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Bottom-UP assembly of nanorobots: extending synthetic biology to complex material design

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Commentary

Today nanotechnology is being researched in a variety of different fields like sustainable energy, life extending medicine, material science and electronic [1]. Nanotechnology enables researchers to program and control the matter at the atomic level using cutting-edge tools like atomic force microscopy and scanning tunneling microscopy [2]. This idea could be used as a step ahead assembling molecules, drugs, and materials at the atomic scale and making nanomachines smaller, which would allow more room for complexity accuracy, and evolution. Future nanotechnology taking inspiration from nature will open routes for the molecular manufacturing for the construction of macroscopic products with nanoscopic precision via bottom-up nanorobot mass fabrication for the drug delivery [3]. This will complement the current nanorobotics manufacturing via top-down approaches used for targeting the therapeutics to inaccessible sites in vivo. It will be essentially 3D chemical printing of large functional molecular structure from basic biochemical building blocks one atom at a time. the broad idea of a nanomachine is that could be programmed to turn even the most basic raw materials into complex structures like microchips, therapeutic proteins, custom DNA or a therapeutic device. However, a single nanomachine on its own cannot perform complex function; we need further to manufacture more of these tiny machines via coding and programming the DNA/RNA/amino acids complementary sequences using Artificial Intelligence (AI), and machine learning, and then integrate into living cells like *E. coli*. The envisioned future is possible via bio-assembly using synthetic biology approaches (Figure 1) [4].

In fact, inside biological cells, there are tiny nano factories inside each of our cells called ribosomes. Recently, biological cells have been shown to manufactures complex structures at nanoscale made from gold chloride [5-7]. The ribosome is simple protein assembler which can assemble 20 different amino acids into an infinite combination of proteins making up the vast complexity of the cellular machine. Another example is the virus particles, nature´s nanoreplicators which are able to hijack the ribosomes of biological cells to make the desired proteins they want including copies of themselves. Viruses reprogram the ribosome to make new DNA and protein assembly, and then use them to infect other cells. The viral nanomachines repeat the process until they take over whole cell functions to manipulate the threat against them. The nature has already made the ribosomes and all we have to do is to edit it, so that they can create more nanostructure out of covalently bonded carbon chains [8].

The future scientific communities might be able to develop a synthetic nanoreplicators personalized medicine. However, it won't be easy since the human genome is 3 billion base pairs long and converting it into a finite amount of size/shape nanomachine with spatiotemporal control is very complicated. Overall if it ever becomes practical, interdisciplinary science and bio-assembly together will have hundreds of times the societal impact of the Industrial Revolution. If not, more it would mean a world of objects that disassemble and reassemble themselves everywhere in our daily lives. The nanoreplicators will most certainly be met with both fear and excitement knowing that this technology could appear out of anywhere since we'd only have to build one nano machine to get trillions. In future, the nanoreplicators will be the next logical step after the biotech revolution ends. This concept has the potential to change not just our bodies and minds but our entire world. The programmable matter is the idea that matter can change its shape and physical properties just by reconfiguring its atoms. All of these miraculous wonders definitely won't happen in the near future but it's still an interesting idea to see what direction this technology could go without making any mistake. The industrial manufacturing of anything larger than a few micrometers using the simplest bacterium is more than decades away since today's technology in these prospects is still are in infancy [9].

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Special Issue: Nanotechnology: Challenges and Perspectives in Medicine

