12-month post-doctoral position (renewable once)

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Random walk on a DNA origami to solve mazes: a biophysical study

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DNA programming is a field that uses biochemistry to design artificial systems made of DNA/RNA that can fold in 2D or 3D structures, embedding computation abilities. Those systems are based on two main techniques:

- DNA origamis [1] which allow to build reliably and with a high yield the initial support for the computation
- algorithmic self-assembly as theorized and later implemented in DNA by Erik Winfree in 1998 whose principle is to design short DNA strands that will collectively assemble into a larger shape, while conducting computations as tiles do in theoretical algorithmic tilings.

We focus here on solving graph algorithms and our goal in this project is to design artificial DNA strands that attach to each other's in such a way that it solves a maze self-assembled onto an origami platform that we design [2]. Such origami mazes have already been solved using DNA navigators [3] that bind to the origami in such a way that drawing a path on the maze is irreversible (hairpins are consumed). In this project we will solve the maze using a random walk that will stop walking only when it reaches the exit. To do so, we use DNA strand displacement mechanism where the kinetics of molecular rearrangement is controlled by toehold DNA sequence and length designs [4]. The biophysical approach we propose will rely on fluorescence quenching kinetic measurements as well as single molecule AFM imaging (see Figure 1).

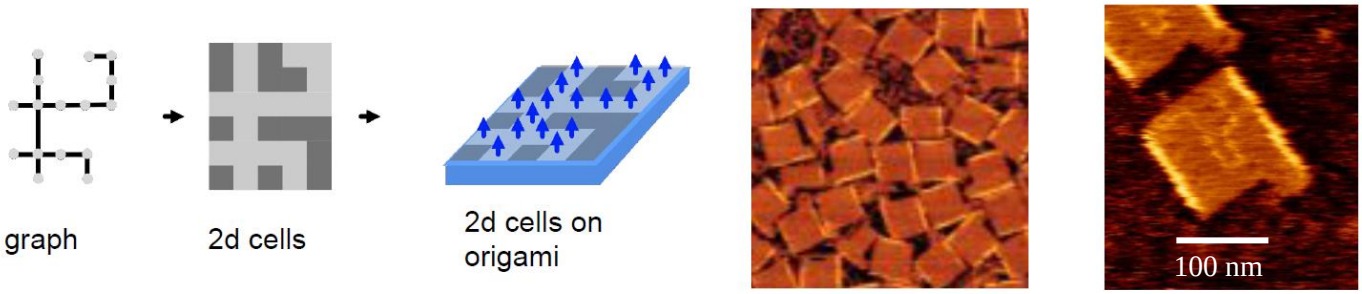

Figure1: The graph solving problem is converted onto a DNA origami self-assembled from DNA cells. To form a maze, there is a ssDNA docking strand coming out of each accessible position only. AFM imaging of several mazes self-assembled as DNA origamis. Preliminary result: we observe on an AFM image at high resolution, the DNA path assembled correctly on the origami encoding a maze consisting of a unique path.

This postdoctoral project is an interdisciplinary collaboration between two teams with complementary expertise in DNA programming, DNA origami design, graph problem solving, biophysics of DNA, AFM imaging and single molecule techniques for DNA and proteins [5,6], nano-mechanics of viral capsids [7]. The work will take place in the Physics Lab at *Ecole Normale Supérieure de Lyon*, where 2 AFM set-up are available and will benefit from the close environment of several labs (Physics, Informatics & Biology) and facilities for sample preparation and characterization.

Recent or upcoming PhD graduates with high motivation and experience in some of the following topics: biophysics, atomic force microscopy and soft condensed matter are strongly encouraged to apply. For the application, we request a short motivation letter along with CV to both of the contacts noted above.

[1] Rothemund P. *Folding dna to create nanoscale shapes and patterns*. Nature, 440, 297 (2006)

[2] Levy N. & Schabanel N. *ENSnano: a 3D modeling software for DNA nanostructures* Schabanel. DNA27, LIPIcs 205(2021)

[3] Chao J. *et a*l. *Solving mazes with single-molecule dna navigators*. Nature Materials, 18, 273 (2019)

[4] Srinivas N. *et al*. *On the biophysics and kinetics of toehold-mediated DNA strand displacement*. Nucleic Acid Res. 22, 10641 (2013)

[5] Carrasco-Salas Y *et al.*; *The sequence of the extruded non-template strand determines the architecture of R-loops*; Nucl. Acid. Res. 47, 6783 (2019)

[6] Montel F., Castelnovo M., Menoni H., Angelov D., S. Dimitrov & C. Faivre-Moskalenko; RSC *remodeling of oligo-nucleosomes: an Atomic Force Microscopy study;* Nucleic Acids Res. 39, 2571 (2011)

[7] Menou L.*, Carrasco Salas Y.*, Lecoq L., Salvetti A., Faivre-Moskalenko C. & Castelnovo M. *Stiffness heterogeneity of small viral capsids*; Physical Review E 104, 064408 (2021)