Algorithmic Design of DNA Nanostructures

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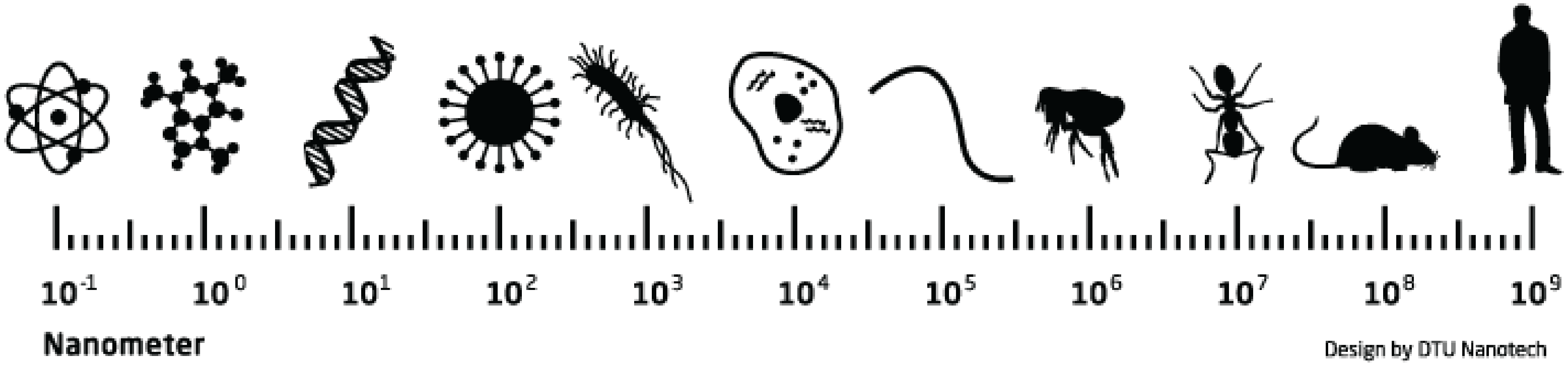
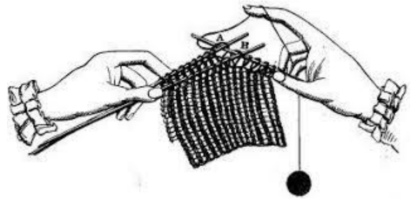
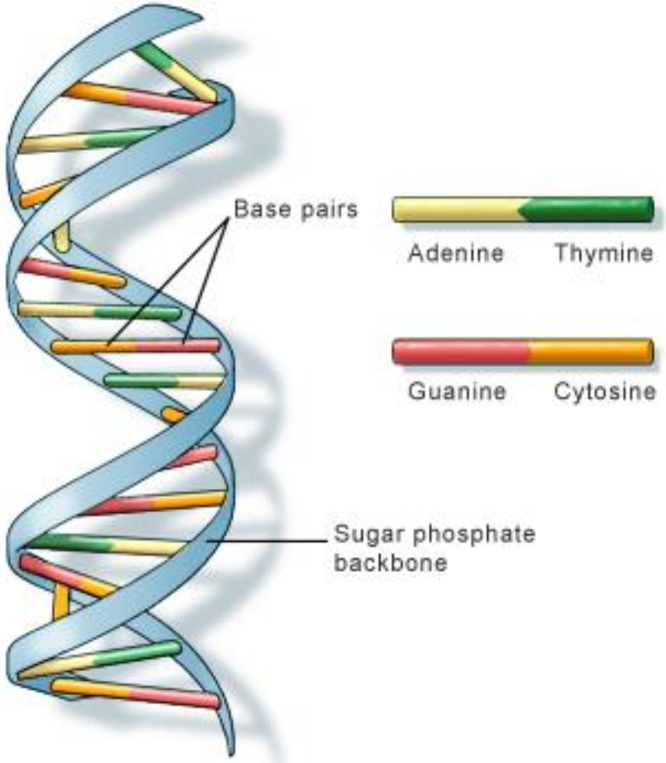
Nanotechnology



