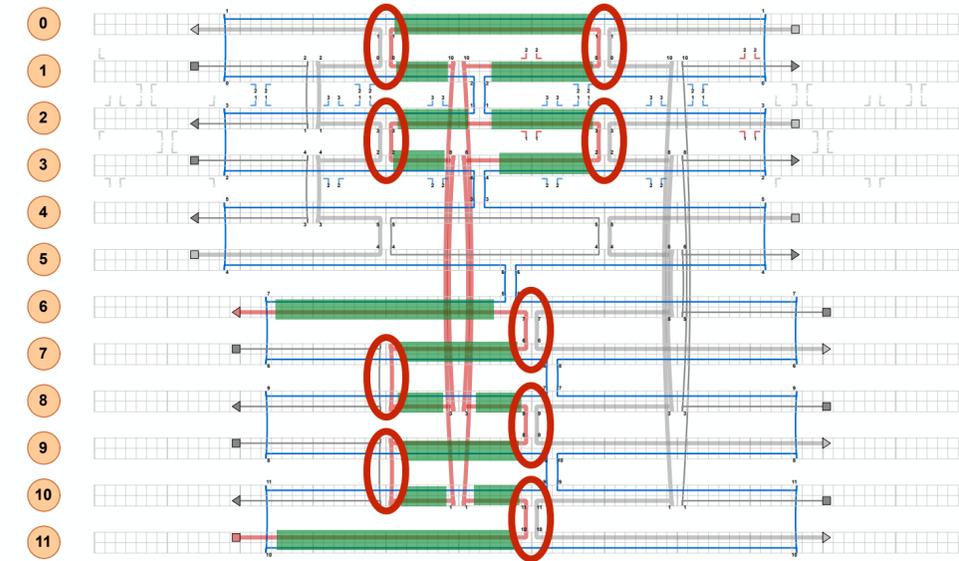
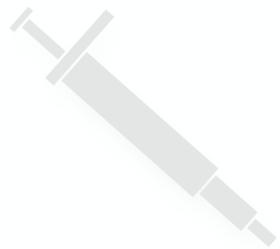
Recommended:

Sequence permutation in
read-only mode

staple length constraints:

- Max staple length:60
- Min staple length:14

autopipette



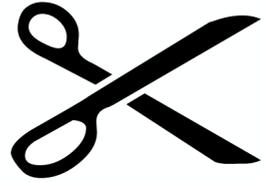
`xstap.all3`

```
autobreak.py -i design_autobreak.json -readonly -permute -npermute 8064
```

design1.json

CTK

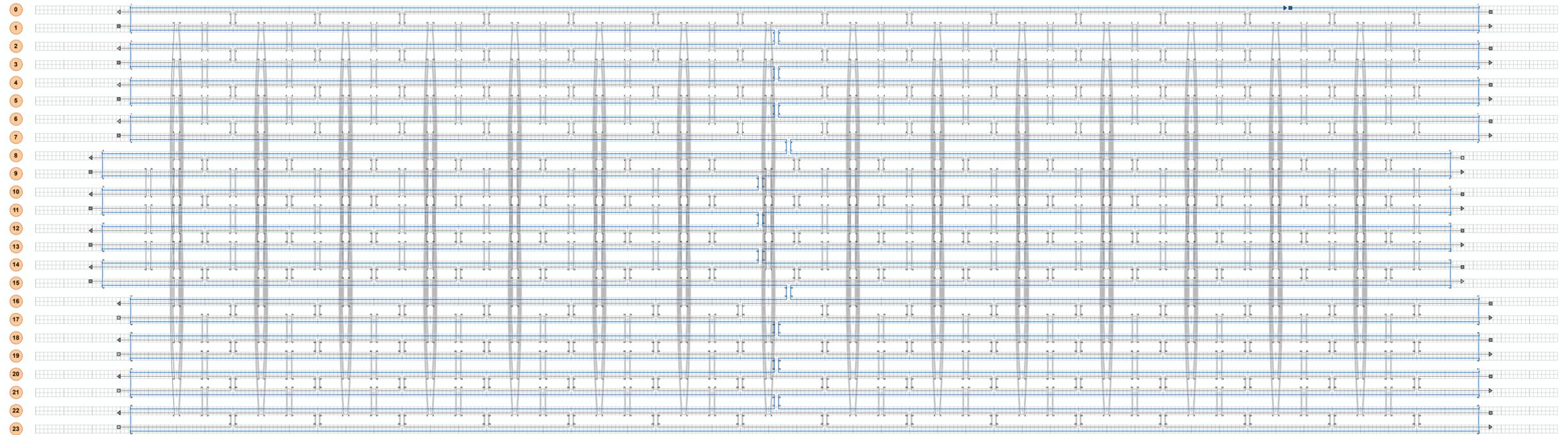
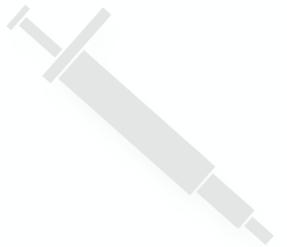
autobreak



origamisim



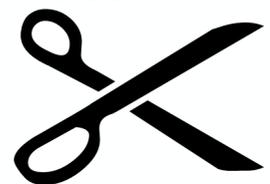
autopipette



design1_autobreak.json

CTK

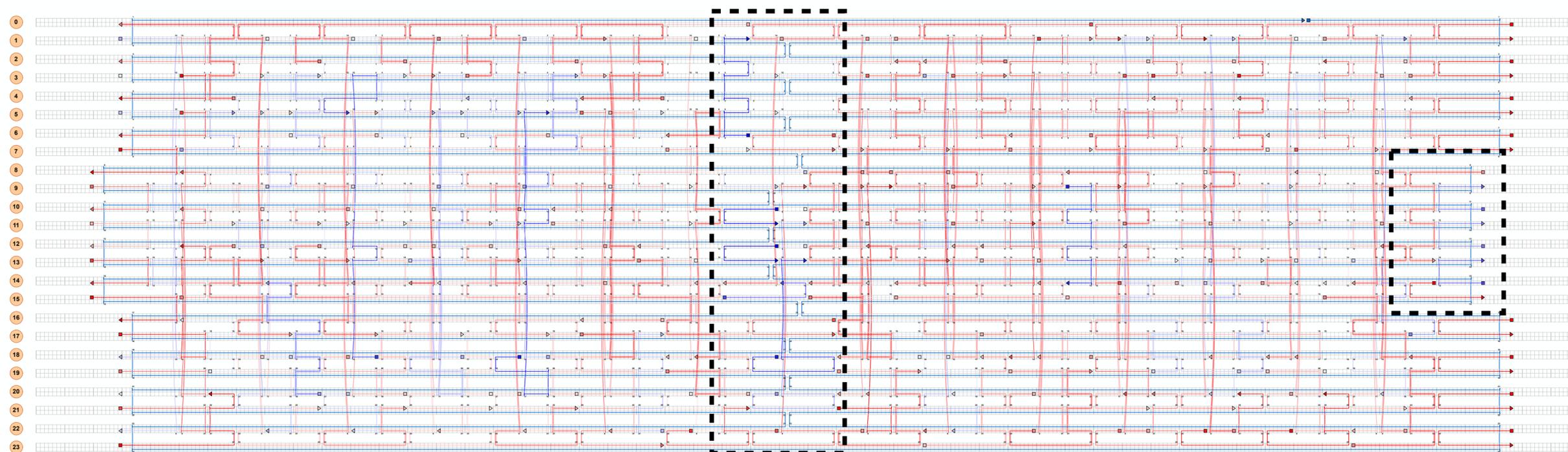
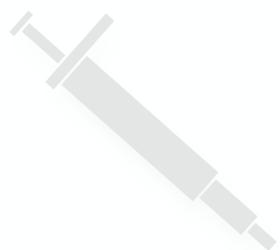
autobreak



origamisim



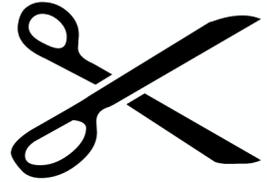
autopipette



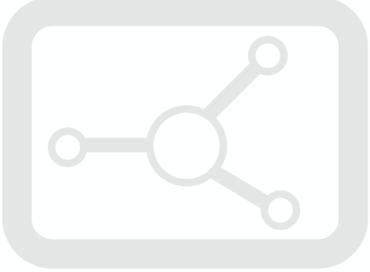
design2.json

CTK

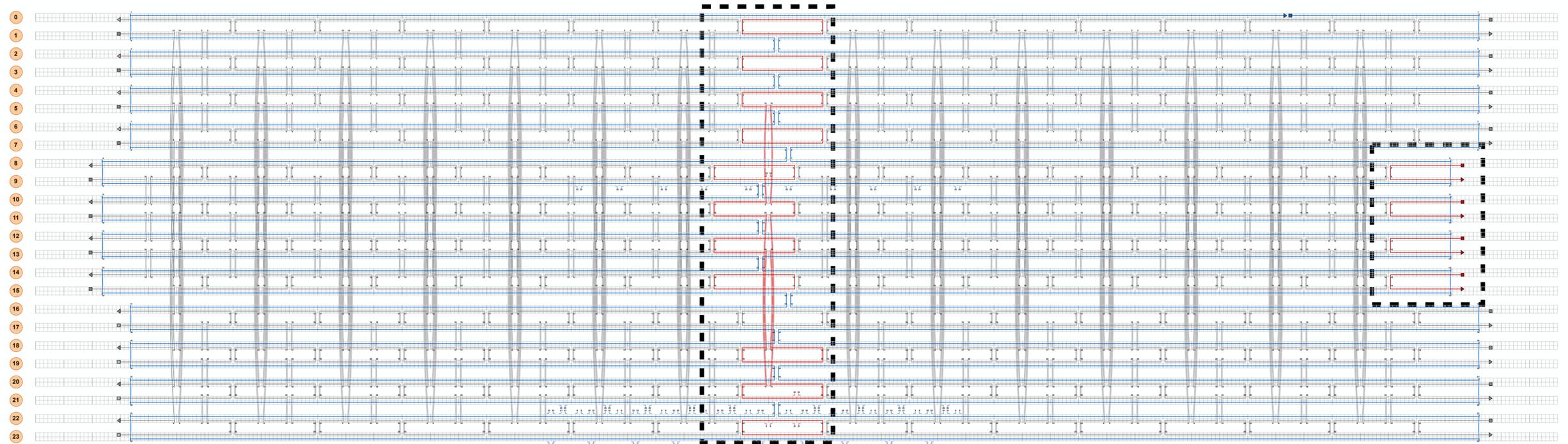
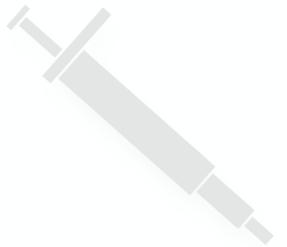
autobreak



origamisim



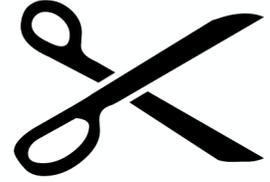
autopipette



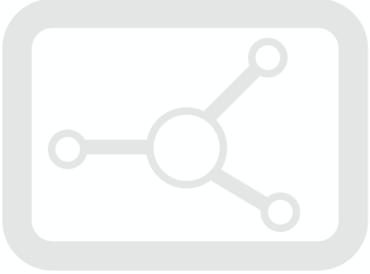
design2_autobreak.json

CTK

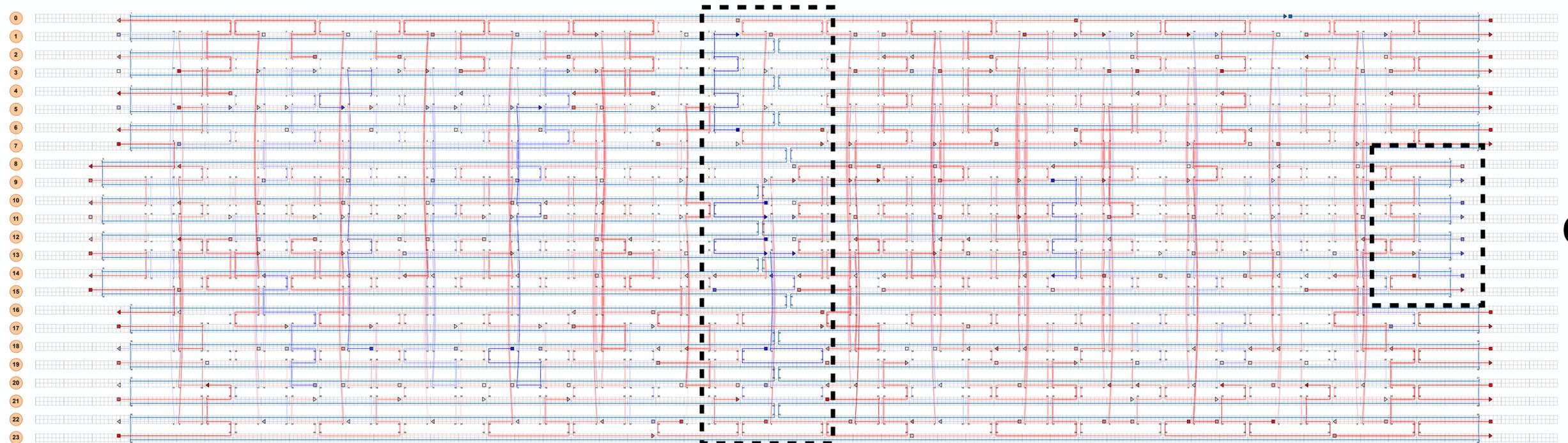
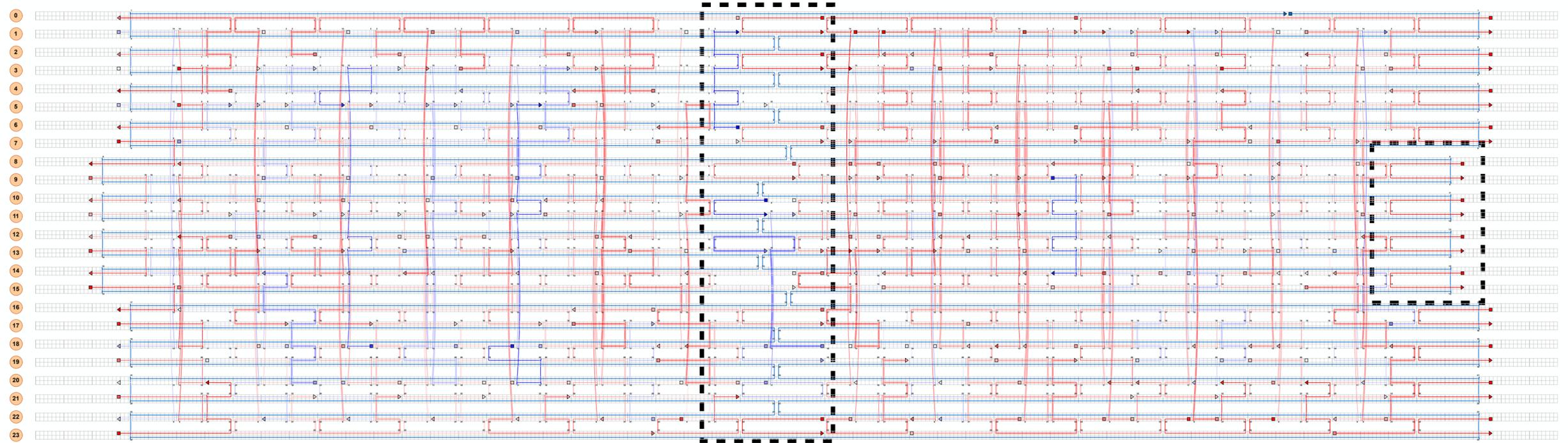
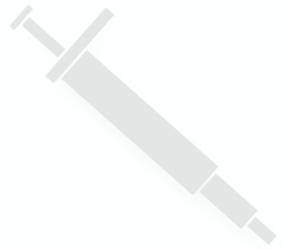
autobreak



origamisim



autopipette



old

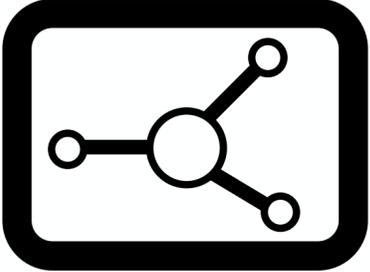
origamisim for rapid DNA origami structure prediction

