STATEMENT OF RESEARCH PLAN

At the junction of top-down and bottom-up

The emerging interest in nanostructures results from their numerous potential applications in various areas such as biomedical sciences, electronics, materials, optics, electrochemistry. Traditional microfabrication, which is built on photolithography, either might be approaching its limits, or continues to achieve reductions in feature sizes at great expense. As suggested by the Nobel Laureate Richard Feynman, "There is plenty of room at the bottom", research has been directed towards alternative ways to achieve nanostructures instead of the conventional top-down approaches. The truest example of bottom up nanotechnology is nature. Nature continuously constructs complex, efficient self-organizing and self-regulating molecular machinery and systems for all processes in living organisms. These molecular machinery and systems can now be used to build materials from the bottom up. Nanostructured assemblies have been constructed by biofabrications[1] using biological materials: from DNA[2] to peptide,[3] from biopolymer[4] to protein,[5] even virus.[6] Does nature, however, provide unexhausted resources for this bottom up strategy? Can researchers and scientists manipulate the nanostructures with nanoscale precision and reproducibility in the same manner as those biological systems?

The multidisciplinary field of nanobiotechnology[7] is of great interest, which opens up the possibility to explore the interface between biology and electronics at the single-molecule level. The research endeavors will be directed towards using nanotechnology for the study or manipulation of biological macromolecules at the nanoscale to contribute to advancement and understanding in frontier biological science, or taking advantage of bioscience concepts for the development of the next generation of nanomaterials. Typically, the goals comprise the construction of nanoarrays for analyzing complex mixtures of DNA, RNA, proteins as well as the design of ultra-sequencing devices, such as molecular machines, sensors or transistors at nanoscale.

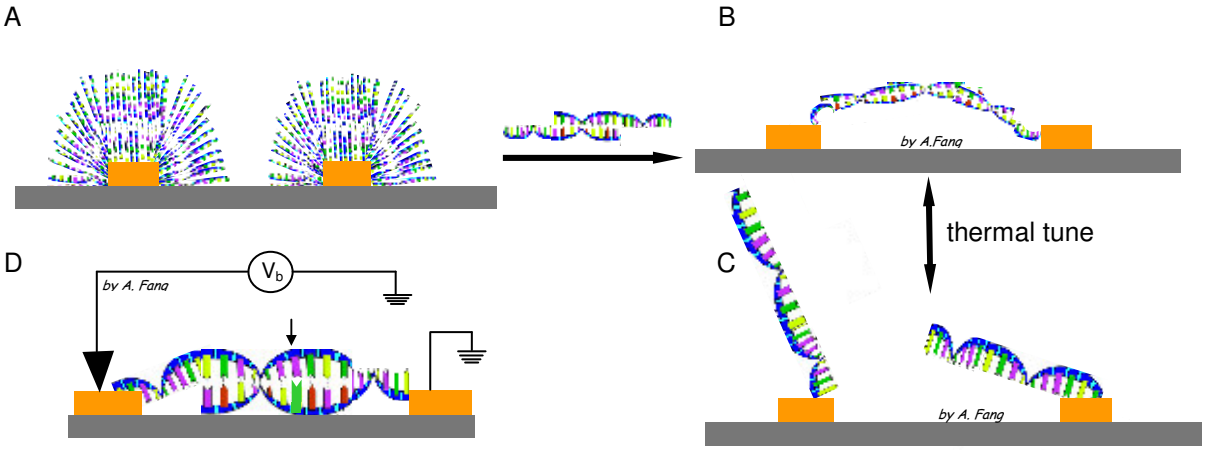

Figure 1 Schematics of molecular switches and its potential for SNPs diagnostics. (A) Patterning of 2 ssDNAs on Au nanostripes; (B) Introducing a complementary DNA duplex to bridge the Au nanostripes; (C) thermal tune for switching the bridge; (D) SNPs, as indicated by the arrow, will be possible to read out from its I(V) characteristics. Only one DNA duplex bridge is shown for clarity.

One of the promising approaches is to build up nanostructures for nanobiotechnology by integration of top-down with bottom-up approaches. Figure 1 illustrates one example of the possible applications of the nanopatterning derived from the hybrid technique. Two single strand DNAs (ssDNA) are immobilized on the neighbouring gold nanostripes in a site-specific manner. The gold nanostripes are separated with a distance of 20 nm on Si surface. The ssDNAs are 40mer non-complementary oligonucleotides. Due to the space and their non-

complementary character, the two grafted ssDNA are in a relaxation state (Fig. 1A). When introducing a solution of an oligonucleotide duplex with protruding ends which are complementary to the two grafted sequences, the neighbouring gold nanostripes are bridged with a DNA duplex (Fig. 1B). This DNA bridging can be reversed by thermal denaturation. By fine tune of the temperature for a hybridization-dehybridization cycle, it will be also possible reversibly to turn the bridging on or off. Together with the pivotal role of base pair in electron as well as charge transport in DNA,[8] this reversible switching behaviour can be directed towards switches for molecular electronics, and *vice versa*, based on the I(V) characteristics of the "nano-bridge", it will be also possible to detect single nucleotides polymorphisms (SNPs) in targeted DNA fragments.

Microfluidic Devices: Lab-on-a-Chip

Miniaturized systems composed of microfluidic channels and microvials provide unique opportunities for parallel, efficient chemical analysis[9] and synthesis,[10] or testing of catalysts.[11] Those chemical analysis devices are commonly referred to as micro-total analytical systems (μTAS),[12] while the miniaturized chemical reaction systems are referred to as microreactors.[13] The conception of μTAS proposes the integration of the different steps of an analytical process into a miniaturized flow system, thereby creating the right conditions for faster, automated analysis. The capability of microchemical reaction systems with sub-millimeter length scales have the potentials to exceed conventional macroscopic systems by the large surface to volume ratios for rapid heat transfer and reduction of concentration gradients, by miniaturized dimensions for fast mass transport and response, and by microfabrication technology for

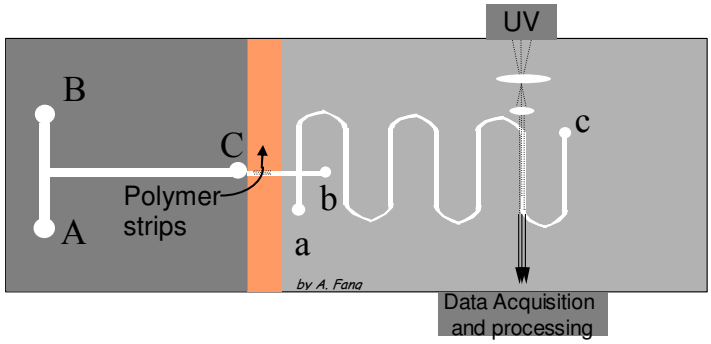

Fig 1. Tentative design for the concept of *lab-on-a-chip*. ■ Reaction zone: A + B⟶ C; the microfluidic channels can be functionized with catalyst.[10d)] ■ Sampling handling zone, the micro-fluidic channels are embedded with polymer strips for preconcentration. ■ On-chip separation and detection, The separation mode can be capillary electrochromatography or capillary electrophoresis, while detection can be optical, electrochemical or other detection methods.[14]

greater control over reactor geometry and integration of heaters and sensors. An attractive feature in utilizing microfabricated structures is the integration of different kinds of manipulation on a single device. One of the clear trends over the recent years has been towards more complex microfludic networks, incorporating chemical synthesis, sample manipulation, separation and detection, towards the fundamental of Lab-on-a-chip. Figure 1 depicts a tentative design of a more integrated device.

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