RECORDING TEMPORAL DATA WITH MINUTES RESOLUTION INTO DNA

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Recording complex biological signals is a crucial application of synthetic biology and essential for a deeper understanding of biological processes. An ideal "biorecorder" would have the ability to record biological signals over a wide spatial distribution of cells with high temporal resolution. However, the genetically encoded biorecording tools available have very good spatial resolution (cellular level), but currently rely on turning on and off transcription and translation of a protein (e.g., Cas9 or a recombinase) to record the biological signal, making their temporal resolution on the order of hours. Here we introduce a DNA polymerase based biorecorder that can record cationic concentration fluctuations into DNA sequence with a resolution of ~1 minute. We use a template independent DNA polymerase; terminal deoxynucleotidyl transferase (TdT) that randomly incorporates bases onto a single strand of DNA. The preference of base incorporated by TdT changes with the concentration of cations in TdT's environment. Therefore, by analyzing a strand of DNA that was extended in fluctuating cation concentrations, we can determine the temporal profile of cation concentration from the bases added. Using this method, we can measure a change in Co²⁺ concentration during a one hour period with an accuracy of 1 min. We also show the approach works for Zn²⁺ and Ca²⁺. We will present our methods for optimizing this biorecorder and characterize its performance in vitro. Recording data onto DNA with minutes time resolution could solve many challenging data acquisition problems in neuroscience and developmental biology, and could aid in the use of DNA as a data storage medium.