CTK

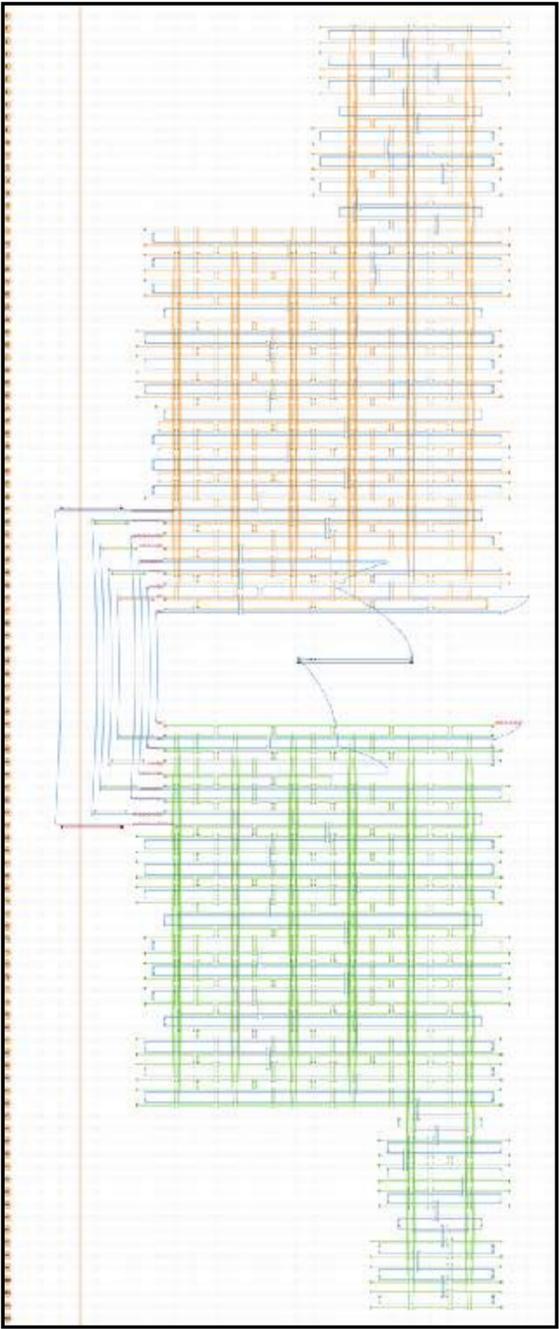
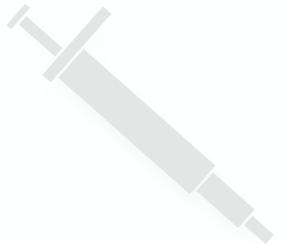
autobreak



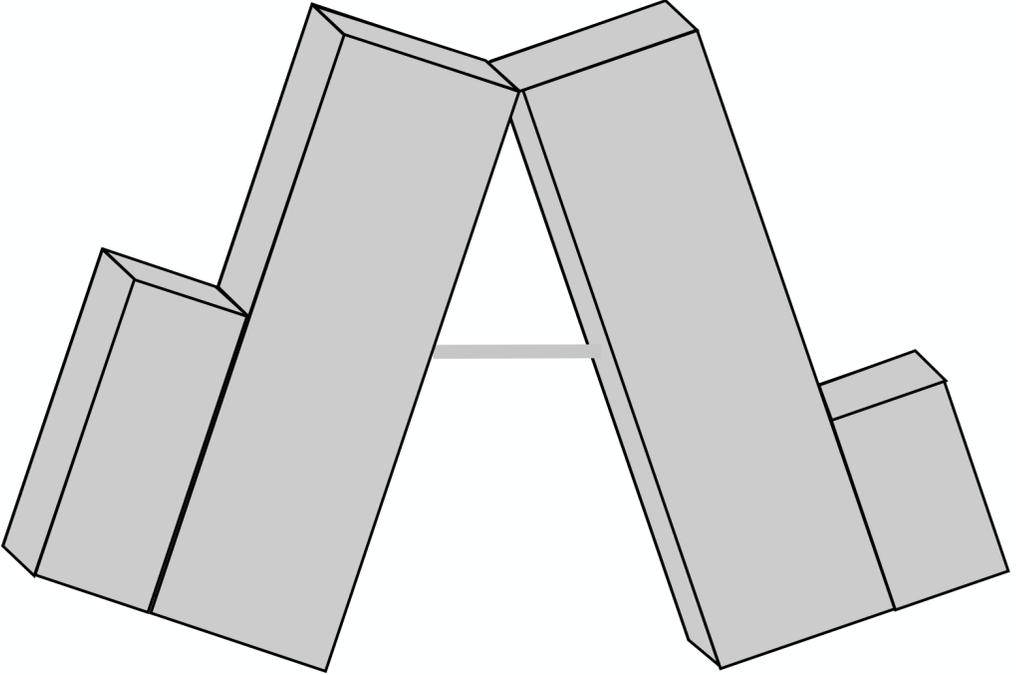
origamisim



autopipette



HOOMD-blue



Thanks to Pablo Damasceno

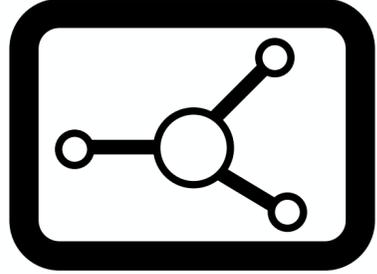
origamisim for rapid DNA origami structure prediction

CTK

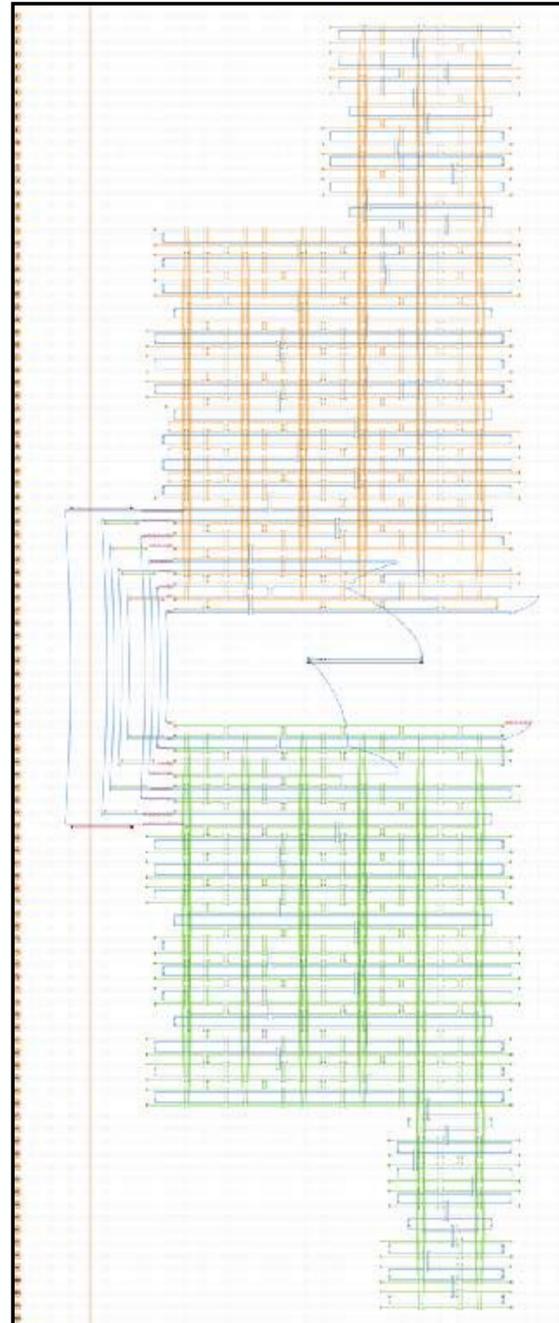
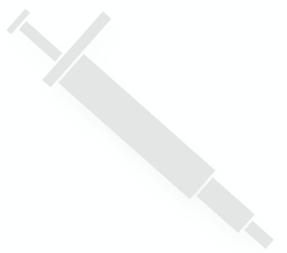
autobreak



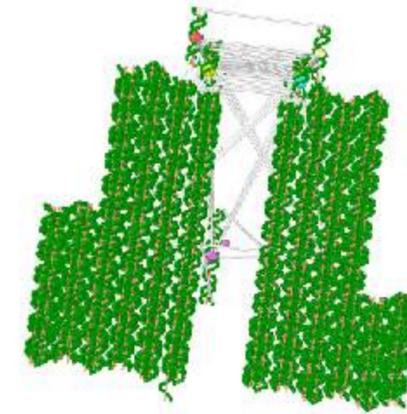
origamisim



autopipette



1. rigid body simulation



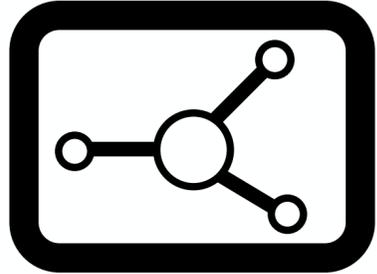
origamisim for rapid DNA origami structure prediction

CTK

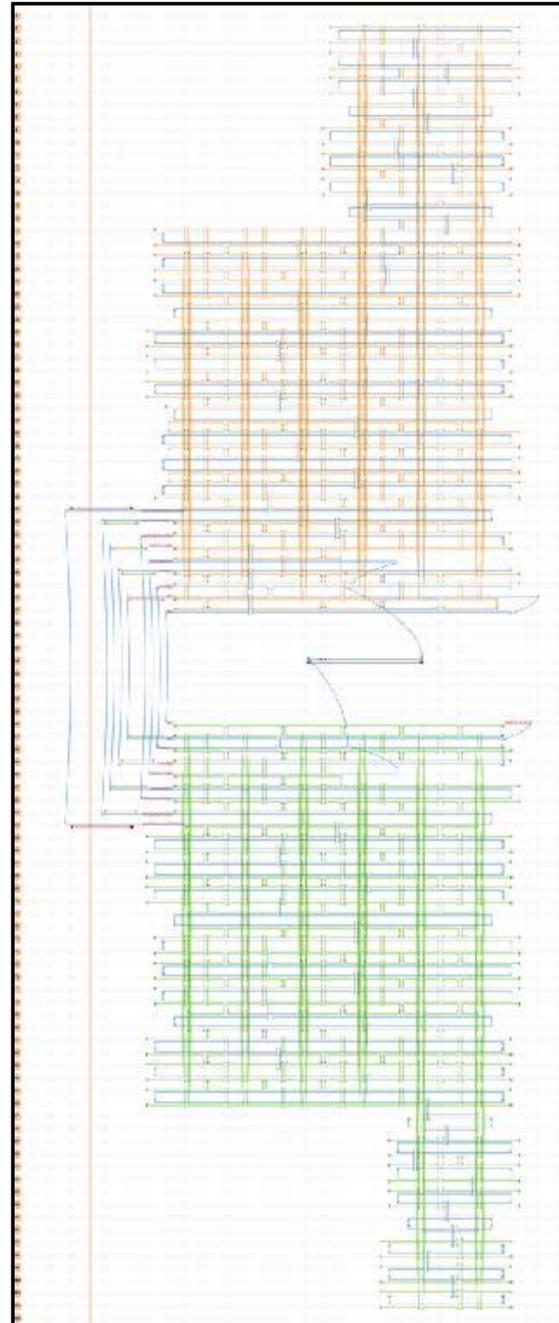
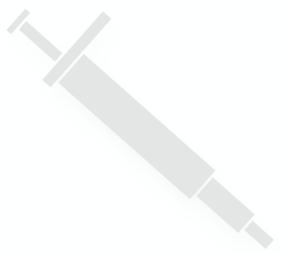
autobreak



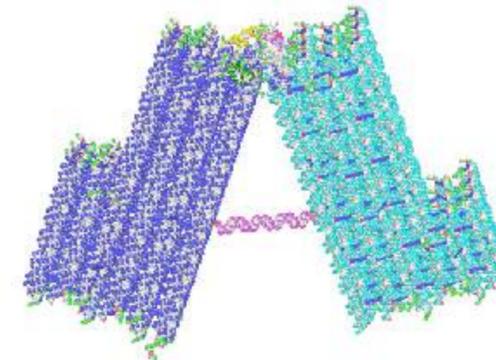
origamisim



autopipette



2. coarse grained simulation



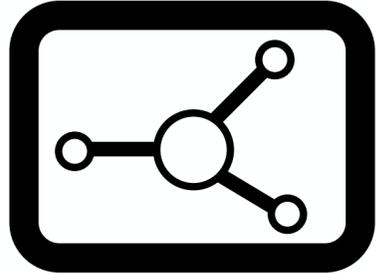
origamisim for rapid DNA origami structure prediction

CTK

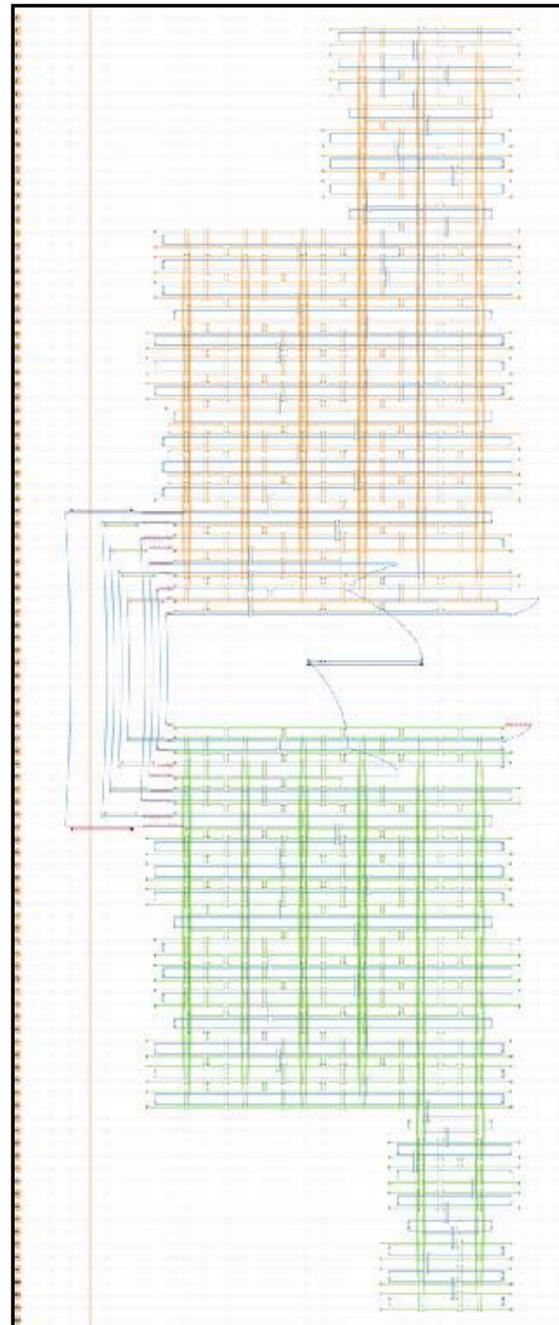
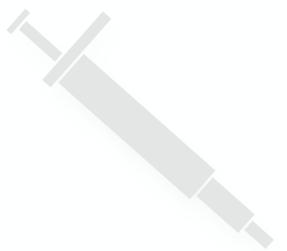
autobreak



origamisim

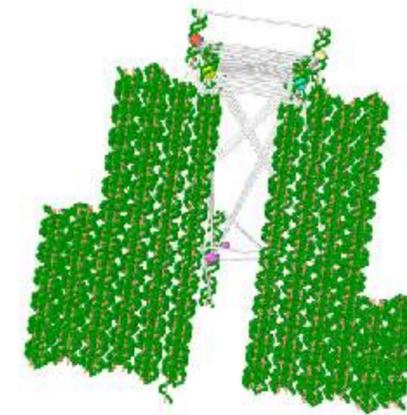


autopipette



1. rigid body simulation

time 0



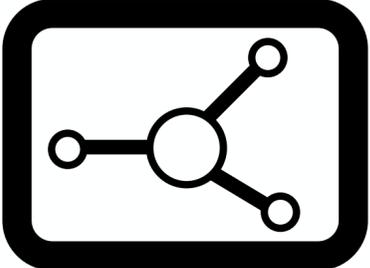
origamisim for rapid DNA origami structure prediction