Design by DTU Nanotech

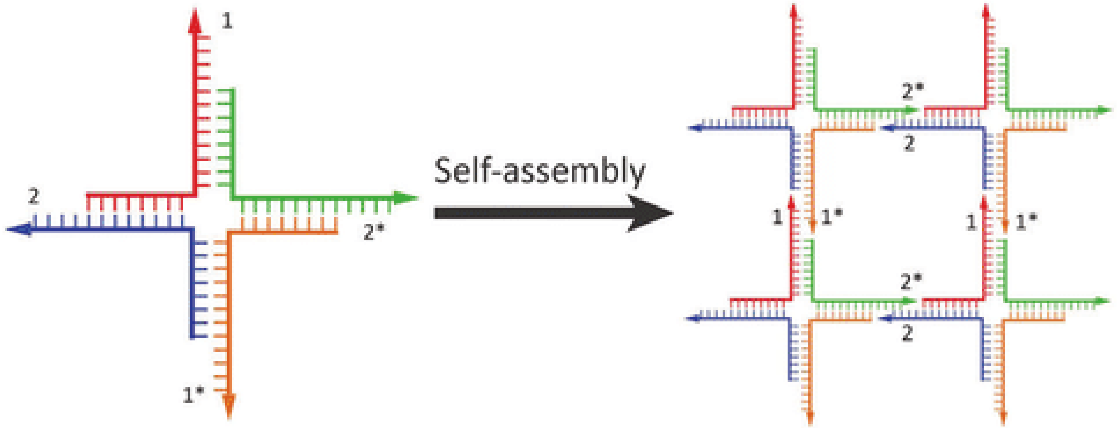


DNA has well-understood interactions and a predictable structure

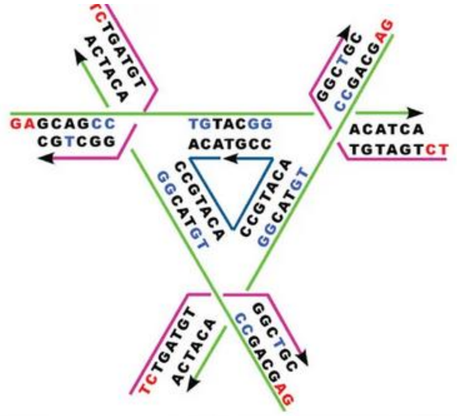


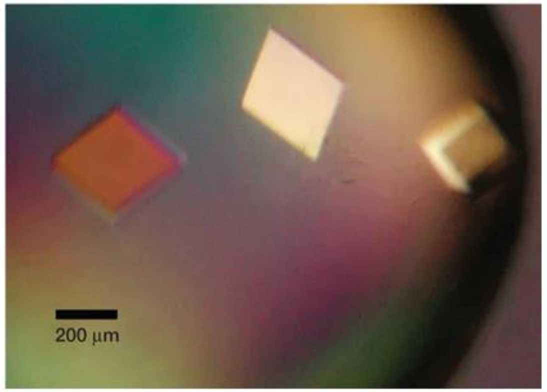
U.S. National Library of Medicine

Stable branched DNA motifs and the birth of DNA nanotechnology (Seeman 1982)



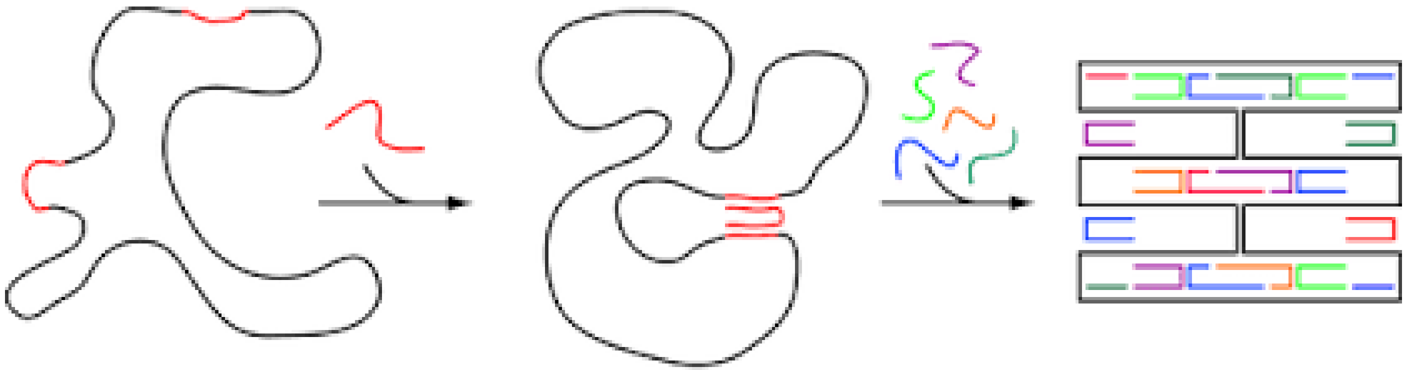
Nadrian C. Seeman (NYU)



