**ABSTRACT**

PicoSeq and the lab of Vincent Croquette are developing a sequencing technology called SIMDEQ™ (short for SIngle-molecule Magnetic DEtection & Quantification). In our novel approach, individual DNA molecules are tethered to micron-sized paramagnetic beads and then manipulated using a ‘magnetic tweezers’ instrument. We have demonstrated that a wide variety of different genetic assays can be performed using SIMDEQ™. The approach is simple, accurate, and has the potential to be run at very high throughput. Here we present preliminary data showing partial and full re-sequencing of individual DNA molecules of up to 10kb in length. We also demonstrate the high resolution mapping of DNA modifications (such as 5-methylcytosine) on unamplified DNA fragments, achieved by analysing the binding of modification-specific antibodies.

**REFERENCES**


**INTRODUCTION**

Our sequence detection process revolves around the ability to determine the 3-dimensional position of a paramagnetic bead to an extremely high resolution. This is achieved by shining a red LED light onto the beads (left panel) which generates a diffraction pattern that can be imaged on a video camera (centre panel). Moving the detector by precise increments while keeping the bead immobile allows the generation of a 3-dimensional calibration image (a lateral section of which is shown on the right panel). This system can accurately detect bead movement of 1-3 nm.

**RESULTS**

Interrogating long fragments of DNA

Sequencing CEB25, a 286 bps, 72% GC-rich, repetitive fragment

**CONCLUSIONS**

**SIMDEQ™ technology allows:**

- Interrogation of DNA fragments ranging from 100 bp to more than 10 kb
- Sequencing repetitive, GC-rich regions such as the human minisatellite CEB25, without error
- The rapid characterisation and identification of bacterial species, for example through 16S- or operon-based fingerprinting
- The detection of modified bases on genomic DNA, with amplification-free hairpin library preparation and antibody-assisted detection

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