CTK

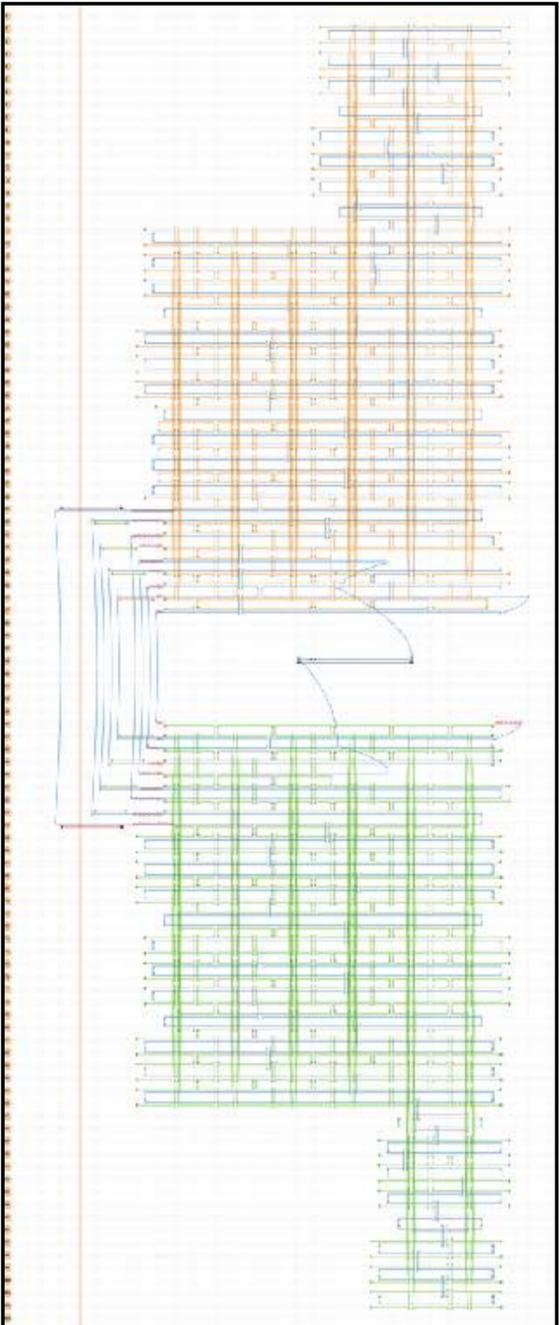
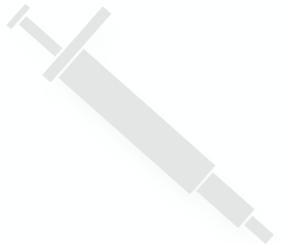
autobreak



origamisim

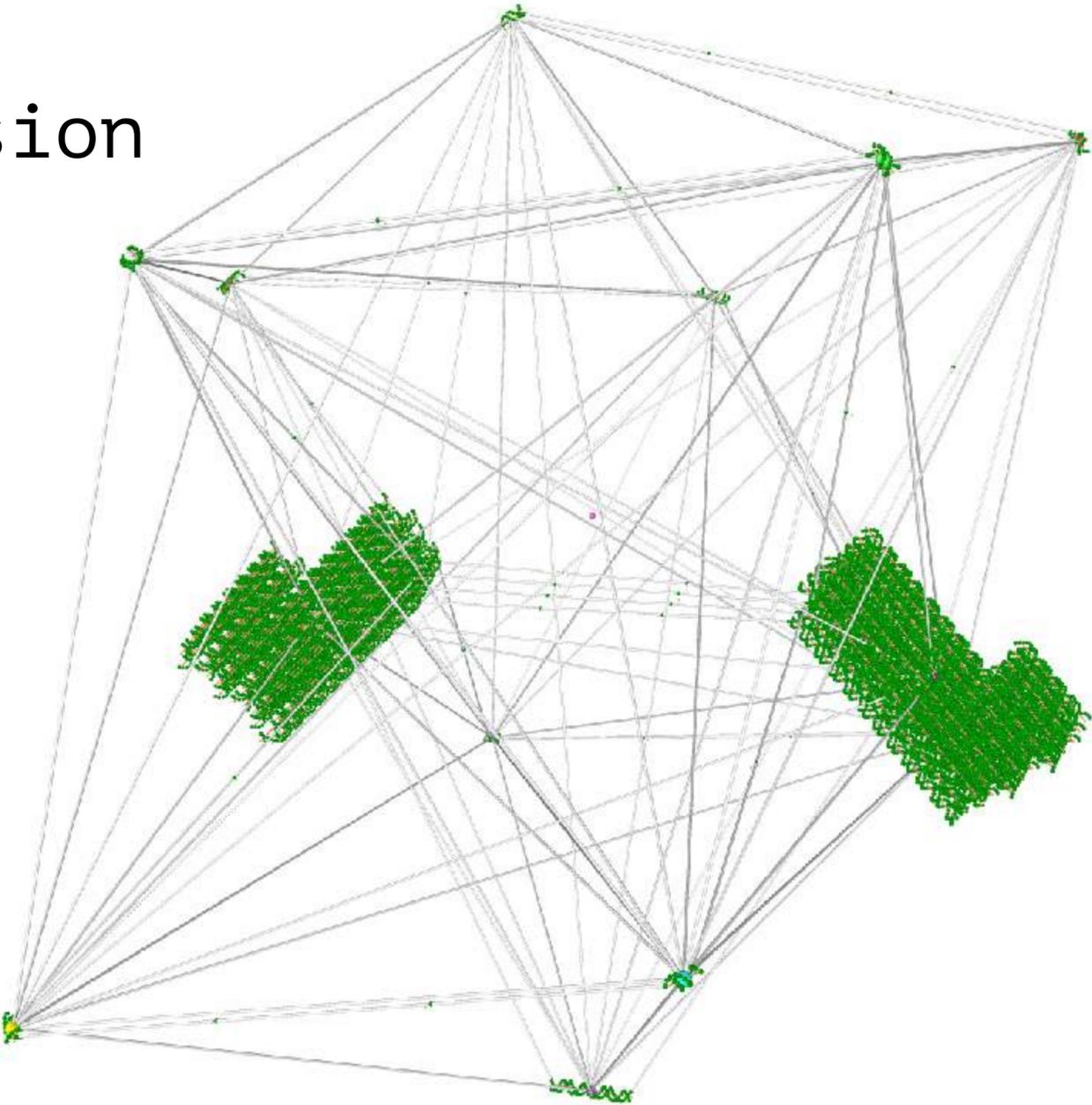


autopipette



1. rigid body simulation

Expansion



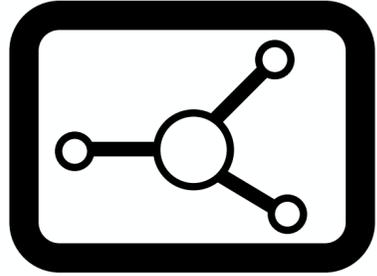
origamisim for rapid DNA origami structure prediction

CTK

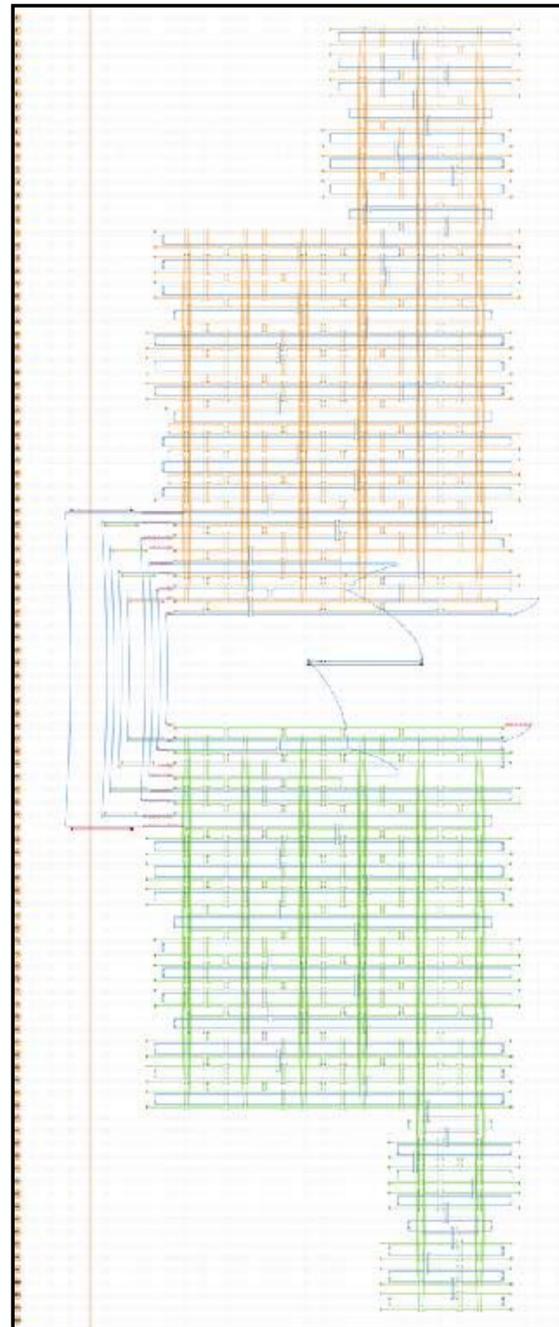
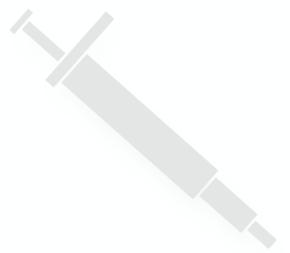
autobreak



origamisim

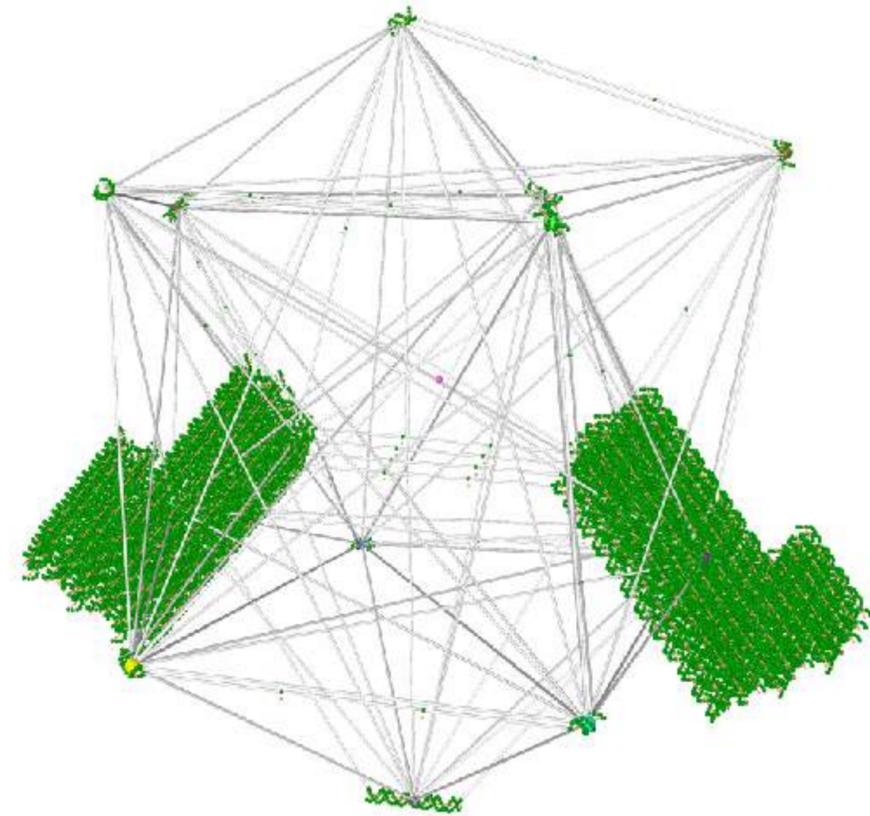


autopipette



1. rigid body simulation

Compaction



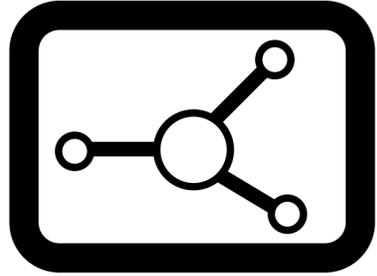
origamisim for rapid DNA origami structure prediction

CTK

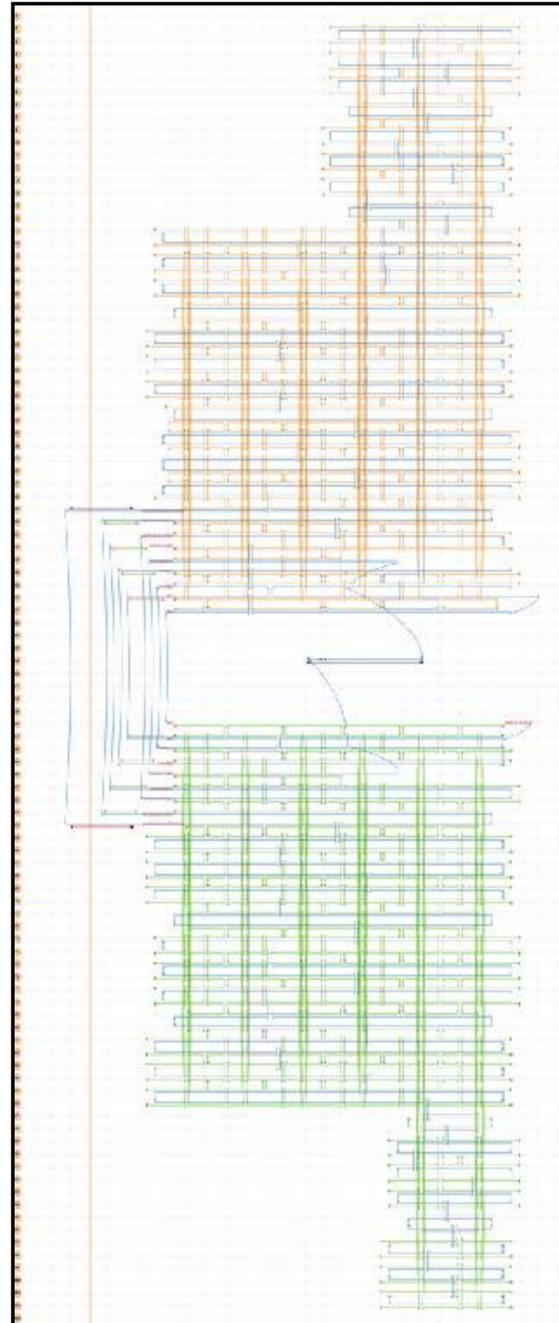
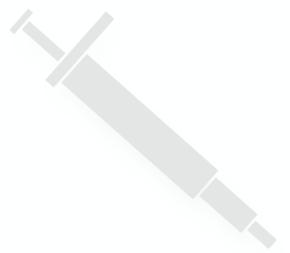
autobreak



origamisim

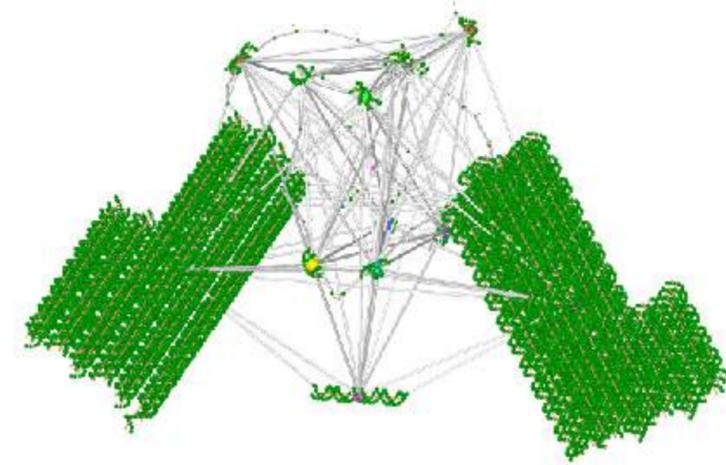


autopipette



1. rigid body simulation

Soft repulsion



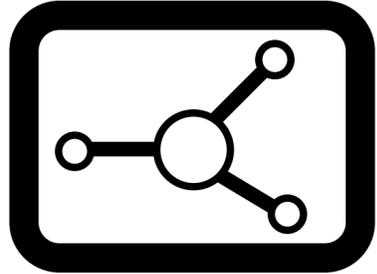
origamisim for rapid DNA origami structure prediction

CTK

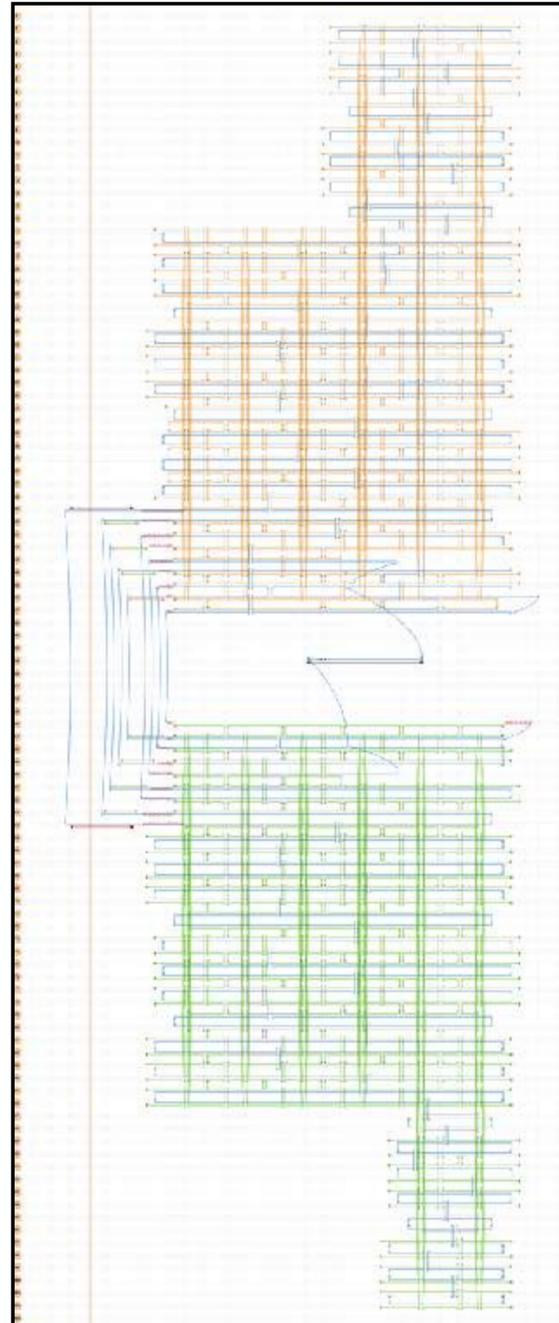
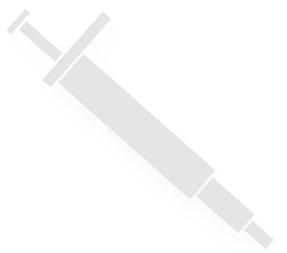
autobreak



origamisim

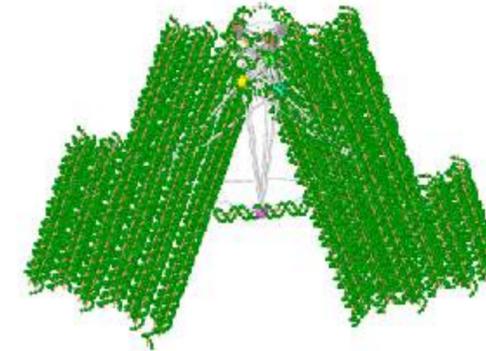


autopipette



1. rigid body simulation

Hard repulsion



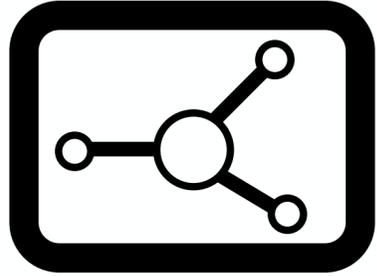
origamisim for rapid DNA origami structure prediction