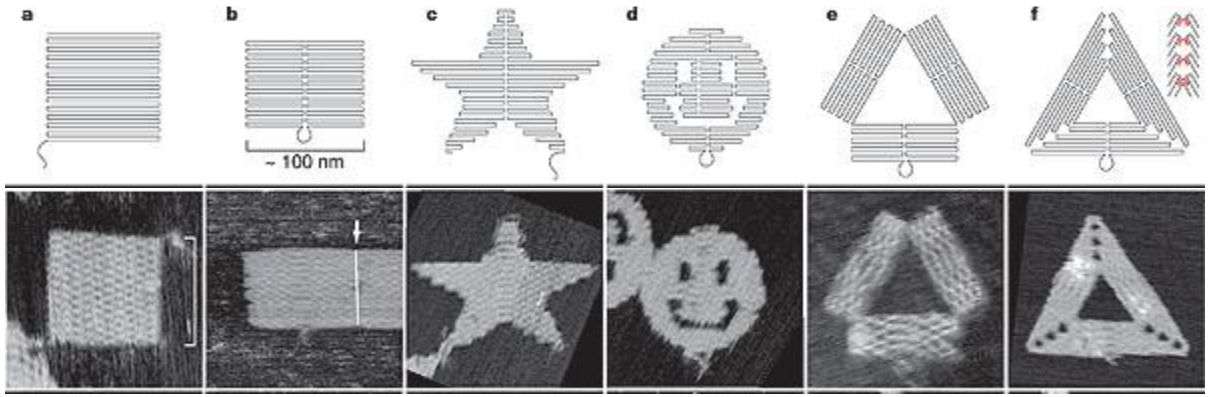


Zheng et al. 2009

DNA origami – a versatile design and synthesis approach

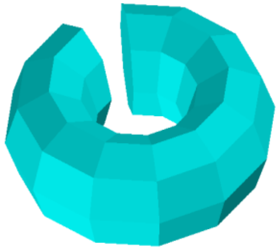


Rothemund 2006



AFM images 165 nm x 165 nm in size

Goal: Biomolecular nanoscale “3D printing”

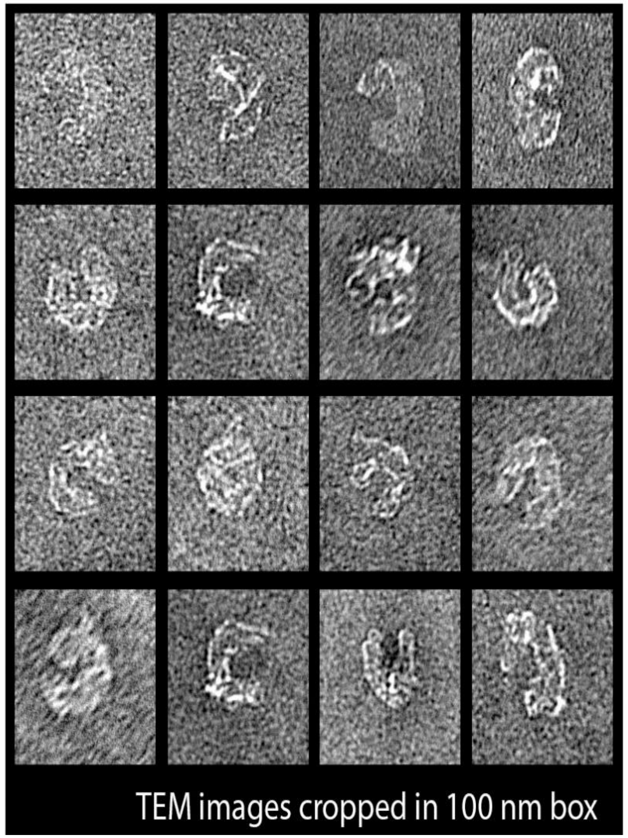


Digital model

```
AAACATGAACAGTAAAGTTTTAACG
GGGTTTAAAGTATTAAGAGGCTATTATTCTG
CCTGCCTATTTCGGAACCAGAGCCGCCGCCAAAGTAAGCGTCAATAATGCCC
GCCCGTATAAACTCAGTACCAGGCGGA
TAAGTAACCCTCATTTTTGCCTTGAGTAACAGT
GGGTCAGACAACGCCTGTAGAGTGTACTGGTAATAATGGCCTGAATTT
ACTTGAGCTGATGATACAGATAAAGGTGAATTATCAACGATTGAGG
ACCGTTCCACATTAAAGCCAGAATGATAGCAGCACCG
CCAGCAAAAAGCGCAGTCAAAATTTGAAAATTTTGTCACACGTCACCG
TAATCAGTAGACAAACAAATAAATCCAGCATTGACAGG
CTTGATATTTTGCCATCTTTTCATAATC
AGAGCCGCGCCACCACCGGAACCGACAGACGATTGGC
AGGTTGAGGCAGGTAGCCGCCACCAGAACCACCACCAAAGAGACTCC
TCAAGAGAAGGATAGAGCCACCACCCTCACCTCCCTC
CCGCCACCCTCTCAGCAGCGAAAGACTGCAGGGAG
GTAAAATACGTAATGCCACTACGACATCGGAACGAGGGTAGCAACAAACACCCTCAGAA
AAAATCACCGGAACCAGAGCTACAGAGGCTTTGA
GGACTAAAGACTTTTTAGCCCCCTTATTAGCGAAGACAGAATC
ATCGGCATTTTCGGTCATCCAGCGATTATACCAAGCG
AACGAGGCGCAAGATTTGTATCATCGCACAGACTGTAGCGCGTTTTC
AAGTTTGCCTTTAGCGTCCAATGAAACCATCGAAATCACCAGT
```

