

Roundtable Session 2 - Table 7 - How Fast Can We Go Without Sacrificing Quality?

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Abstract:

Fast speed separation is the intrinsic nature of CE methods because of its narrow separation channel. High separation voltage can be applied to CE. However, scientists always push for even higher speed on CE. Up to now, we have seen mainly two ways to enhance the speed: 1. use narrower separation channels, such as micro-chips. In this way, short separation channel can be used to facilitate the use of high separation voltage. For example, SDS separation performed on micro-chips can be done within 1 min. The speed is very high. 2. multiple capillaries (multiple channels). In this way, although the separation speed may not increase on each channel, the number of samples analyzed in a given time can be significantly increased.

For solution 1, the separation speed is super high. But there are several issues for solution 1: narrow channel imposes difficulty to detectors. UV absorption detection may not have sufficient sensitivity for the narrow channels. Fluorescence detection may be the only way; sample labeling may be necessary. For the short and narrow separation channels, the chemical conditions may be unique that makes the method transfer between micro-chip based CE and regular CE difficult. Although QC methods based on the micro-chip CE for proteins were reported in the 20 years, many scientists are still complaining that the resolution of the micro-chip CE prevents it from being used in QC. The relatively low resolution is caused by short separation channel.

For solution 2: It needs expensive equipment. If high throughput separation is not always needed in many cases, it may be a waste. An advantage of this solution is that the methods are transferable between regular CE instruments and the multiple capillary instruments. Theoretically, this solution may not sacrifice data quality, just “sacrifice” money.

Discussion Questions:

1. In bio-pharm companies, which areas need the high speed method? Screening?
2. If we look at recently launched multiple capillary CE instruments, it seems that they are targeting gene therapy for genome analysis, such as DNA and mRNA. Does the gene therapy area need high speed/high throughput methods?
3. Which CE method needs high speed the mostly, CE-SDS, CGE or cIEF?

Notes:

Introductions

- Moderator and scribe introduced themselves
- Attendees introduced around the table

Overview

- Moderator reviewed the abstract, highlighting approaches to increasing CE speed:
 - Microchips (CHIPs)
 - Multichannel CE (e.g., Biophase)

Discussion Points

Detectors

- J: Can detectors other than fluorescence be used?
- S: Possible, but performance is poor. Fluorescence remains the better option.
- J: Lasers could replace fluorescence detectors.

Microchip CE

- J: Methods are developed for microchip in QC.
- S: Main issue is reproducibility, not resolution.
 - Chip-to-chip variability is problematic.
 - No NFD developed for microchips.
- J: Biotechnie has NF for IEF.
- S: Fluorescence detection is necessary; QC methods are developed for fluorescence.

Multichannel CE

- Advantage: Can run 8 different samples or replicate 1 sample 8 times.
- Same voltage and pressure apply across 8 capillaries.
- Method development is a possible advantage.

QC Considerations

- Question raised: Why does QC need speed if it isn't a key driver?
- Example from a company:
 - Instruments used: PA800 and GX2
 - GX2 resolves some molecules better (product-specific).
 - Pico prelabeling preferred in GX2: improves robustness for some molecules.
- Trade-off:
 - Low-throughput: limitations accepted.
 - High-throughput: more sample submissions, increasing demand.
- Perspective:
 - Reducing SDS from 60 min to 6 min is valuable.
 - Reducing iCIEF from 10 min to 1 min is less impactful.
 - With 100 samples/day, bottleneck is analysts, not instruments.

Applications in Biopharma

- Question: Which areas need high-speed methods? Screening?
- Early phase development benefits most (e.g., purification step analysis).
- Before QC and formulation, higher speed helps due to more sample submission needs.
- Not required in QC, more useful in exploratory studies.

Trade-offs in Multicapillary CE

- Question during Biophase development: How many capillaries before sacrificing temperature accuracy?
- Decision: 8 capillaries balance speed and performance (~3 min per sample).

Gene Therapy Applications

- New multi-capillary CE instruments target genome analysis (DNA, mRNA).
- Question: Does gene therapy really need high speed/high throughput?
- Points raised:
 - Demand driven by increased CGT/mRNA interest.

- Example: DNA 20kb kit release after demand from industry.
- Some argue no strong throughput need in gene therapy.
- Faster task completion is useful, but not transformative.
- CZE limitations:
 - Requires fluorescence labeling.
 - Method development slower compared to alternatives like Maurice.

Broader Themes

- High throughput requires ****platform methods****.
- Debate: platform methods vs. optimizing individual methods for speed.
 - If optimization takes 1 day, teams will do it.
 - Otherwise, CE is preferred.
- Question: Platform method vs. platform technology?
 - Not all technologies can become platforms.
 - Platform technology difficult to establish for analytical testing.