CTK

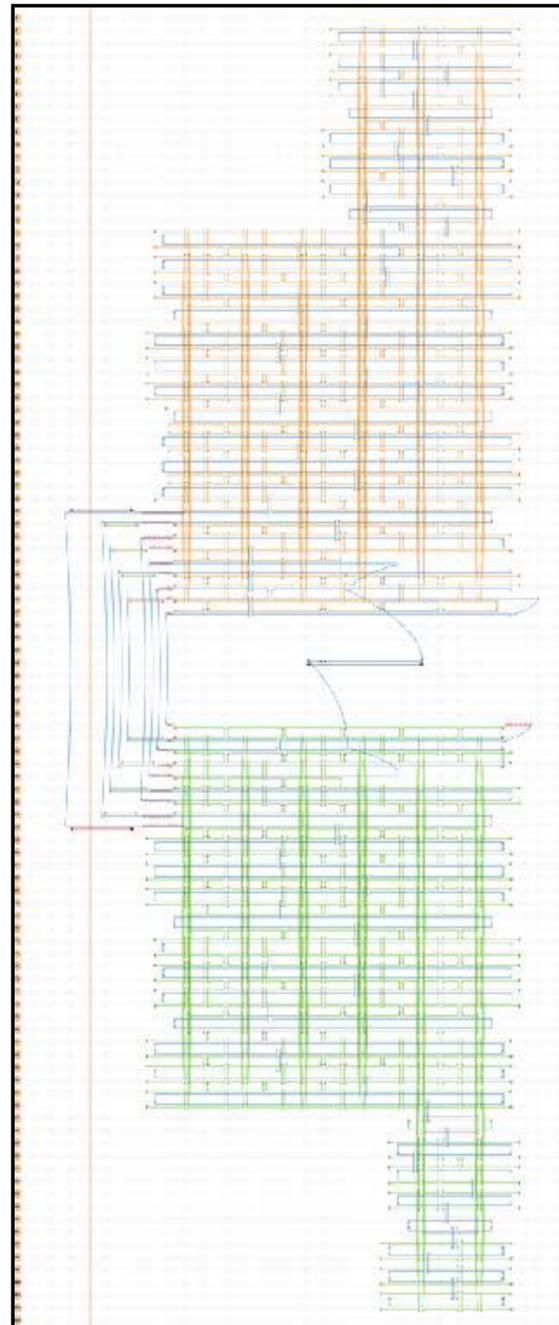
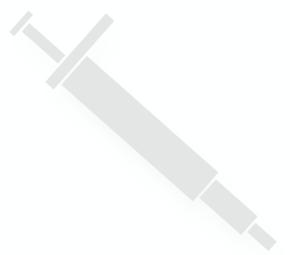
autobreak



origamisim

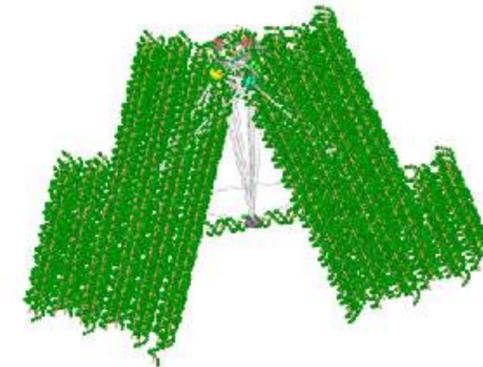


autopipette



1. rigid body simulation

Langevin dynamics



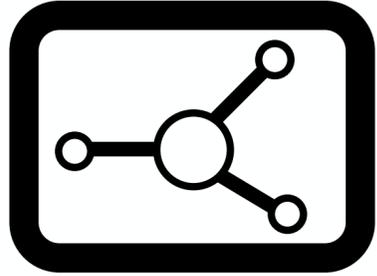
origamisim for rapid DNA origami structure prediction

CTK

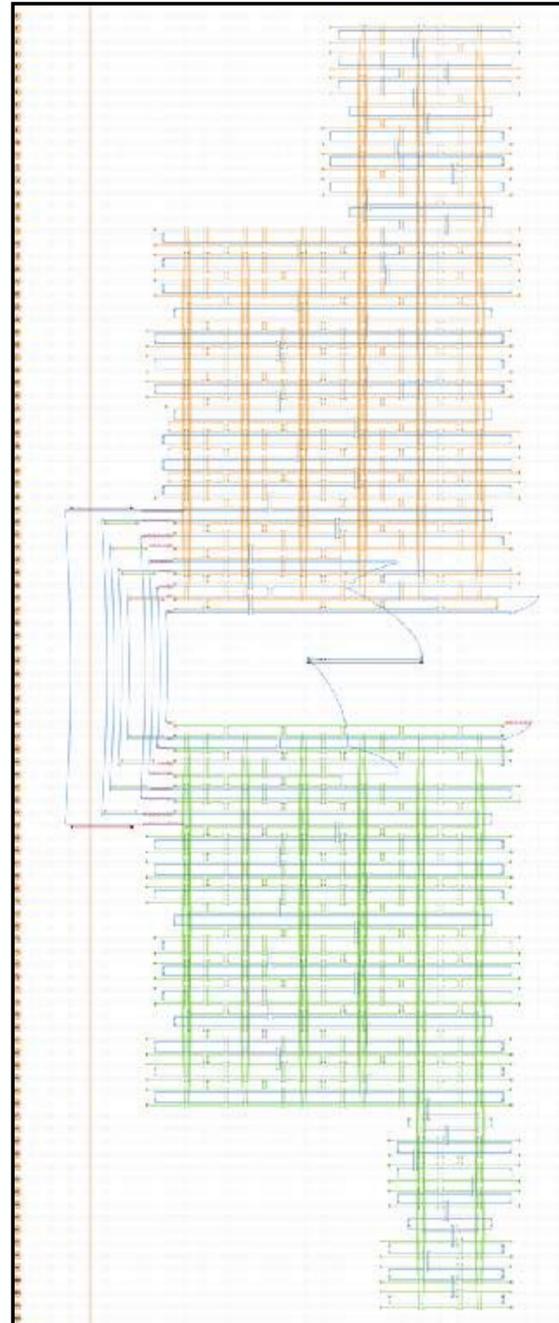
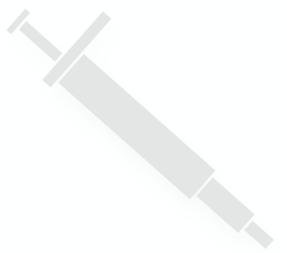
autobreak



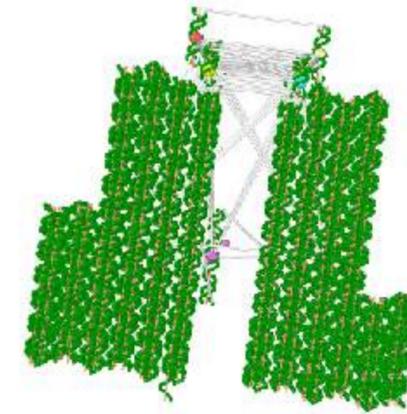
origamisim



autopipette



1. rigid body simulation



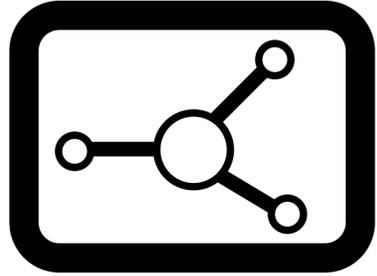
origamisim for rapid DNA origami structure prediction

CTK

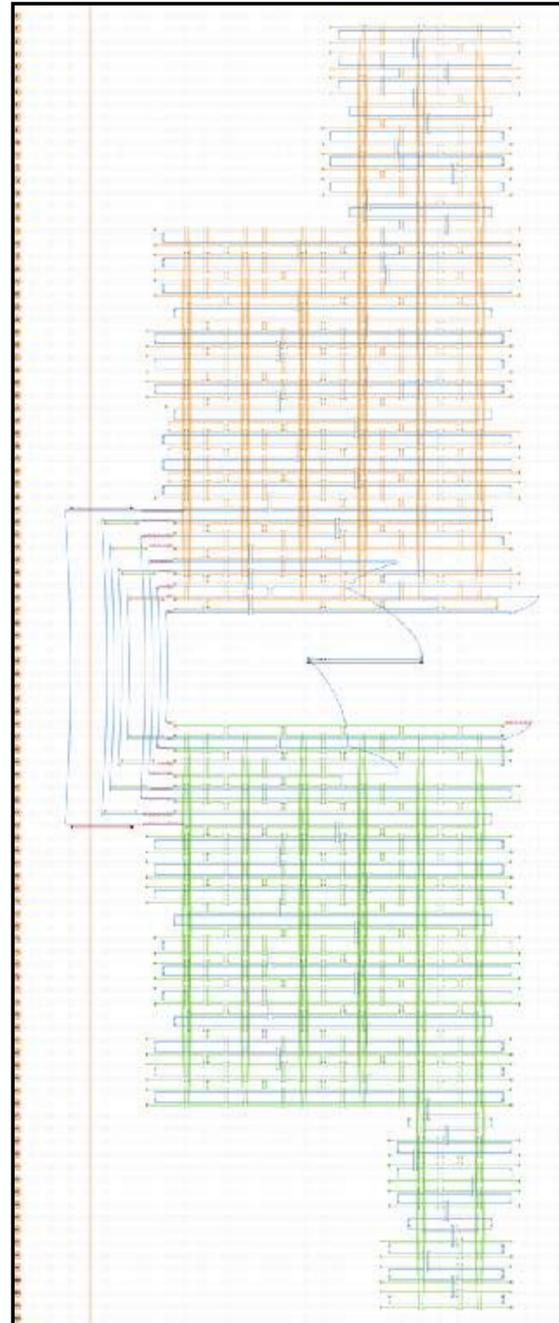
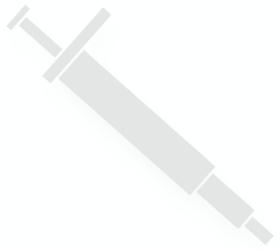
autobreak