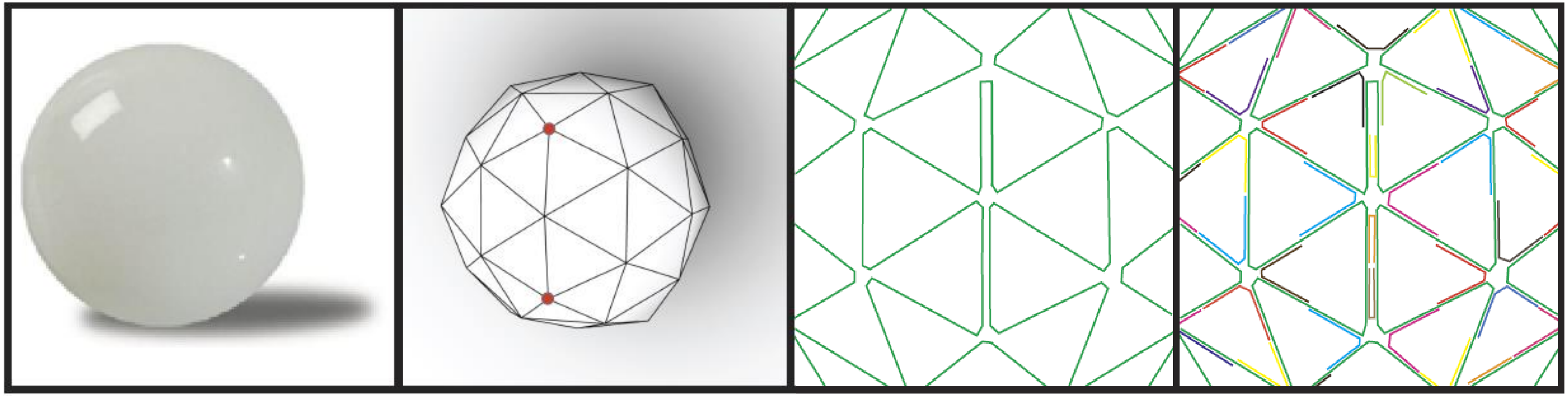
DNA sequences

Chemical reactions



Imaging

Algorithmic design of 3D DNA origami (Benson et al. 2015)



