Docket #: S21-290

MANIfold: Systematic characterization of nucleic acid thermodynamics via high-throughput fluorescence melt experiments

MANIfold is a novel method developed for systematic, high throughput measurements of nucleic acid secondary structure. The method includes a platform that is capable of massively parallel fluorescent measurements yielding quantitative data on the thermodynamics of the nucleic acid secondary structure. Numerous algorithms have previously been developed to predict the DNA/RNA secondary structure thermodynamics, many of which rely on nearest-neighbor models; however a major hurdle limiting such efforts has been the throughput available to methods that characterize DNA and RNA one-by-one. Now with MANIfold, it is possible to measure nucleic acid secondary-structure motif data for multiple classes of motifs (e.g. hairpin loops, mismatches, and bulges) at once. This propensity of diverse data thus allows the development of more accurate deep learning models for prediction of nucleic acid thermodynamics and folding.

Stage of Research

- Proof of concept

Applications

- Predictive models of DNA and RNA structure including secondary structure and base-pairing
- Measuring interactions between nucleic acids and other molecules (e.g. small molecules) at various experimental conditions

Advantages

- Structure prediction in various buffer conditions
- Simultaneous measurement of ~45,000 nucleic acid melt curves (DNA and RNA)
- Measures multiple classes of structural motifs for more accurate prediction of nucleic acid dynamics

Publications

- Ke, Y., Sharma, E., Wayment-Steele, H. K., Becker, W. R., Ho, A., Marklund, E., & Greenleaf, W. J. (2025). High-Throughput DNA melt measurements enable improved models of DNA folding thermodynamics. Nature Communications, 16(1), 5572.

Patents

- Published Application: WO2023028618
- Published Application: 20240352450

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