Synthesis of modified nucleotides and oligonucleotides to improve the storage of digital information in DNA

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Digital data production has seen an exponential growth in the last decade and spawns the need for alternative and efficient storage media. Efficient storage media that could replace existing, materials must encompass several criteria including high storage capacity and density, long-term storage capacity, high access speed, low cost of production, and sustainability[1,2]. DNA represents an alluring nanomaterial to produce such devices since the theoretical storage capacity (~$4.5 \cdot 10^7$ GB/g) exceeds that of traditional media and the Watson-Crick base pairing rules offers a high degree of programmability. In addition, DNA can easily be replicated using polymerases which permits the copy of digital information at low cost and high efficiency; a feature that is not met in traditional media. Simple algorithms can convert strings of bits into actual DNA sequences. These sequences can then be synthesized, mainly by phosphoramidite-based chemistry, in the process called “writing” (Fig. 1)[2]. All these sequences are then grouped together into complex libraries and prepared for long term storage. Retrieving or “reading” of the digital information proceeds then via an inverted process, namely sequencing of the sequences and decoding back using the aforementioned algorithms. Modern sequencing methods such as NGS, nanopore, or sequencing by synthesis offer the possibility of analyzing large libraries of DNA sequences with high fidelity in very short time frames. On the other hand, synthetic access to longer (>150 nt) sequences with large (>10^{10}) diversities is very limited and is certainly trailing behind existing capacity for reading complex DNA libraries which is a strong impediment for storage of digital information with DNA as medium[3].

Our chemoenzymatic strategy involves the preparation of longer DNA templates containing chemically modified nucleotides at defined positions. Polymerases will read through and copy these templates with a higher speed than any chemical synthesis will be capable of doing[4]. We envision that diversity can be obtained using these templates simply by applying a trigger signal on the chemical modifications which in turn will alter the fidelity of polymerases. The direct result will be introduction of different nucleotides than in the absence of stimuli and these differences can be read by sequencing analysis.

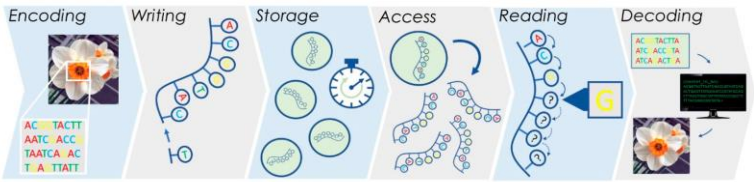

Fig. 1. General strategy for DNA data storage[2].

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