Target shape

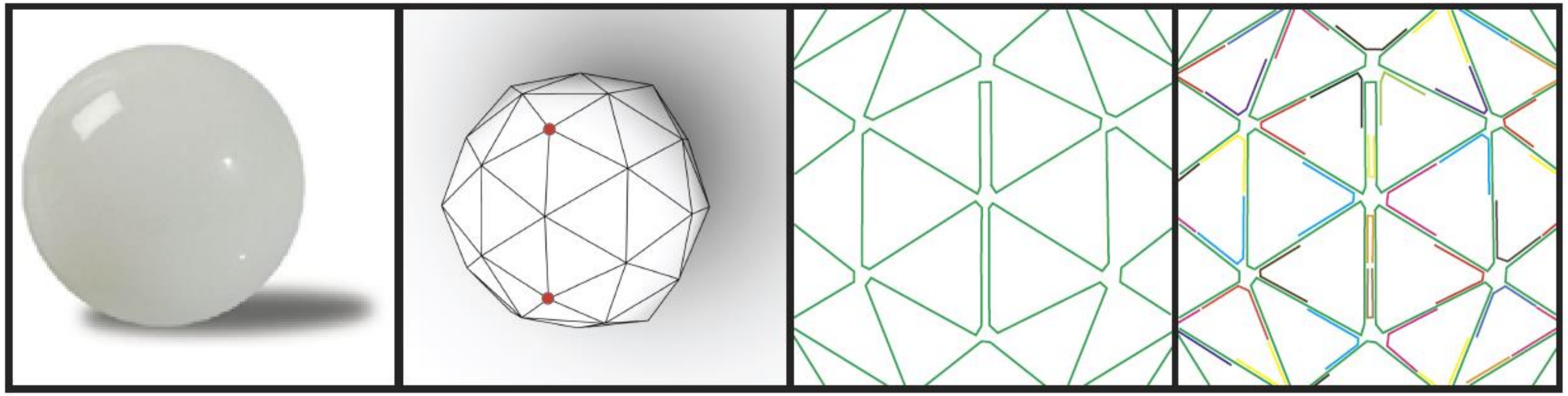
Triangulation

Scaffold routing

Stapling

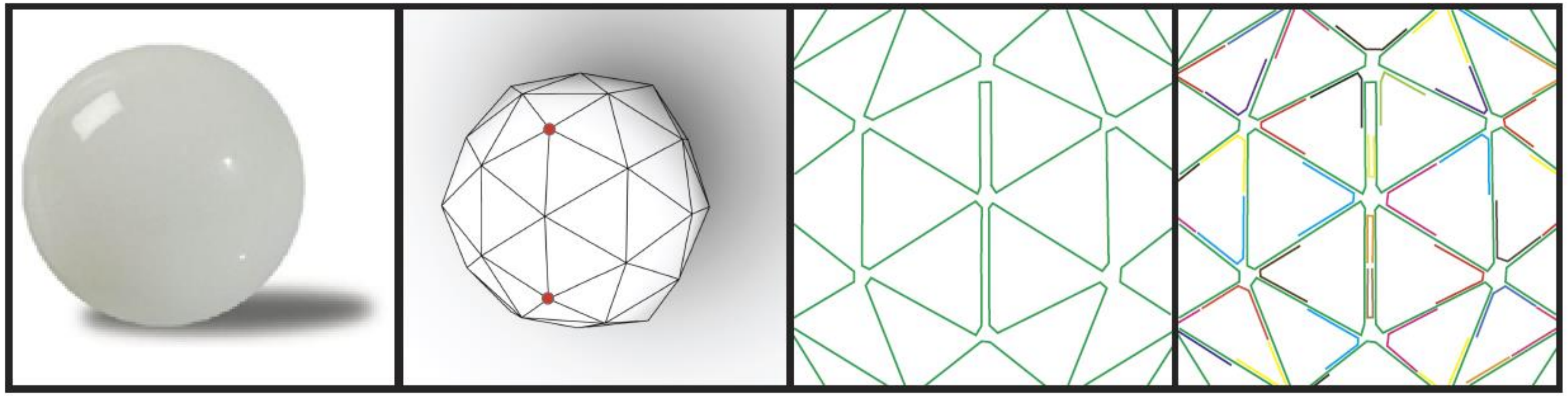
3D DNA origami scaffold routing

1. Each edge replaced by fewest possible number of double-helices. This enables assembly of large structures
2. Scaffold should not cross itself at vertices . This avoids potential knottedness of circular scaffold strand’s routing



3D DNA origami scaffold routing

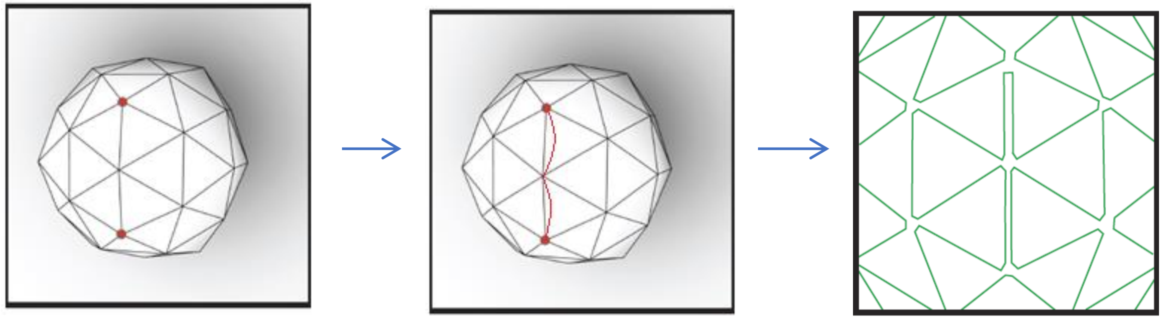
1. Each edge replaced by fewest possible number of double-helices => the scaffold routing should correspond to a "Chinese postman tour"
2. Scaffold should not cross itself at vertices => the Chinese postman tour should be "non-crossing"



Chinese postman tours -- background

1. Each edge replaced by fewest possible number of double-helices =>
   the scaffold routing should correspond to a Chinese postman tour

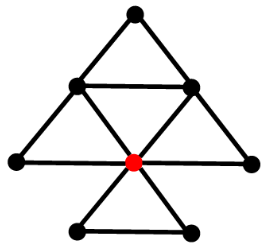
- A *Chinese postman tour* (CPT) on a graph is a minimum-length closed walk which traces every edge.
- A CPT corresponds to an Eulerian tour in an augmented graph where a minimum subset of edges are doubled (Edmonds & Johnson 1973).



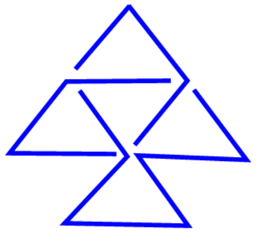
Eulerian tours on embedded graphs

2. Scaffold should not cross itself at vertices => the Eulerian tour should be non-crossing

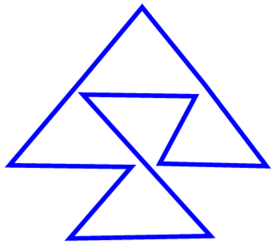
- A graph embedded on a (closed, connected, orientable) surface/plane determines, for each vertex, a cyclic CCW order of edges incident to the vertex, i.e. a rotation system
- Types of Eulerian tours on surface-embedded graphs:
  - a *non-crossing Eulerian tour:* no two pairs of edges *(a,c), (b,d)* incident to a vertex *v* s.t. *(a,v,c)* and *(b,v,d)* are in the tour interleave in the order *(…,a,…,b,…,c,…,d,…)* around *v*.
  - an *A-trail:* any two consecutive edges in the tour are neighbors in the rotation order around their shared vertex



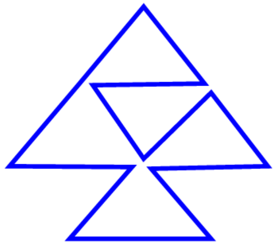
(a) An Eulerian graph.



(b) A crossing Eulerian tour.



(c) A non-crossing Eulerian tour.



(d) An A-trail.

