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# Faster DNA sequencing

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## Abstract

A newly developed high-throughput DNA-sequencing method is five times as fast as current commercially available techniques

# Significance and context

Improvements in DNA sequencing technology have made it possible to sequence prokaryotic and eukaryotic genomes in a reasonable time frame. Nevertheless, efficient sequencing of large genomes, such as the human genome, and characterization of sequence variations in them, would greatly benefit from advances in sequencing technologies. To reach this goal, recent efforts have focused on microfabricated electrophoretic analysis systems. These are microchips that rapidly separate mixtures of fluorescent dyes or fluorescently labeled amino acids, but they have also been shown to be suitable for DNA sequencing. Advantages of microfabricated capillary array electrophoresis include the possibility of large-scale array construction, precise volume usage and integrated low-sample-volume processing. The method presented by Paegel *et al*. is based on the use of a 96-lane radial microchannel plate layout equipped with a rotary confocal scanning detector, initially used for genotyping but now adapted for high-throughput DNA sequencing.

# Key results

The microchannel plate consists of a radial array of 96 capillary microchannels, organized in pairs around a central anode reservoir. Each of the channels is folded to ensure effective separation and a compact set-up. The use of four hyperturns and pinched-turn geometries avoided deleterious effects of the channel folds on electrophoretic separation. The microchannels were filled with a polyacrylamide matrix and scanned with the Berkeley four-color rotary confocal scanner. Paegel *et al*. present figures describing both the layout of the microchannel plates and the scanner. M13mp18 sequencing vector DNA was used as a template to test the new method. The sequencing speed using this device was as high as 1,700 bp/min (five times as fast as currently available technologies) and the accuracy was higher than 99% with an average read length per lane of 430 bp. Essentially, these improvements in DNA sequencing are achieved by the construction of a new injector system that allows uniform sieving matrix loading, and the architecture of the microchannel plates that ensures a more effective, high-resolution

DNA separation. Paegel *et al*. further demonstrated that continuous buffering of protons and hydroxyl groups generated during electrophoresis is necessary to avoid shifts in DNA mobility.

# Links

More information about R. Mathies' research group and related papers is available at the Mathies' lab homepage.

# Reporter's comments

Although particular parameters, including for instance matrix composition, still need to be optimized, it is clear that Paegel *et al.*'s new methodology will facilitate sequencing projects in general and may be used in the next generation of high-speed DNA sequencing devices. The authors state in the title of their article that this technique is suitable for high-throughput DNA sequencing, but no hard data, apart from indications of the speed and accuracy, support this statement at present. It would have been useful if the authors had addressed the question of whether it will eventually be practicable to sequence around 2.5 Mbp per 24 hours using the microfabricated capillary array electrophoresis bioprocessor device, and, if so, how much it would cost to reach this ambitious goal.

# Table of links



## References

1. Paegel BM, Emrich CA, Wedemayer GJ, Scherer JR, Mathies RA: High throughput DNA sequencing with a microfabricated 96-lane capillary array electrophoresis bioprocessor. Proc Natl Acad Sci USA. 2002, 99: 574-579. 0027-8424