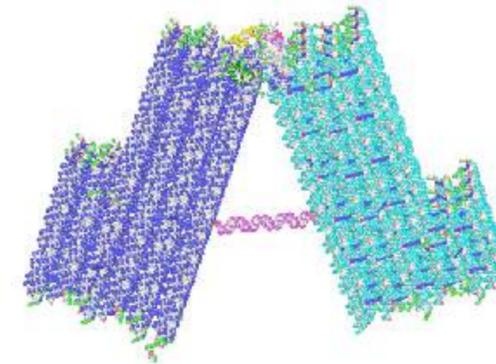
origamisim



autopipette



2. coarse grained simulation

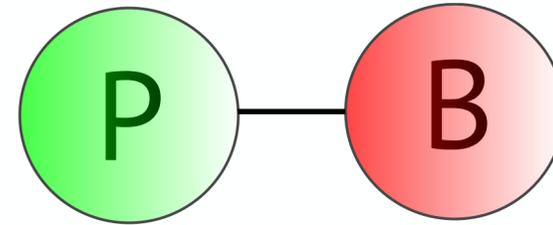


origamisim for rapid
DNA origami structure prediction

Coarse grained model

Nucleotides

ssNucleotide

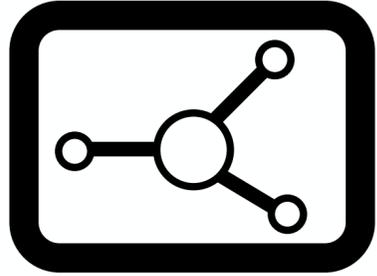


CTK

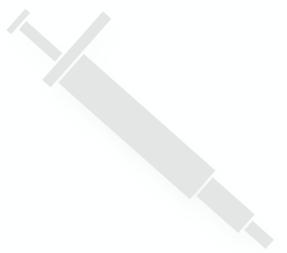
autobreak



origamisim



autopipette

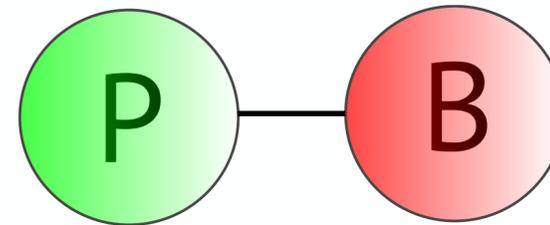


`origamisim` for rapid
DNA origami structure prediction

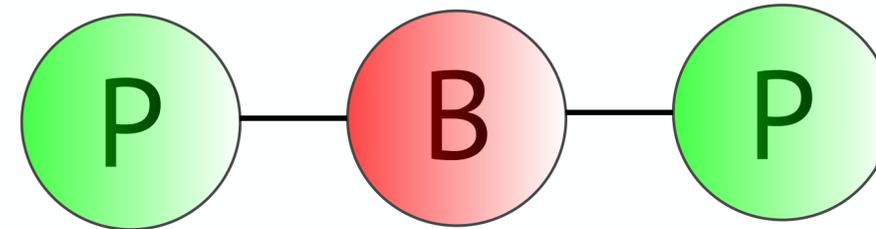
Coarse grained model

`Nucleotides`

`ssNucleotide`



`dsNucleotide`

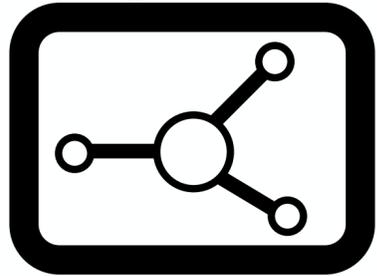


`CTK`

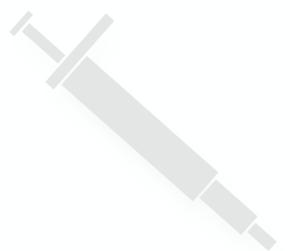
`autobreak`



`origamisim`



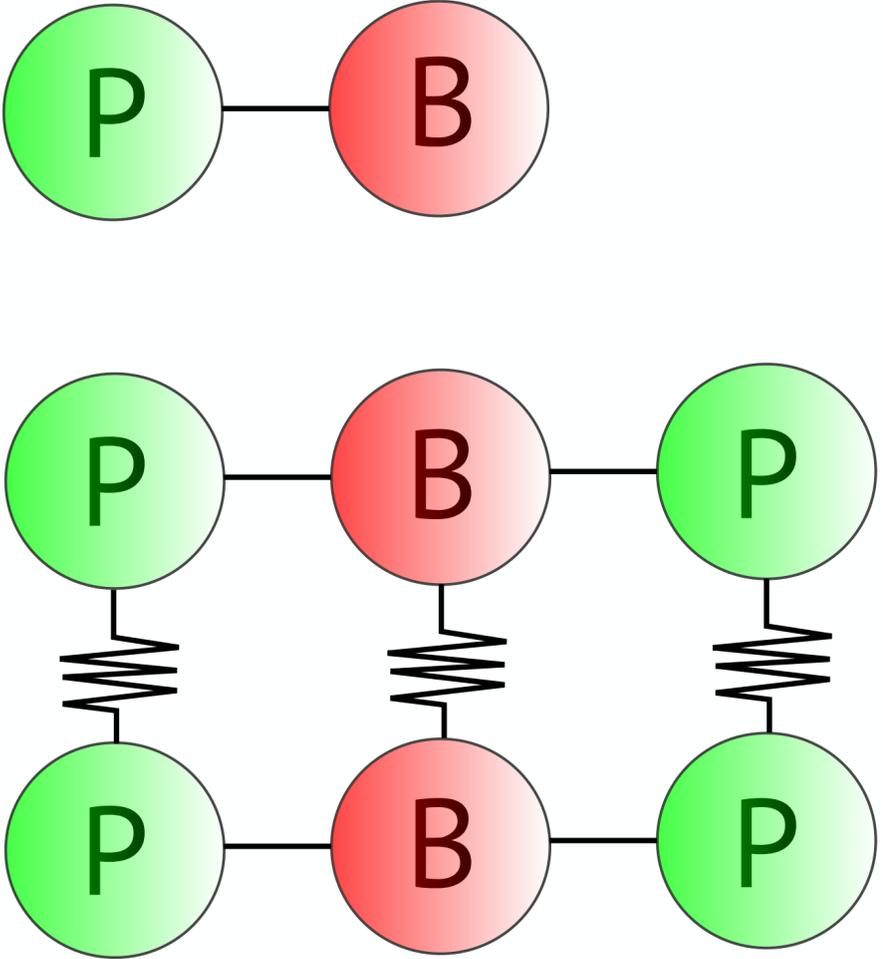
`autopipette`



origamisim for rapid
DNA origami structure prediction

Coarse grained model

Potentials



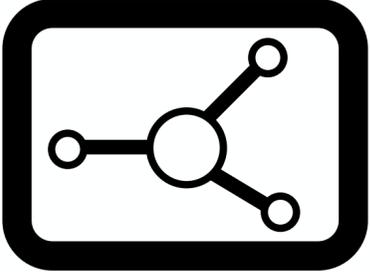
harmonic
bonds

CTK

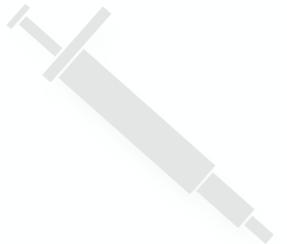
autobreak



origamisim



autopipette

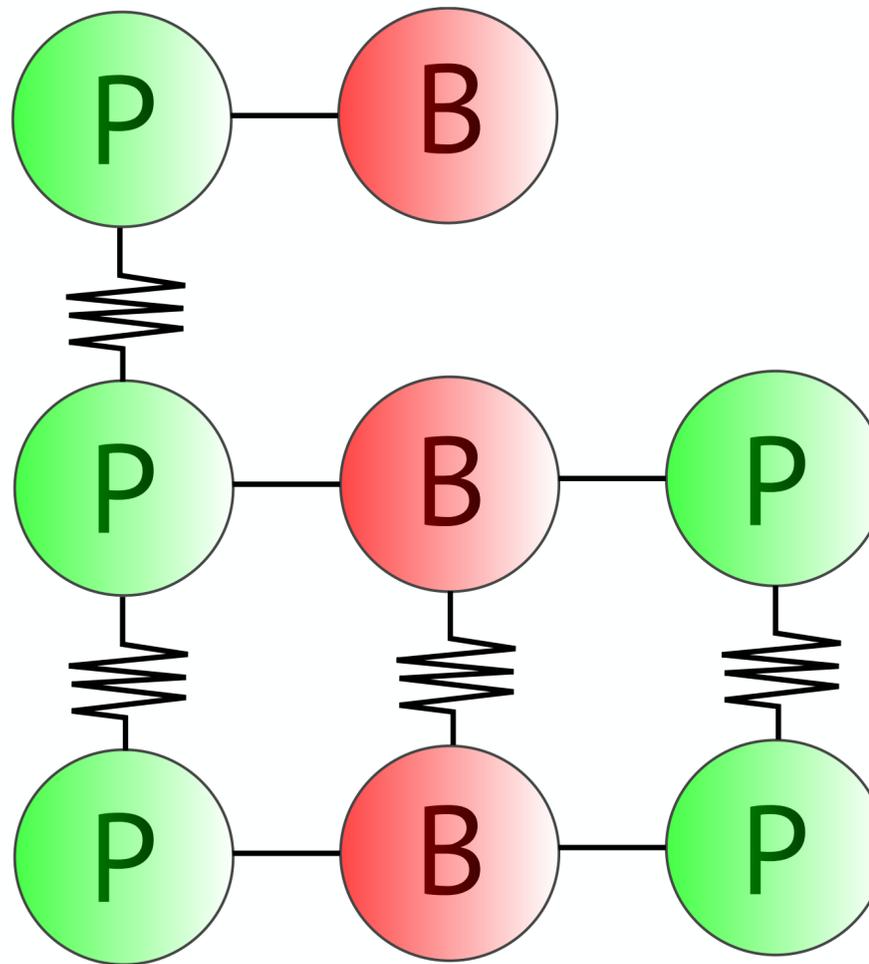


origamisim for rapid
DNA origami structure prediction

Coarse grained model

Potentials

harmonic
bonds

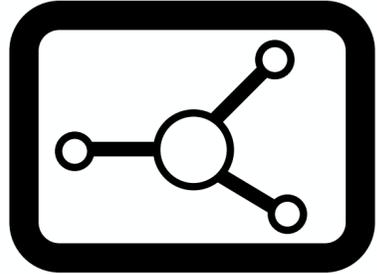


CTK

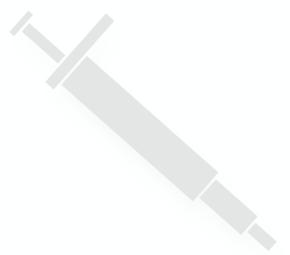
autobreak



origamisim



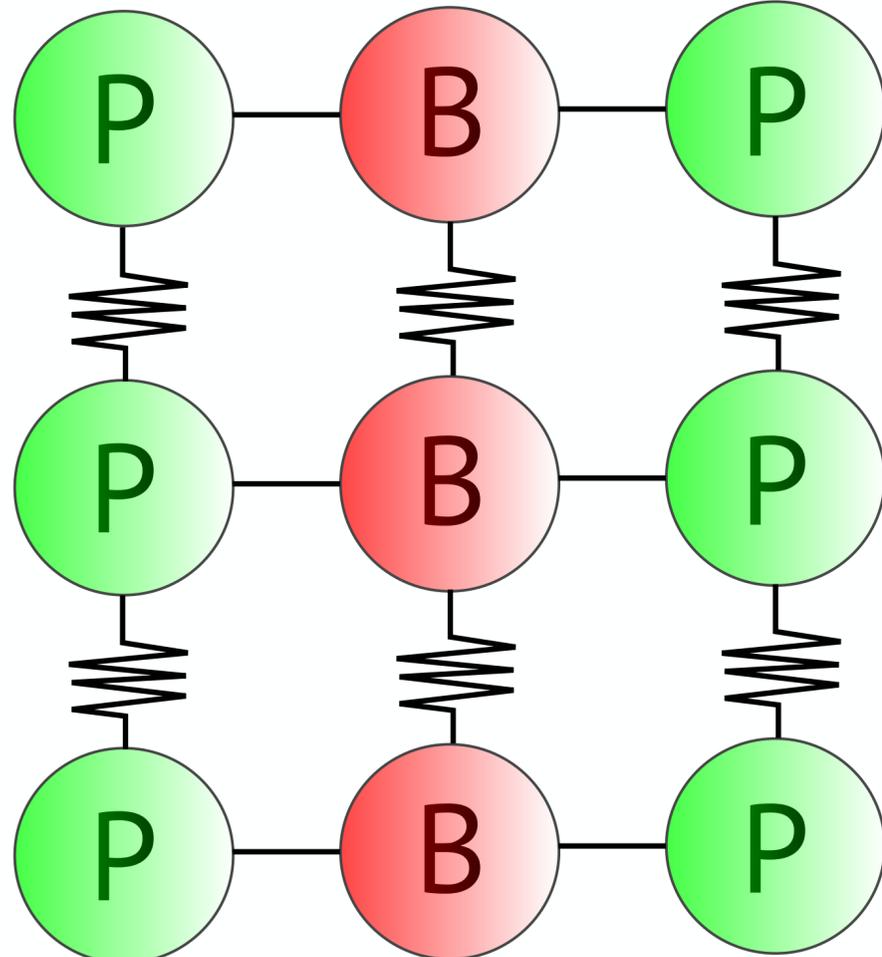
autopipette



origamisim for rapid
DNA origami structure prediction

Coarse grained model

Potentials



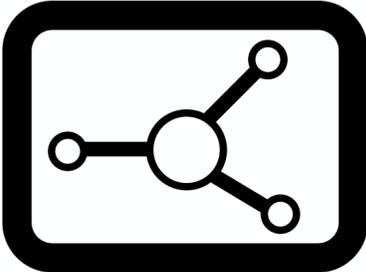
harmonic
bonds

CTK

autobreak



origamisim



autopipette



origamisim for rapid
DNA origami structure prediction

Coarse grained model

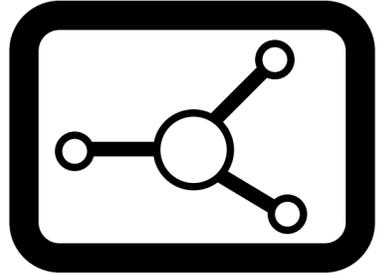
Potentials

CTK

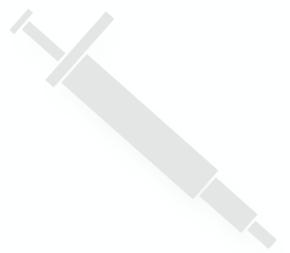
autobreak



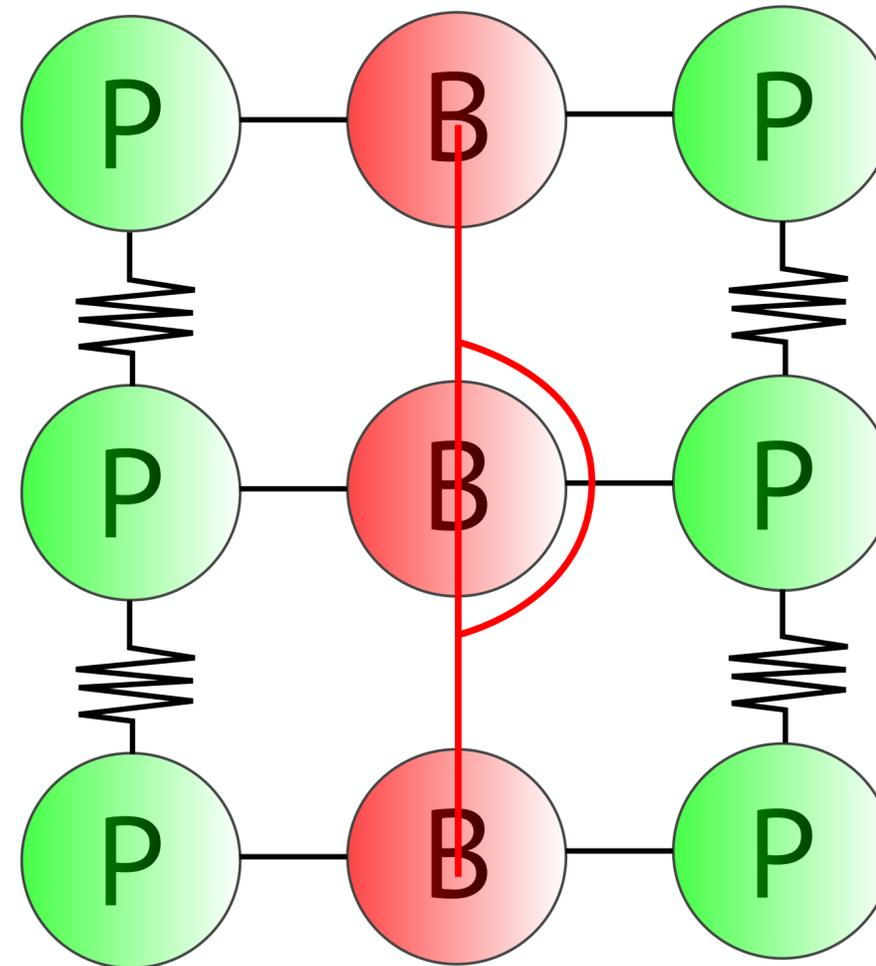
origamisim



autopipette



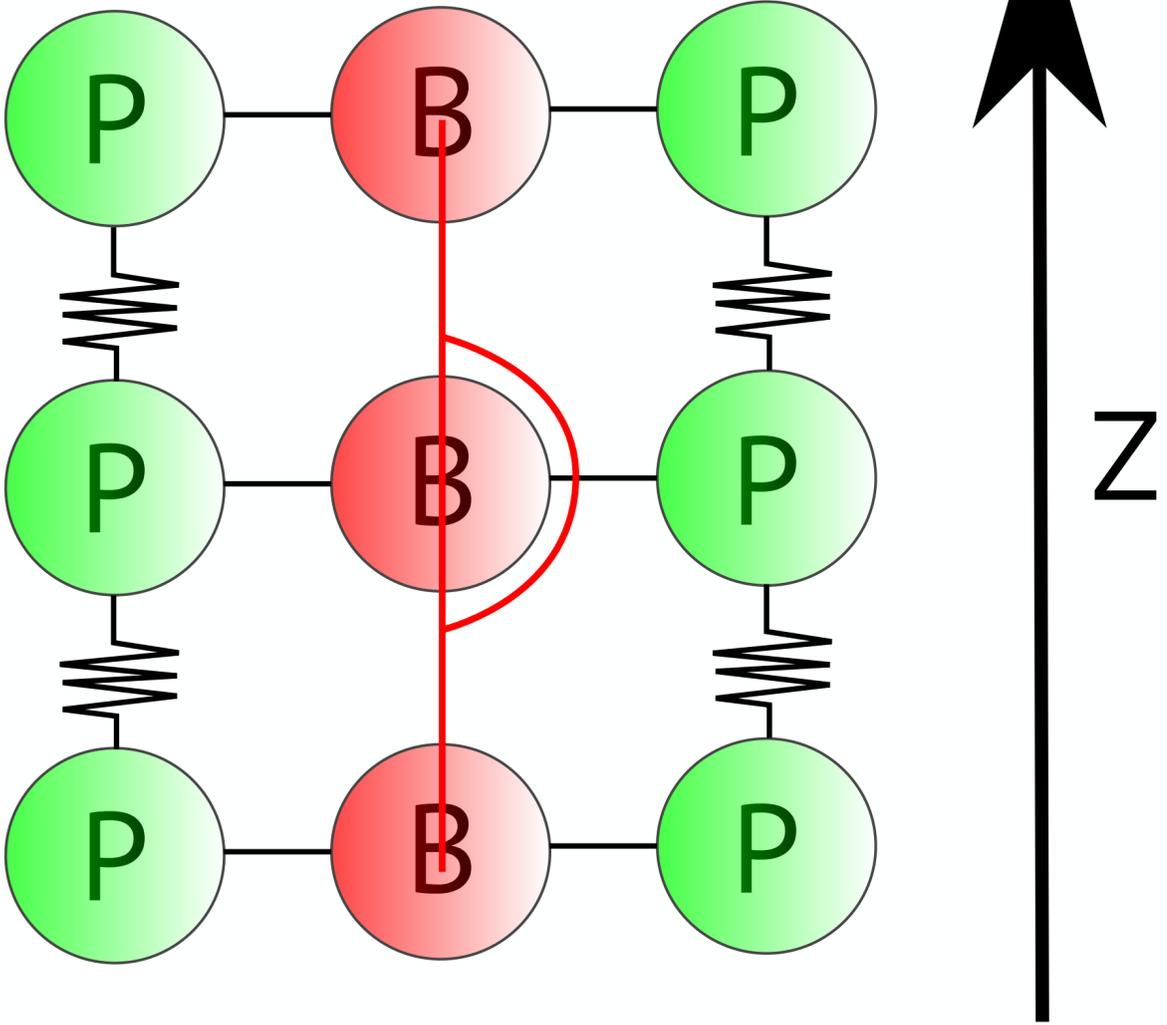
harmonic
angle



origamisim for rapid
DNA origami structure prediction

Coarse grained model

Potentials



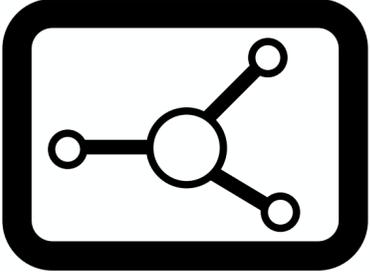
harmonic
angle

CTK

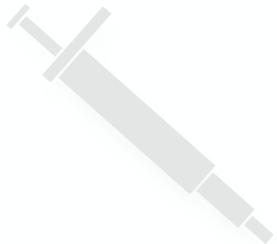
autobreak



origamisim



autopipette



origamisim for rapid
DNA origami structure prediction

Coarse grained model

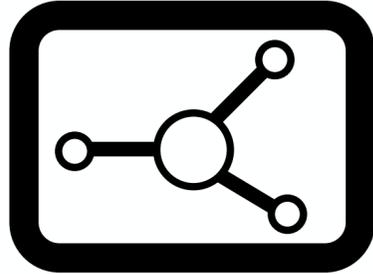
Potentials

CTK

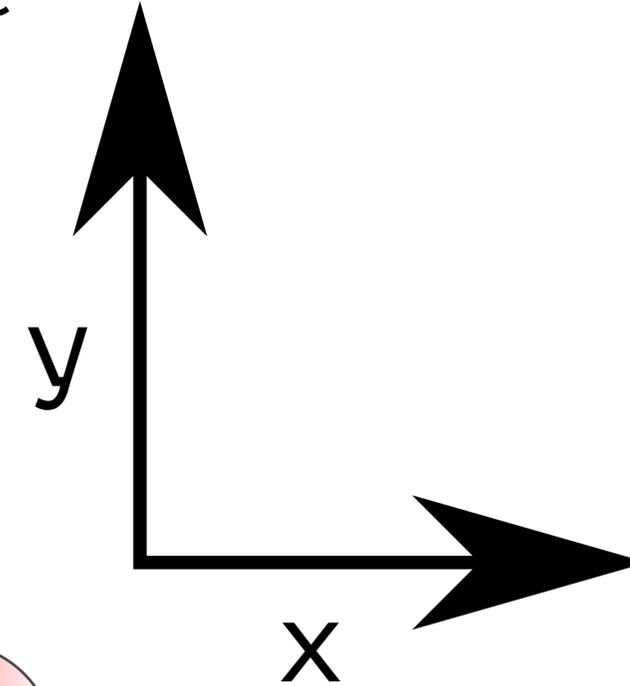
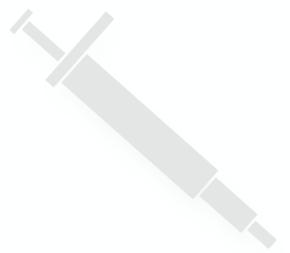
autobreak