Eulerian tours on embedded graphs

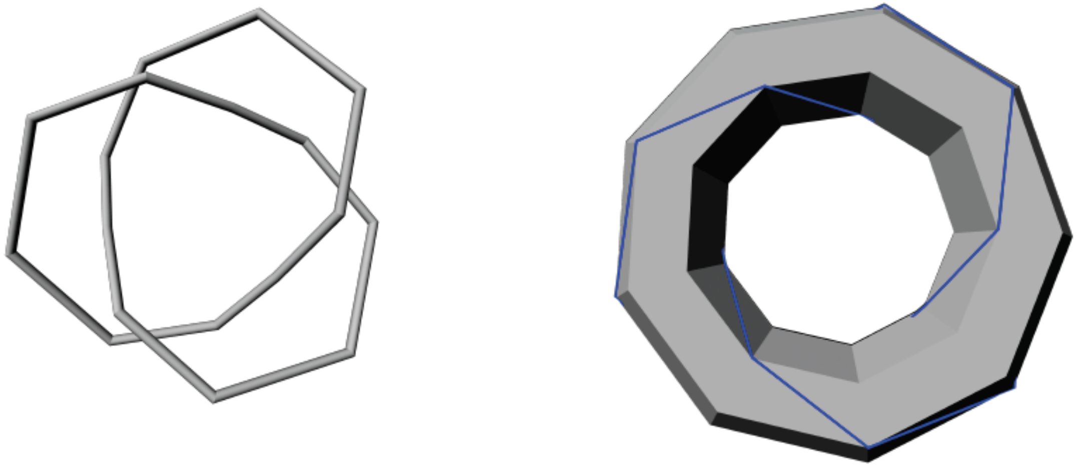
Non-crossing Eulerian tours

- Exist for any plane Eulerian graph (Abraham & Kotzig 1979)
- A polynomial time algorithm for embeddings on orientable surfaces (Mohammed & Hajij 2017)

A-trails

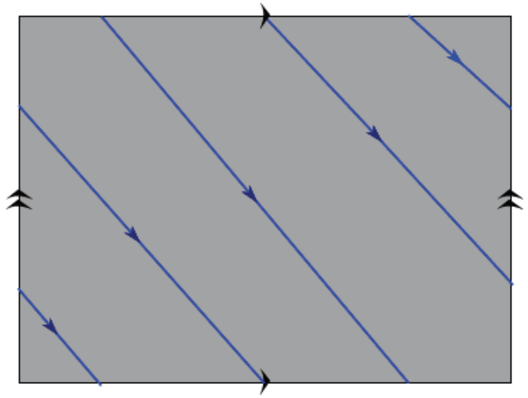
- **NP**-complete for plane graphs (Bent and Manber 1987)
- **NP**-complete for polyhedral graphs with triangular and quadrangular faces (Anderson and Fleischner 1995)
- $O^*(2^{\text{\# of vertices with degree >= 6}})$ algorithm (Mohammed 2014)

Knots and higher-genus surfaces



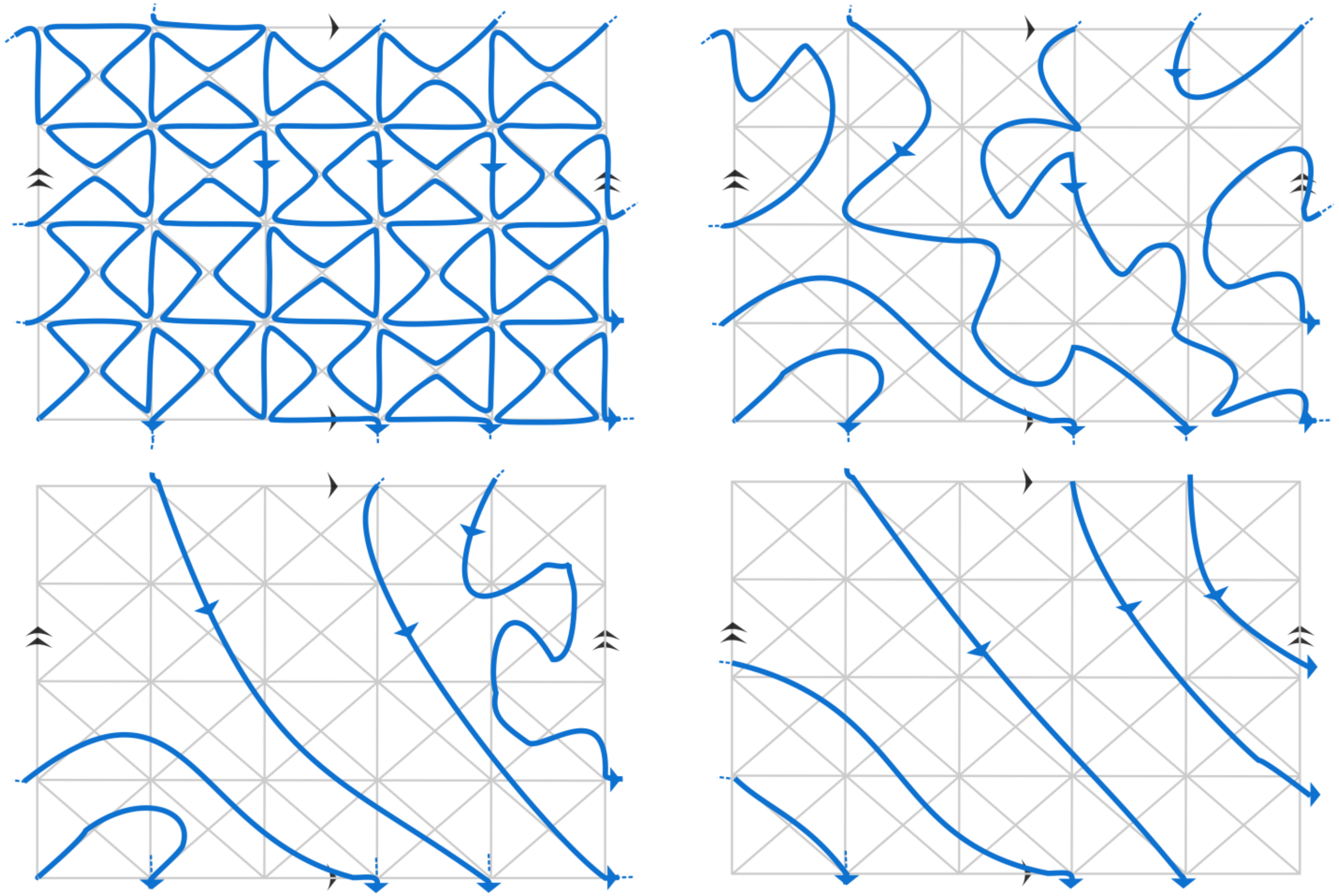
(a) A trefoil knot.

