Editorial

DNA Sequencing and Genotyping

Annelise Barron

The past few years, since the last special issue of ELECTROPHORESIS on this topic, have been an incredibly, and increasingly exciting time in the development of DNA sequencing technology. However, the excitement is being generated mostly by non-electrophoretic approaches, rather than any extension of conventional Sanger sequencing. Pyrosequencing, sequencing by synthesis, sequencing by hybridization or ligation within hydrogels, and single-molecule sequencing technologies are all new technologies that are evolving rapidly and do not involve electrophoresis. So far, these mostly "short-read" technologies seem better suited to "re-sequencing" of human genomes and may not yet be up to the challenge of *de novo* sequencing of a large, complex genome on the same size scale as the human. They are just terrific for sequencing microorganisms with modest-sized genomes. But these technologies are getting better and cheaper all the time. We wait with bated breath to see if the "nanopore"-based sequencing technologies will work someday. It has been fascinating to watch these new technologies compete with each other as they move forward, and try to sift the hard scientific fact and well-supported figures of merit from corporate braggadocio. The jury is still out – when will we have our $1000 genome? Do we really already have a $60 000 genome, from sequencing-by-ligation? Time will tell.

Meanwhile, our beloved "workhorse" electrophoresis methods such as CE, the domain of this journal, have for the past few years improved only incrementally; the cost *per* base of DNA sequencing has not dropped very much, even while average read lengths have increased, due to optimization of polymer sieving matrices and base-calling software. The primary complaint, which led the charge to develop non-electrophoretic methods, was high cost and in particular, the need for better scalability of both sample preparation and sequence resolution methods. The new "next-gen" sequencing technologies lend themselves much more easily to massive parallelization than CE. That being said, Craig Venter's genome, obtained by CE on ABI 3730XL instruments, surprised us with its large-scale rearrangements and other interesting and rather major differences from the "reference" human genome, which go well beyond the expected SNPs. We were not quite sure what to think of Jim Watson's genome, which was obtained by "re-sequencing" and relied on the reference genome for its assembly. Clearly, putting a complex genome together correctly will remain challenging even when different human individuals are "re-sequenced", and something like a "cancer genome" (the full, correctly assembled sequence of the mutant DNA in a tumor) will present us with even more surprising rearrangements than one sees between human individuals. The salmon genome project, just announced, will rely on CE since they do not know what to expect but do know that they will benefit from long reads and high quality. Such challenging projects will continue to rely upon long-read separations of Sanger sequencing fragments by electrophoresis. So, it seems there is still room to contribute.

At the same time, technologies for DNA sequencing and genotyping on microfluidic devices continue to advance. Microchip-based electrophoresis analyses of DNA well represented in this issue, may surge to the fore for medical sequencing applications on individual DNA samples, as well as for forensic applications. We shall see! In the mean time, please enjoy the many interesting contributions, which advance microchannel electrophoresis technologies, offered among the 22 articles in this special issue.

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Editor