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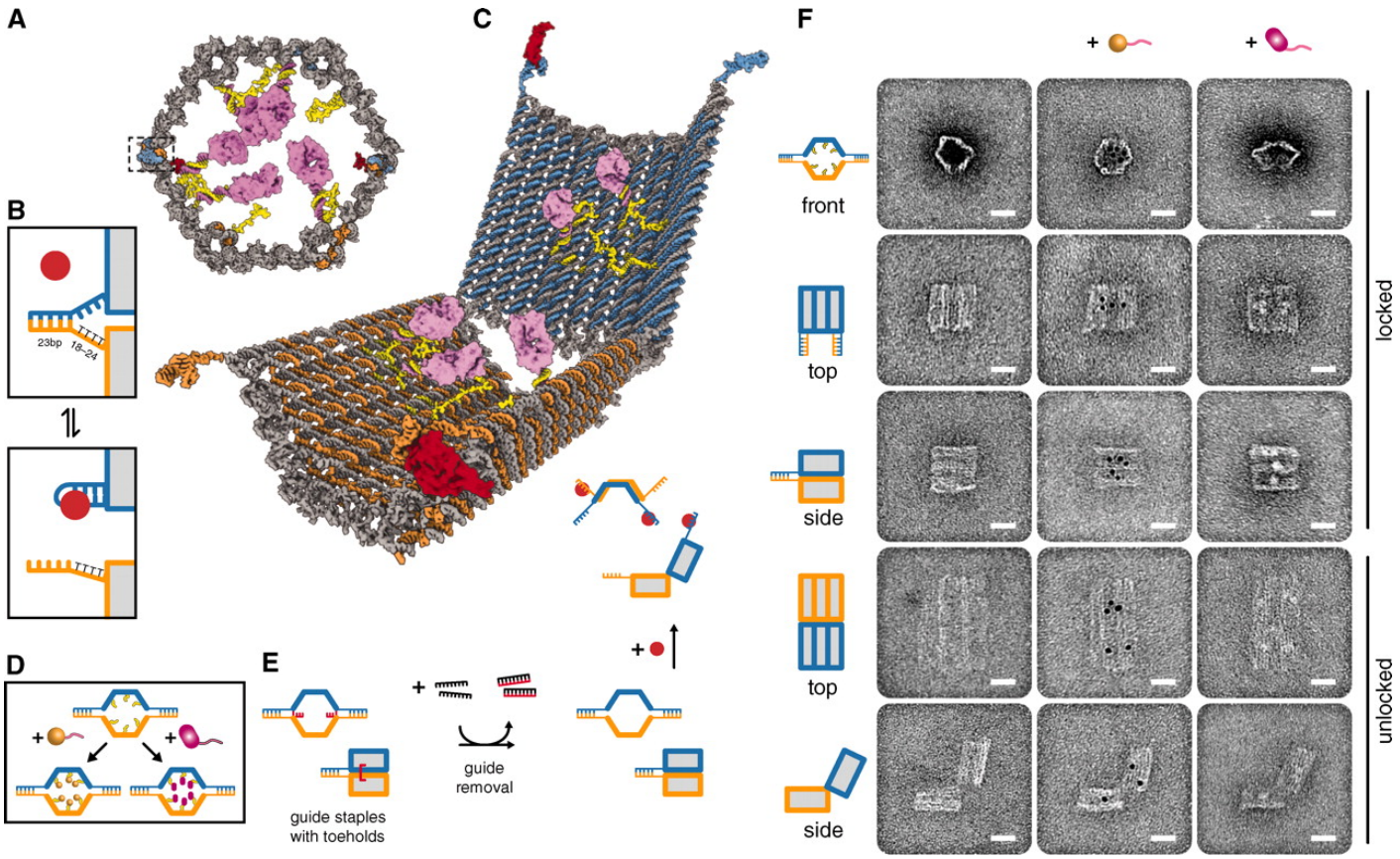

Figure 1. Design and TEM analysis of aptamer-gated DNA nanorobot. (**A**) Schematic front orthographic view of closed nanorobot loaded with a protein payload. Two DNA-aptamer locks fasten the front of the device on the left (boxed) and right. (**B**) Aptamer lock mechanism, consisting of a DNA aptamer (blue) and a partially complementary strand (orange). The lock can be stabilized in a dissociated state by its antigen key (red). Unless otherwise noted, the lock duplex length is 24 bp, with an 18- to 24-base thymine spacer in the nanoptamer strand. (**C**) Perspective view of nanorobot opened by protein displacement of aptamer locks. The two domains (blue and orange) are constrained in the rear by scaffold hinges. (**D**) Payloads such as gold nanoparticles (gold) and antibody Fab′ fragments (magenta) can be loaded inside the nanorobot. (**E**) Front and side views show guide staples (red) bearing 8-base toeholds aid assembly of nanorobot to 97.5% yield in closed state as assessed by manual counting. After folding, guide staples are removed by addition of fully complementary oligos (black). Nanorobots can be subsequently activated by interaction with antigen keys (red). (**F**) TEM images of robots in closed and open conformations. Left column, unloaded; center column, robots loaded with 5-nm gold nanoparticles; right column, robots loaded with Fab′ fragments. Scale bars, 20 nm. (Reproduced with permission from the American Association for the Advancement of Science (AAS) from reference [4].

Conflict of Interest

Authors state no conflict of interests.

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