(b) On a standardly embedded torus.



(c) On an identification space for a standardly embedded torus.

A knotted A-trail on a toroidal mesh

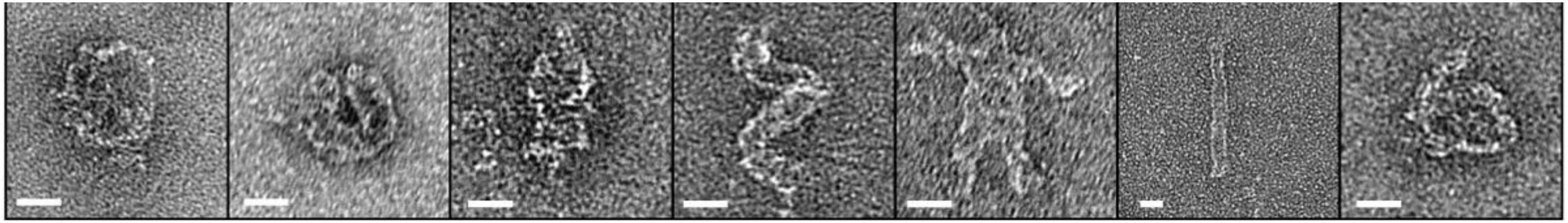


Finding unknotted scaffold routings in higher-genus triangulated surface meshes

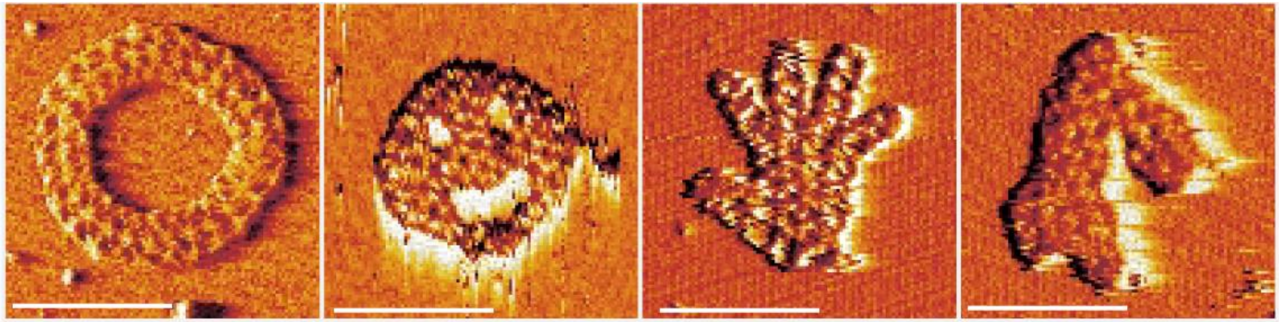
1. Cut the input higher genus surface to a topological disk
2. Remove one edge from each partnered pair of edges in the boundary of the disk
3. Find a non-crossing Chinese postman tour on the processed topological disk

- Yields an unknotted routing which repeats *at most two-thirds* of the edges
- No edge of the surface mesh is routed more than twice

