Using Living Cells as Nanotechnology Factories

At the Biodesign Institute at Arizona State University (ASU), researcher Hao Yan makes DNA-based nanostructures inside living cells by using the cells as factories. Cells are good at making copies of double-stranded DNA, and Yan and his colleagues have used the cell's own machinery to produce many, many copies of complex DNA nanostructures in a simple, efficient process. Researchers in synthetic biology have been searching for a versatile method for replicating artificial DNA nanostructures with complex secondary structures, and Yan's work brings that goal closer.

To test the nanoscale manufacturing capabilities of cells, Yan and fellow researchers Chenxiang Lin, Sherri Rinker and Yan Liu at ASU and their collaborators Ned Seeman and Xing Wang at New York University (NYU) went back to reproducing the very first branched nanostructures made up of DNA: a cross-shaped, four-arm DNA junction and another DNA junction structure containing a different crossover topology. To copy these branched DNA nanostructures inside a living cell, the research team first introduced material inside a bacteria cell. They cut and pasted the DNA necessary to make these structures into a phagemid, a virus-like particle that infects a bacteria cell. Once inside the cell, the phagemid used the cell to reproduce millions of copies of the DNA. By starting with just a single, theoretical phagemid infection, and a single milliliter of cultured cells, Yan found that the cells could churn out trillions of the DNA junction nanostructures. Moreover, the DNA nanostructures produced in the cells were also found to fold correctly, just like the previously built test tube structures. The fact that the natural cellular machinery can tolerate artificial DNA objects is quite intriguing, and opens new research directions.

C. Lin, S. Rinker, X. Wang, Y. Liu, N. C. Seeman, and H. Yan. 2008. In vivo cloning of artificial DNA nanostructures. *PNAS*, **105** (46): 17626–17631. Published online before print October 16, 2008, doi: 10.1073/pnas.0805416105

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