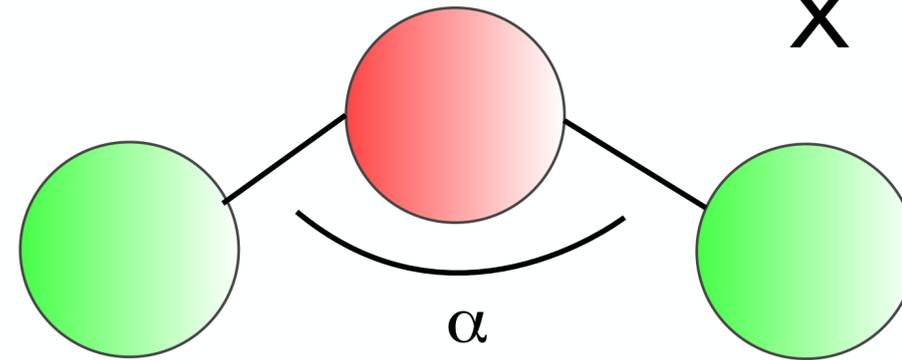
origamisim



autopipette



harmonic
angle



origamisim for rapid
DNA origami structure prediction

Coarse grained model

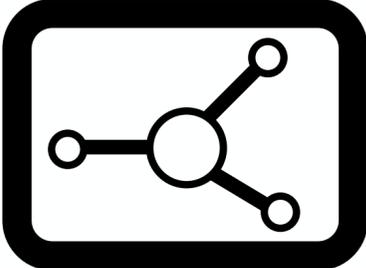
Potentials

CTK

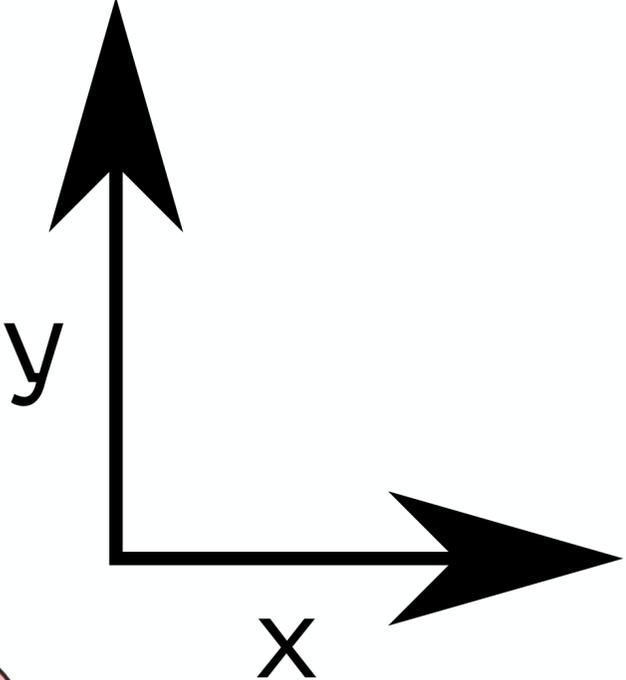
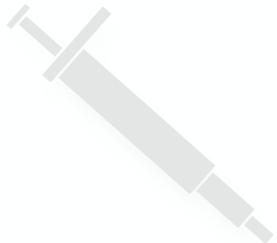
autobreak