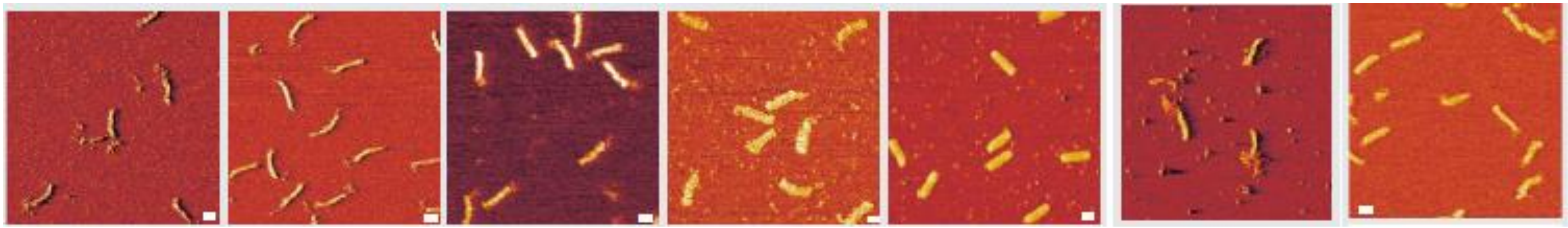
Experimental results



Spherical meshes
20 nm scale bars
Benson et al. 2015

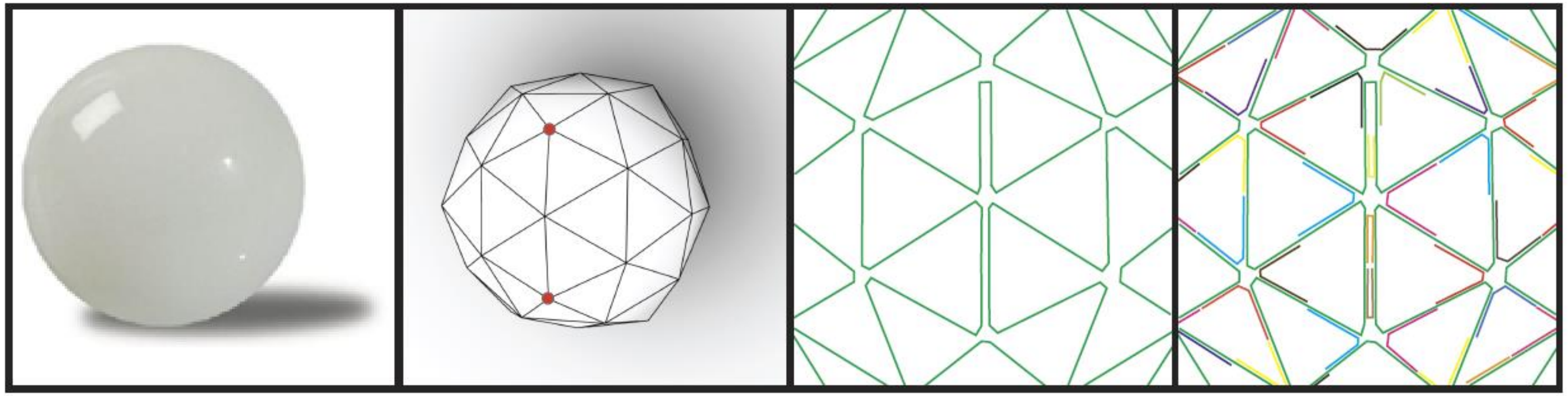


2D meshes with boundary
100 nm scale bars
Benson et al. 2016

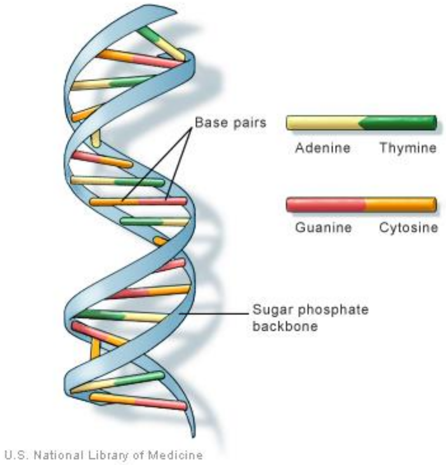


Stiffness of DNA wireframe rods
50 nm scale bars
Benson et al. 2018

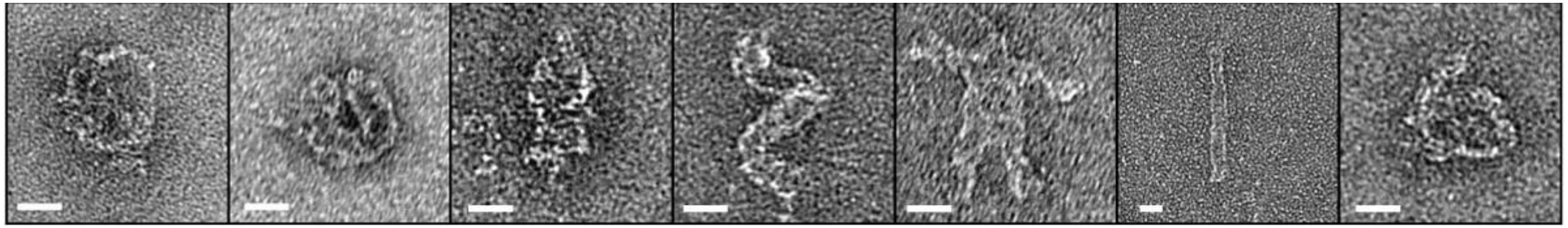
Conclusions



Algorithmic design



Biomolecular nanoscale fabrics



Nanoscale “3D printing”

Ongoing work and future directions

- Exploring knottedness of non-crossing Eulerian circuits on higher-genus surfaces
    - Connections with checkerboard-colorability of the graph embedding
- Design of other linearly embedded spatial graphs
    - Crystallographic structures
    - Edge skeleta of 3-manifold polyhedral complexes

Acknowledgments

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