Molecular encryption for controllable random access in DNA data storage

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Abstract

DNA data storage offers exceptional density and millennial-scale stability, with advances in encoding schemes and reduced synthesis costs making large-scale archiving increasingly viable. However, while efforts have focused on reliable data retrieval, securing DNA-encoded information against unauthorized access remains largely unexplored. Here, we introduce DNA-GUARD (DNA Gated Unlocking and Access Restriction of Data), a molecular-level access control system that physically restricts data retrieval rather than relying on computational encryption. DNA-GUARD integrates with PCR-based random access by selectively blocking amplification of protected sequences. Chemically modified "locker strands" outcompete PCR primers and block polymerase extension through 3' inverted dT modifications, preventing amplification of key sequences required for file decoding. To restore access, complementary "password strands" tethered to magnetic particles sequester locker strands, enabling their removal and restoring unbiased amplification. We demonstrate DNA-GUARD's scalability from 600-byte to 1-MB files without performance loss, orthogonal control of multiple files within mixed libraries, and reliable repeated locking-unlocking cycles. This approach enables physically-controlled molecular encryption compatible with established DNA storage workflows, providing a foundation for secure archival storage with implications for molecular information security.