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High-throughput DNA Stretching in Continuous Elongational Flow for Genome Sequence Scanning ROBERT MELTZER, JOSHUA GRIFFIS, MIKHAIL SAFRANOVITCH, GENE MALKIN, DOUGLAS CAMERON, PathoGenetix — Genome Sequence Scanning (GSS) identifies and compares bacterial genomes by stretching long (60 – 300 kb) genomic DNA restriction fragments and scanning for site-selective fluorescent probes. Practical application of GSS requires: 1) high throughput data acquisition, 2) efficient DNA stretching, 3) reproducible DNA elasticity in the presence of intercalating fluorescent dyes. GSS utilizes a pseudo-two-dimensional micron-scale funnel with convergent sheathing flows to stretch one molecule at a time in continuous elongational flow and center the DNA stream over diffraction-limited confocal laser excitation spots. Funnel geometry has been optimized to maximize throughput of DNA within the desired length range (>10 million nucleobases per second). A constant-strain detection channel maximizes stretching efficiency by applying a constant parabolic tension profile to each molecule, minimizing relaxation and flow-induced tumbling. The effect of intercalator on DNA elasticity is experimentally controlled by reacting one molecule of DNA at a time in convergent sheathing flows of the dye. Derivations of accelerating flow and non-linear tension distribution permit alignment of detected fluorescence traces to theoretical templates derived from whole-genome sequence data.

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