

Abstract Title**Functional DNA nanodevices****Symposium Track**

Engineering Applications to Nanobiology

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The unique chemical and mechanical properties of DNA can be used to construct simple nanoscale devices [1]. Their operation principle usually relies on the specific recognition between complementary DNA strands, the "unzipping" of DNA strands by DNA "branch migration", and the different mechanical properties of single and double-stranded DNA.

Two strands of DNA will only bind together if they contain complementary base sequences, i.e. each guanine on one strand finds a cytosine on the other, each adenine finds a thymine. This allows to "program" DNA sequences which are partly single-stranded and partly double-stranded. Due to the fact that single-stranded DNA is a considerably more flexible molecule than DNA in its double-helical form, this results in supramolecular structures composed of a combination of flexible and rigid elements. Furthermore, a biochemical process known as "branch migration", in which two DNA strands with the same sequence compete for binding to another strand can be used to selectively remove DNA strands from such a supramolecular structure. Using branch migration, the mechanical properties of such a structure may therefore be reversibly switched between different states. These principles have been previously used to realize motion on the nanometer scale as well as the binding and controlled release of other molecules. The latter was achieved by incorporating functional nucleic acids such as DNA aptamers into DNA nanodevices.

Aptamers are oligonucleotides which strongly and specifically bind to small molecules or proteins. In some cases they exhibit binding affinities similar to those for antibody-antigen interactions. At the same time, they have the advantage of being compatible with standard DNA methodologies. Once the correct sequence for an aptamer is known, it can be synthesized or amplified much more easily than proteins. Recently, we have shown how an aptamer for the protein thrombin can be easily switched between two conformations in which it binds or does not bind the protein [2]. This allows us to cyclically bind or release the protein. In our original approach, the release of thrombin had to be triggered by a DNA strand whose sequence depended on the aptamer sequence itself. It would be more useful, however, to completely uncouple molecular "input" from "output". We therefore developed a DNA signal transduction scheme based on a DNA molecular automaton by which the rate of protein release by the DNA aptamer could be made dependent on "generic" DNA signals [3]. Being able to reversibly bind or release proteins using switchable aptamers can be used, e.g., to selectively switch on or off enzymatic function. This could be demonstrated recently with a

device based on a DNA aptamer specific for Taq polymerase, switching on and off DNA polymerization at room temperature [4].

For future applications it will be desirable to make the action of DNA-based molecular devices dependent on a variety of environmental stimuli. One natural choice of a biologically relevant environmental input is the presence or absence of mRNA. In a series of preliminary experiments, we could demonstrate that indeed DNA nanodevices can be controlled using mRNA transcribed from an artificial "control gene" [5] and that this gene can even be put under the control of simple gene regulatory mechanisms [6].

Keywords

DNA nanoscience, aptamers, DNA computing, synthetic biology, transcription

References

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