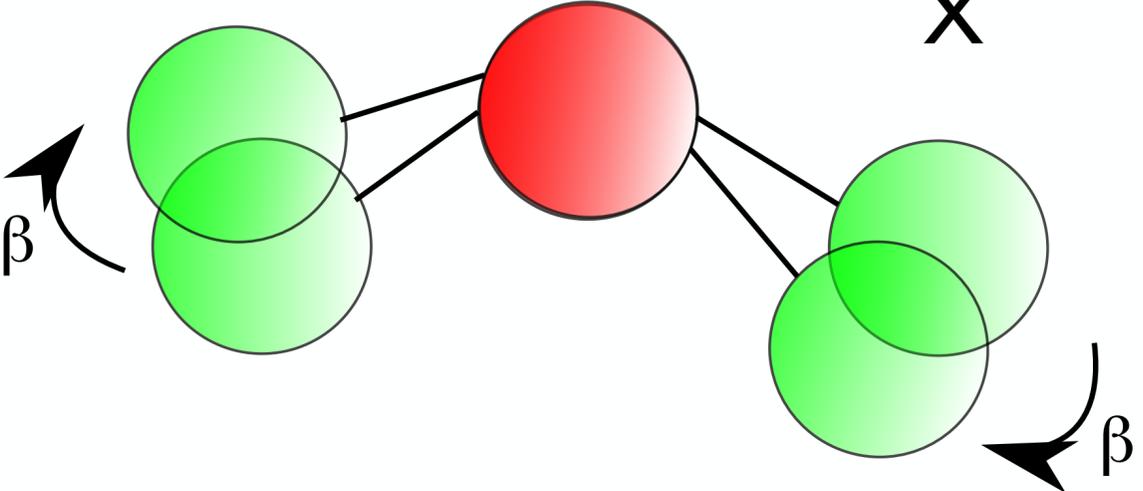
origamisim



autopipette



harmonic
dihedral

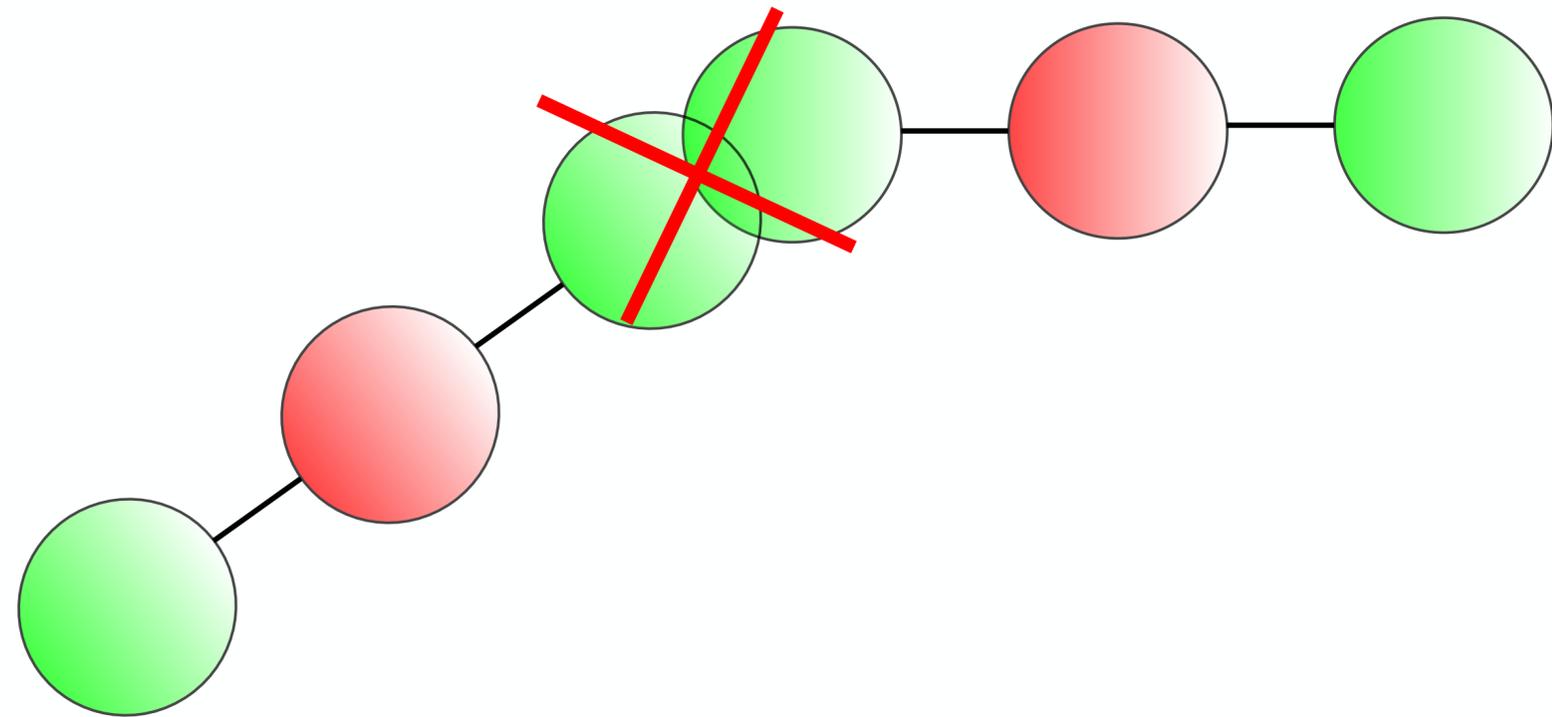


origamisim for rapid
DNA origami structure prediction

Coarse grained model

Potentials

repulsions

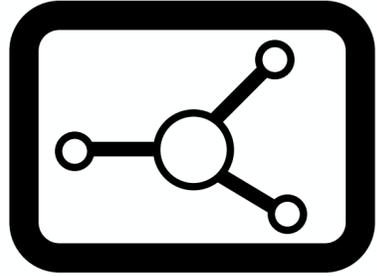


CTK

autobreak



origamisim



autopipette

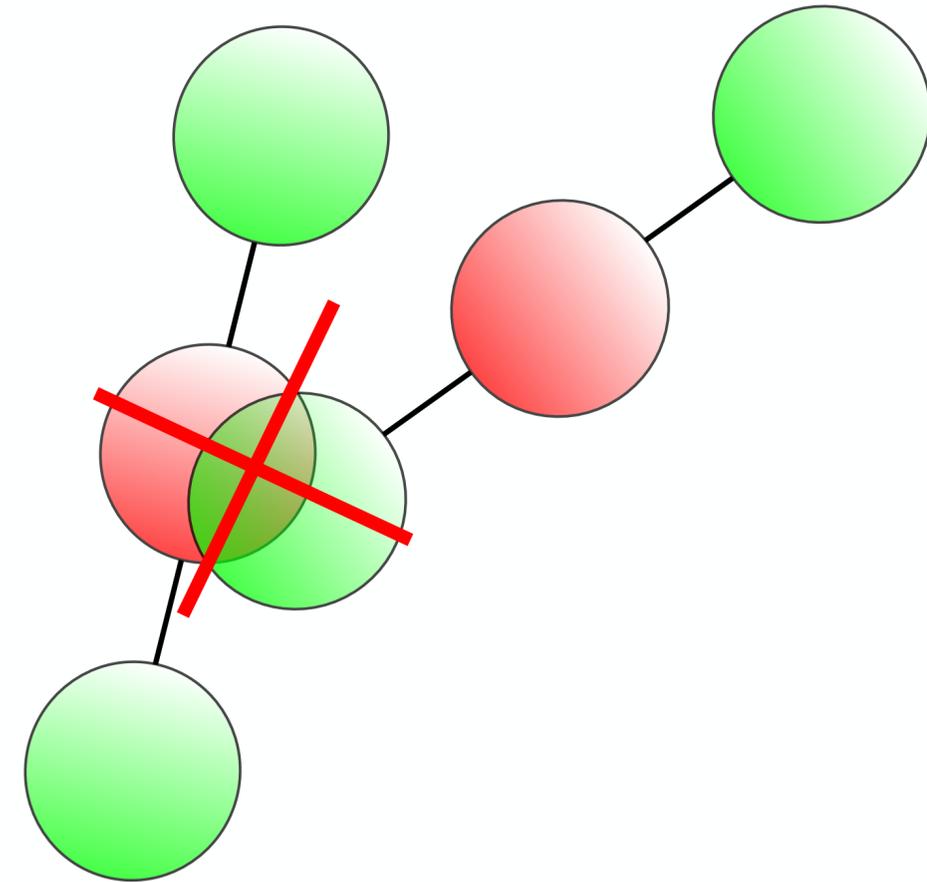


origamisim for rapid
DNA origami structure prediction

Coarse grained model

Potentials

repulsions

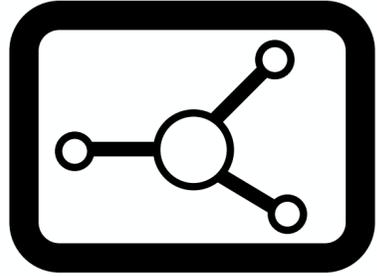


CTK

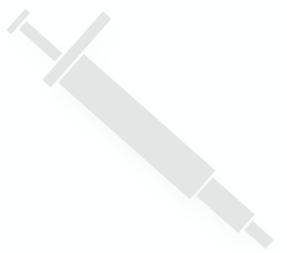
autobreak



origamisim



autopipette

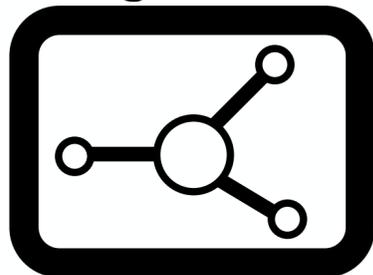


CTK

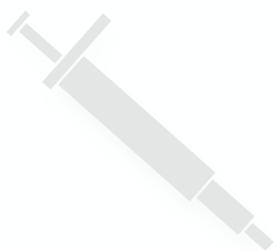
autobreak



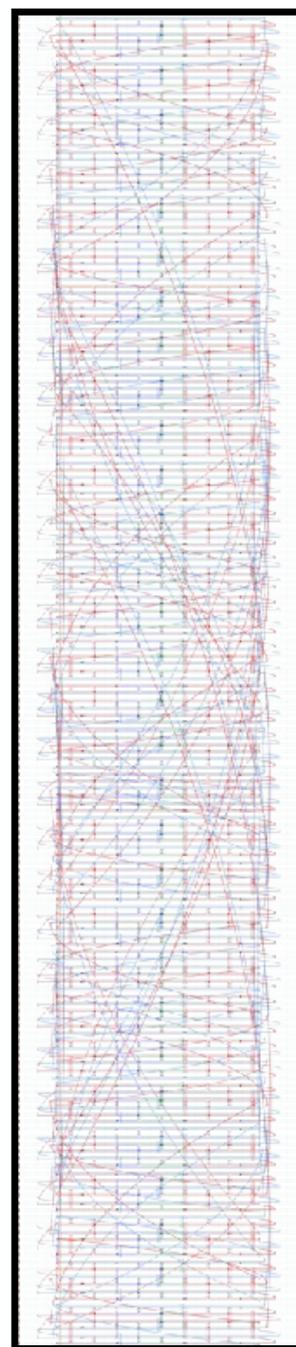
origamisim



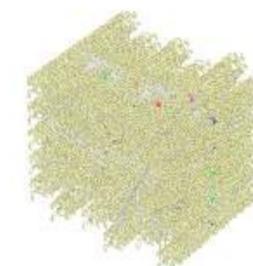
autopipette



design.json



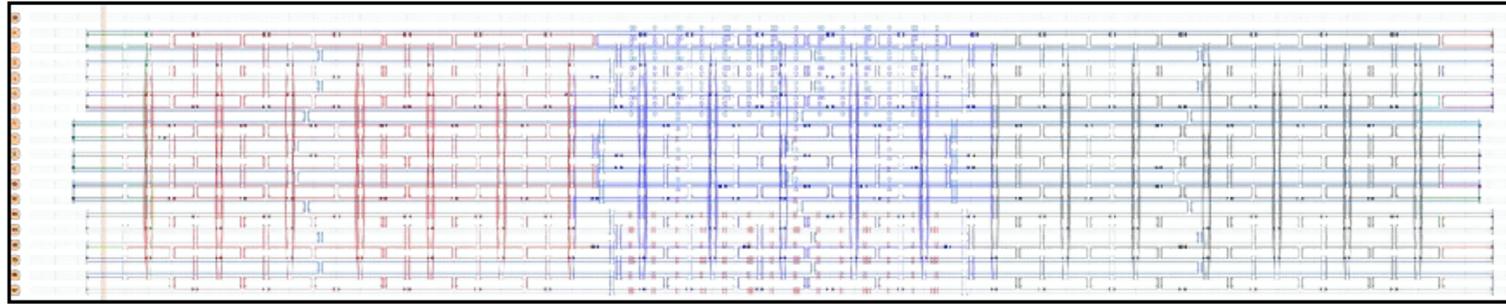
Example 1: Icosahedron



Example 2: Protractor-90

CTK

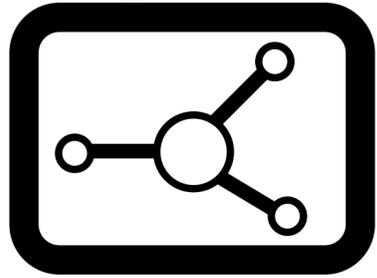
design.json



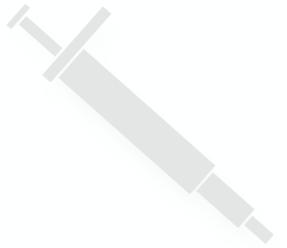
autobreak



origamisim



autopipette

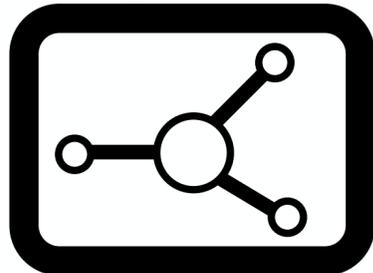


CTK

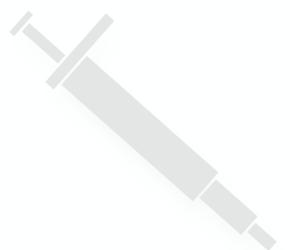
autobreak



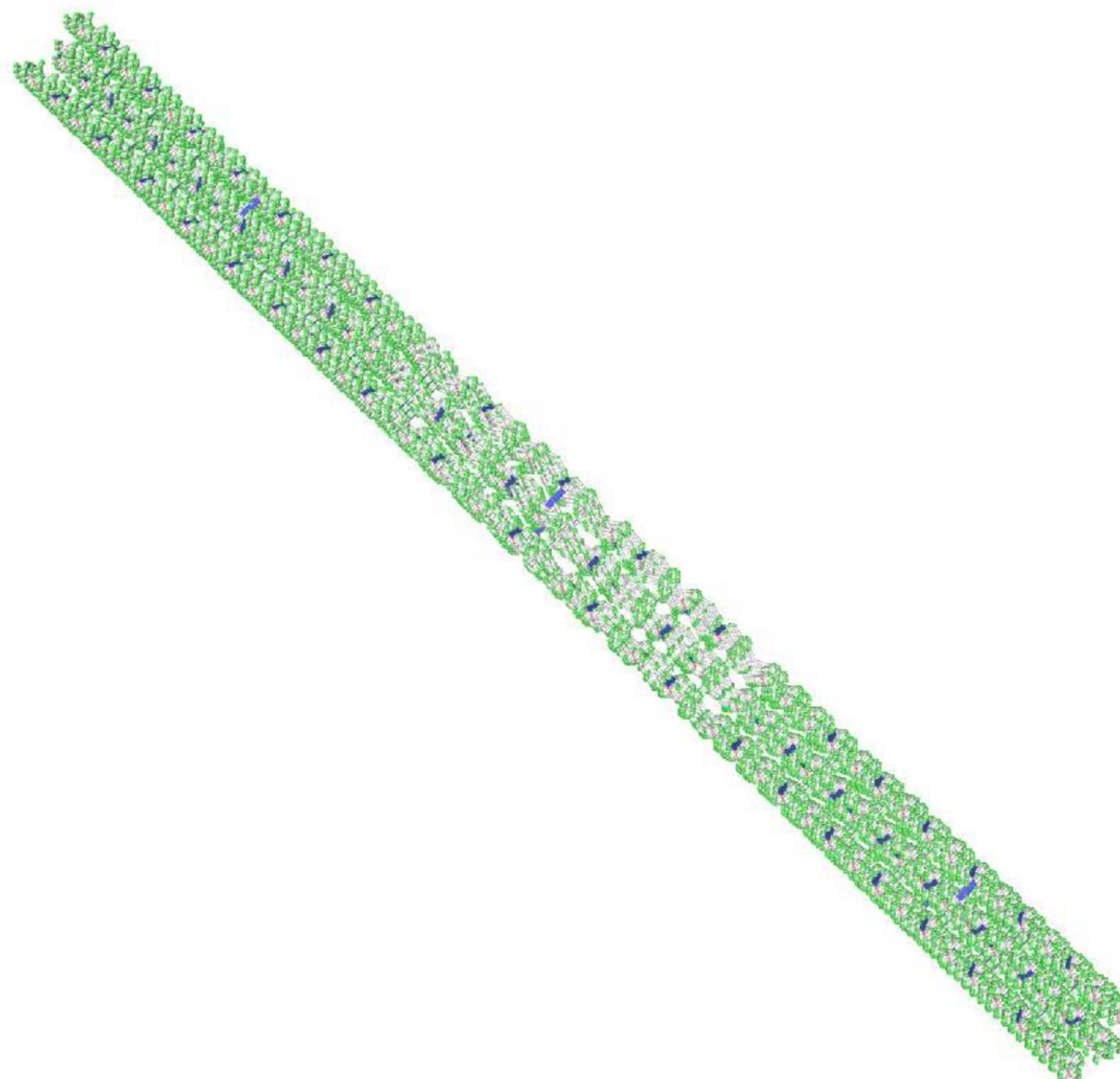
origamisim



autopipette



Example 2: Protractor-90

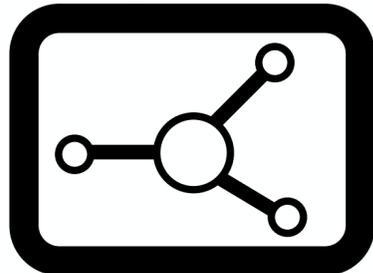


CTK

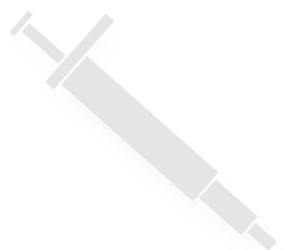
autobreak



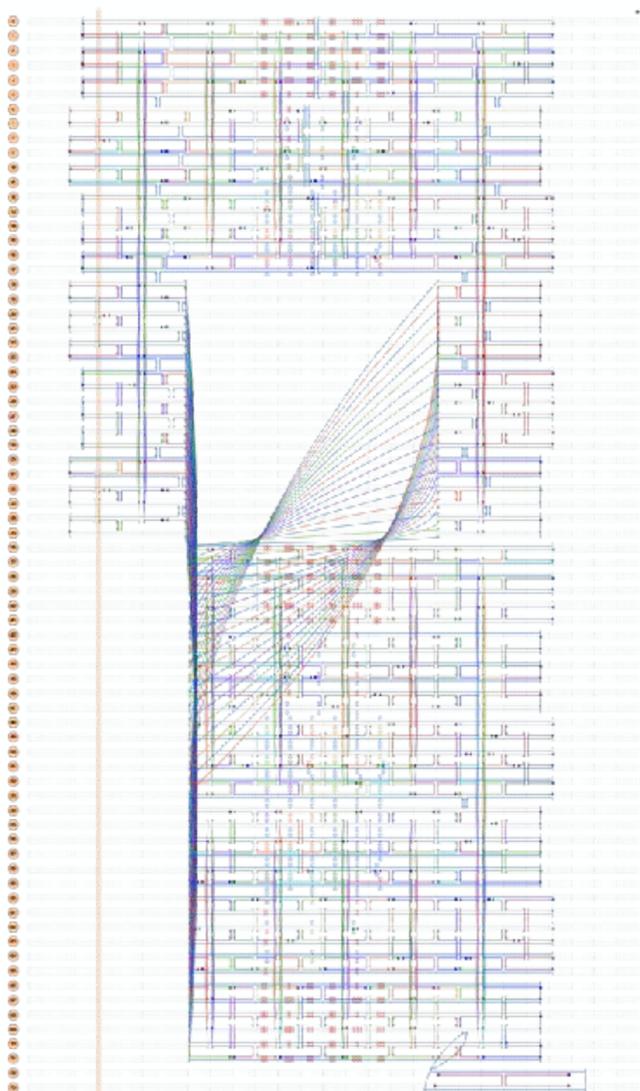
origamisim



autopipette



design.json



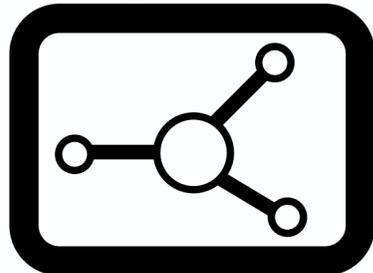
Example 3: tri-120

CTK

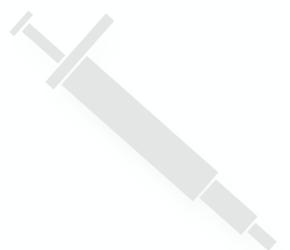
autobreak



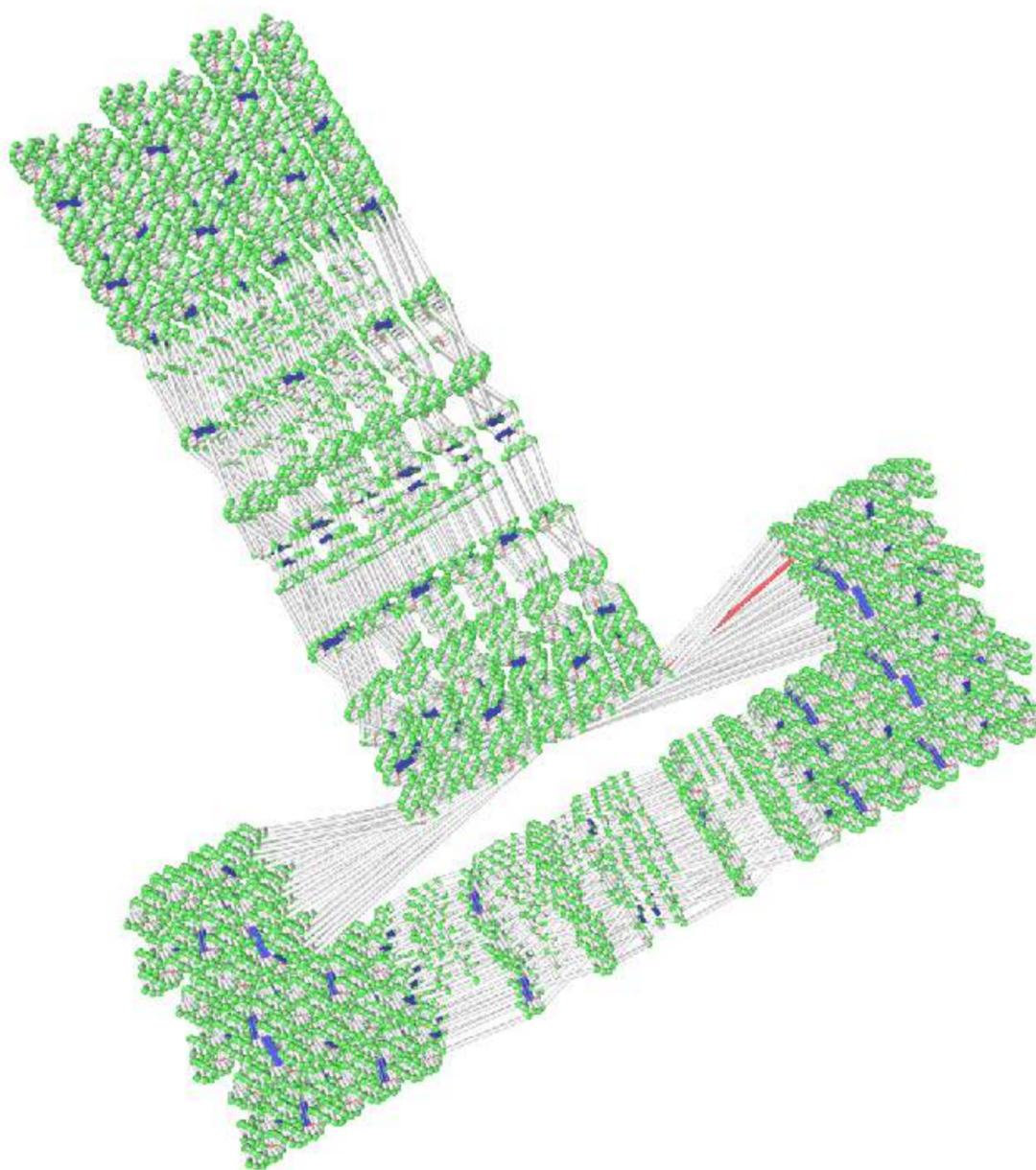
origamisim



autopipette



Example 3: tri-120



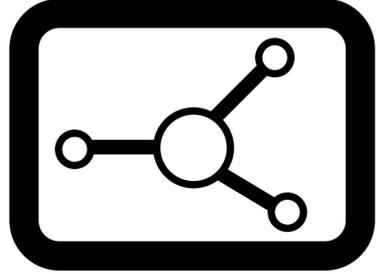
Example 4: DNA pegboard

CTK

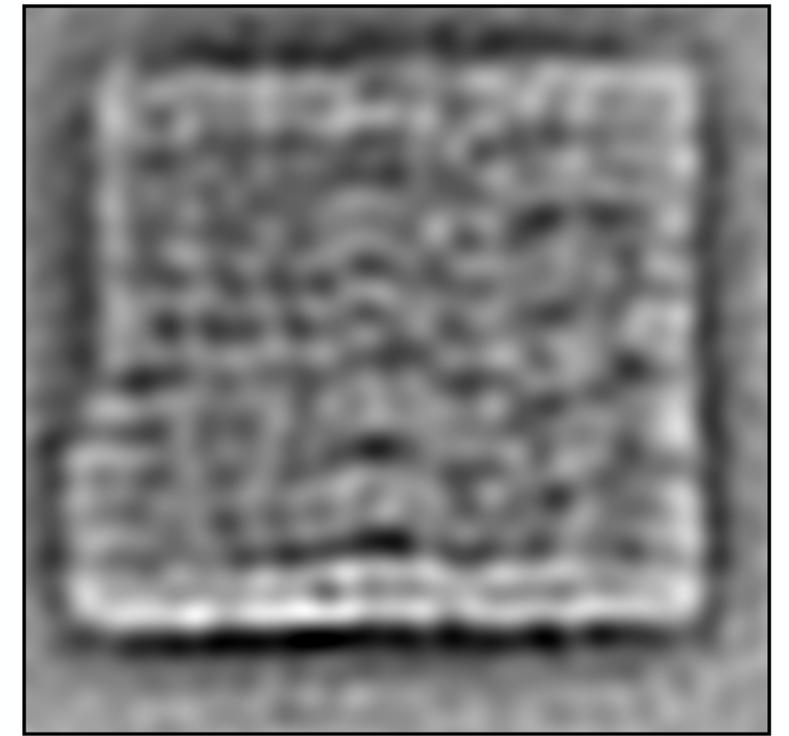
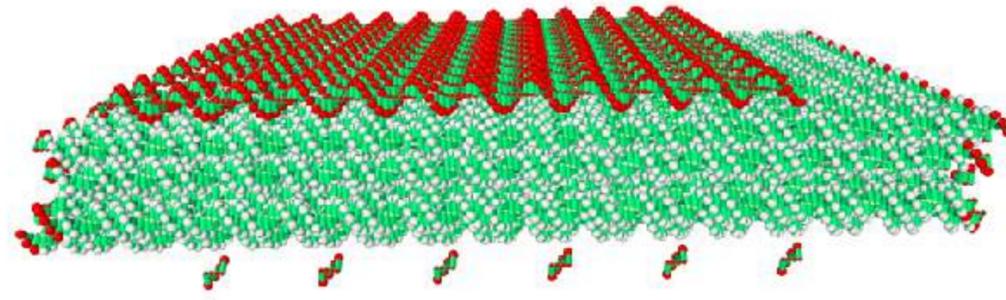
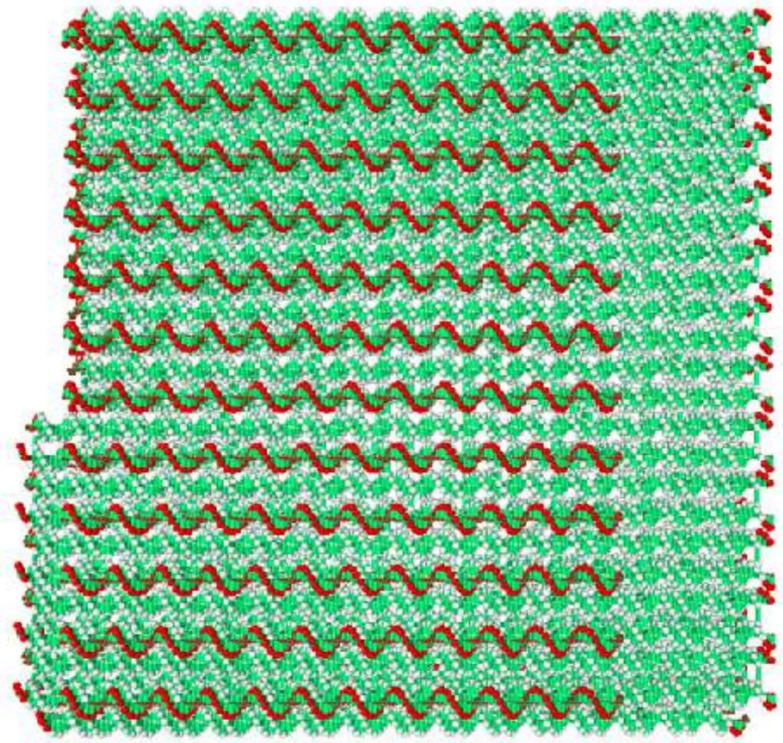
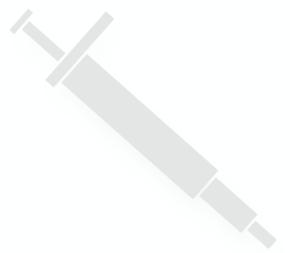
autobreak



origamisim



autopipette



20nm

```
origamisim.py -i design_autobreak.json -vmd -circularize
```

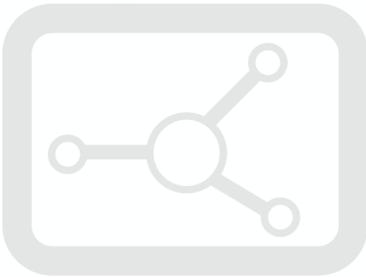
CTK

Autopipette enables the user
to organize the staples ready for order

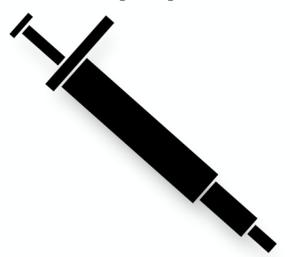
autobreak



origamisim



autopipette



input

design1.json

design2.json

design3.json

output

echo_384well.cvs

oligos_96well.xlsx

oligos_384well.xlsx

```
exportoligos.py -i *.json -seq p8064
```

Autopipette enables the user to organize the staples ready for order

Labcyte Echo input file

CTK

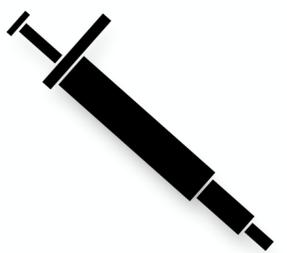
autobreak



origamisim



autopipette



	A	B	C	D	E	F	G
88	Reservoir	A1	DestPlate-0	H3	5500		
89	Reservoir	A1	DestPlate-0	H4	5500		
90	Reservoir	A1	DestPlate-0	H5	5500		
91	Reservoir	A1	DestPlate-0	H6	5500		
92	Reservoir	A1	DestPlate-0	H7	5500		
93	Reservoir	A1	DestPlate-0	H8	5500		
94	Reservoir	A1	DestPlate-0	H9	5500		
95	Reservoir	A1	DestPlate-0	H10	5500		
96	Reservoir	A1	DestPlate-0	H11	5500		
97	Reservoir	A1	DestPlate-0	H12	5500		
98	Plate1by3v9-4-1	A1	DestPlate-0	A1	25		
99	Plate1by3v9-4-1	A1	DestPlate-0	A10	25		
00	Plate1by3v9-4-1	A1	DestPlate-0	A11	25		
01	Plate1by3v9-4-1	A1	DestPlate-0	A12	25		
02	Plate1by3v9-4-1	A1	DestPlate-0	A2	25		
03	Plate1by3v9-4-1	A1	DestPlate-0	A3	25		
04	Plate1by3v9-4-1	A1	DestPlate-0	A4	25		
05	Plate1by3v9-4-1	A1	DestPlate-0	A5	25		
06	Plate1by3v9-4-1	A1	DestPlate-0	A6	25		
07	Plate1by3v9-4-1	A1	DestPlate-0	A7	25		
08	Plate1by3v9-4-1	A1	DestPlate-0	A8	25		
09	Plate1by3v9-4-1	A1	DestPlate-0	A9	25		
10	Plate1by3v9-4-1	A1	DestPlate-0	B1	25		
11	Plate1by3v9-4-1	A1	DestPlate-0	B10	25		
12	Plate1by3v9-4-1	A1	DestPlate-0	B11	25		
13	Plate1by3v9-4-1	A1	DestPlate-0	B12	25		
14	Plate1by3v9-4-1	A1	DestPlate-0	B2	25		
15	Plate1by3v9-4-1	A1	DestPlate-0	B3	25		
16	Plate1by3v9-4-1	A1	DestPlate-0	B4	25		
17	Plate1by3v9-4-1	A1	DestPlate-0	B5	25		
18	Plate1by3v9-4-1	A1	DestPlate-0	B6	25		
19	Plate1by3v9-4-1	A1	DestPlate-0	B7	25		
20	Plate1by3v9-4-1	A1	DestPlate-0	B8	25		
21	Plate1by3v9-4-1	A1	DestPlate-0	B9	25		



CTK

Autopipette enables the user to organize the staples ready for order

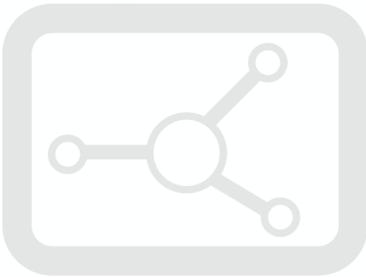
96well format input

Stocks

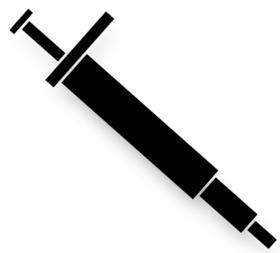
autobreak



origamisim



autopipette



	A	B	C	D	E	F	G
1	Stock Id	Start Plate	Start Well	End Plate	End Well	#Oligos	
2	1	Plate1by3v9-4-1	A1	Plate1by3v9-4-2	A8	104	
3	2	Plate1by3v9-4-2	B1	Plate1by3v9-4-2	F3	51	
4	3	Plate1by3v9-4-2	G1	Plate1by3v9-4-2	G1	1	
5	4	Plate1by3v9-4-2	H1	Plate1by3v9-4-3	D2	50	
6	5	Plate1by3v9-4-3	E1	Plate1by3v9-4-3	E6	6	
7	6	Plate1by3v9-4-3	F1	Plate1by3v9-4-3	F6	6	
8	7	Plate1by3v9-4-3	G1	Plate1by3v9-4-3	G6	6	
9	8	Plate1by3v9-4-3	H1	Plate1by3v9-4-3	H9	9	
10	9	Plate1by3v9-4-4	A1	Plate1by3v9-4-4	A9	9	
11	10	Plate1by3v9-4-4	B1	Plate1by3v9-4-4	B3	3	
12	11	Plate1by3v9-4-4	C1	Plate1by3v9-4-4	C1	1	
13	12	Plate1by3v9-4-4	D1	Plate1by3v9-4-4	D1	1	
14	13	Plate1by3v9-4-4	E1	Plate1by3v9-4-4	E1	1	
15							
16							
17							
18							
19							
20							
21							
22							

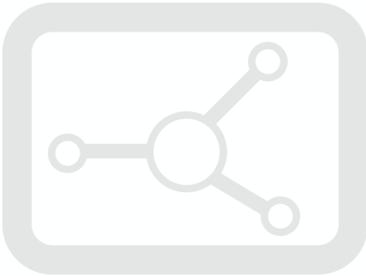
Autopipette enables the user to organize the staples ready for order

CTK

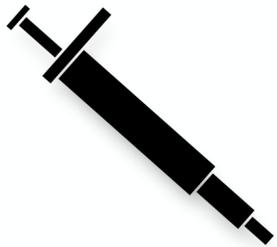
autobreak



origamisim



autopipette

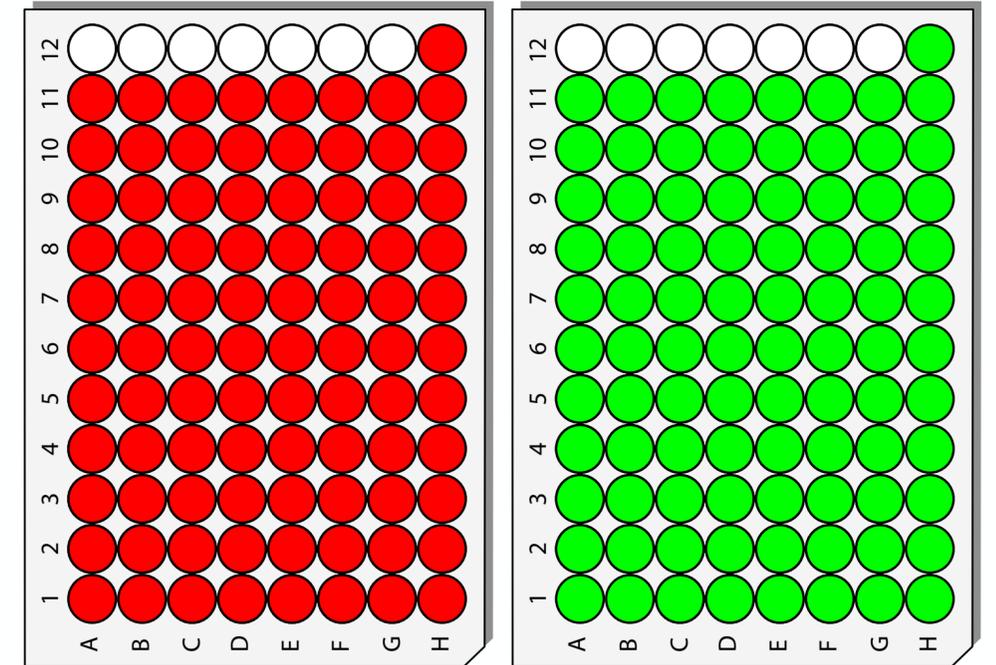
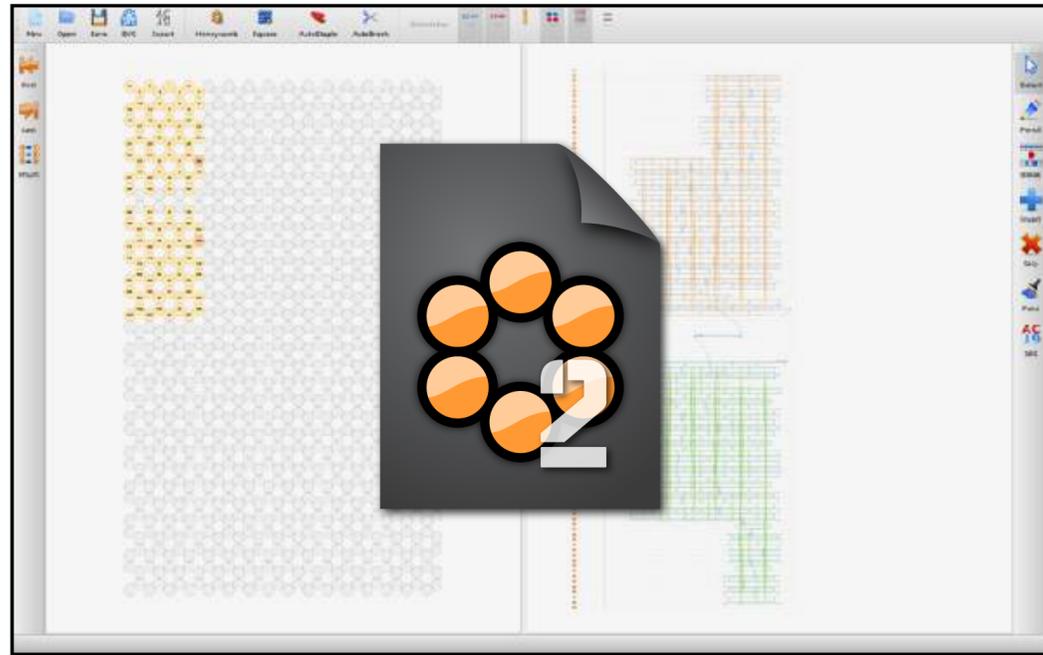


96well format input

Plates

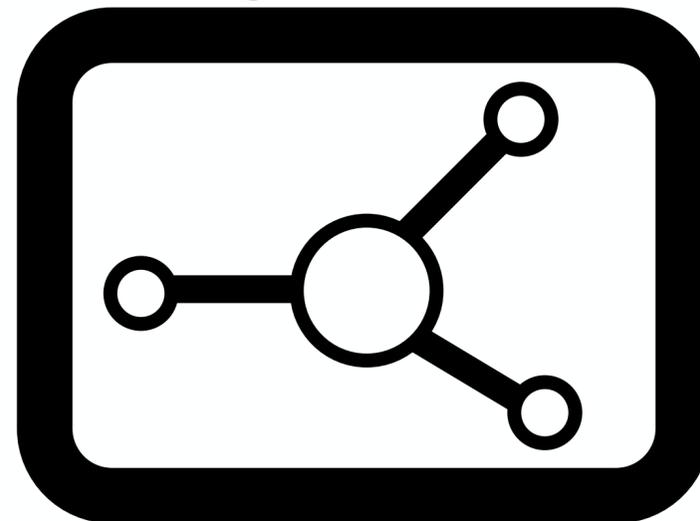
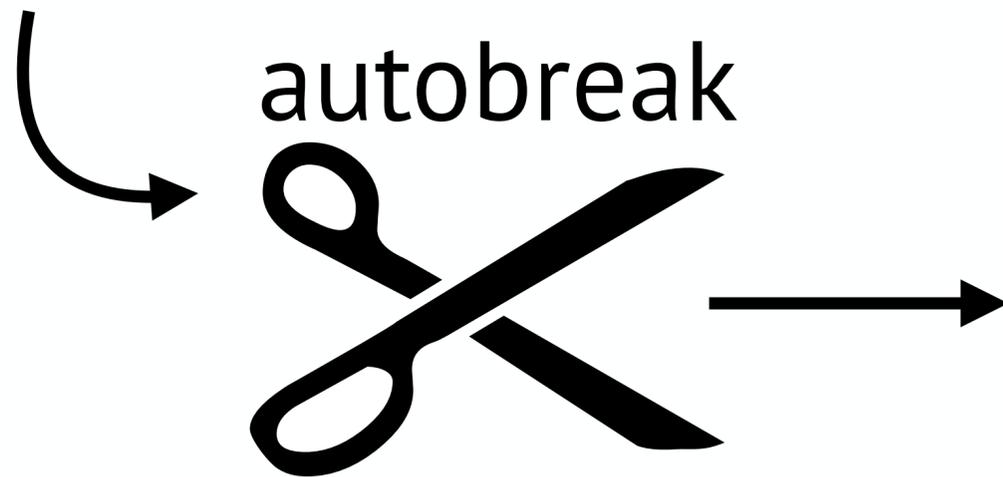
The screenshot shows an Excel spreadsheet titled "of_gos_96well.xlsx". The spreadsheet is organized into columns A through J and rows 1 through 96. Column A contains the plate name "Plate 1 by 96-4-1" for each row. Column B contains the well coordinates (e.g., D11, D12, E1, E2, etc.). Column C contains the DNA sequence for each well. Columns E through J contain numerical values and codes (e.g., 6[249], 15[356], 49, #cc000, 1111111). The spreadsheet is displayed in a window with a standard Excel ribbon and toolbars.

DNA origami design with CTK



origamisim

autopipette



Acknowledgements

Shawn Douglas

Yifan Cheng

David Agard

Erik Navarro

Zanlin Yu

Feng Wang

Pablo Damasceno

Nick Fong

Cryo-EM core facility

Alex Myasnikov

Parsa Nafisi

David Bulkley

Suraj Makhija

Rebecca Wheeler



CHEAT SHEET

cadnano2

```
autobreak.py -i design.json -seq p8064
```

```
origamisim.py -i design_autobreak.json -vmd -circularize
```

```
exportoligos.py -i *.json -seq p8064
```