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# AUTOMATED CAPILLARY ELECTROPHORESIS: A TECHNOLOGICAL RENAISSANCE AT THE HEART OF BIOPHARMACEUTICALS

## PROF. DR. HERMANN WÄTZIG DISCUSSES THE BENEFITS OF CAPILLARY ELECTROPHORESIS AND AUTOMATED SOLUTIONS IN THE MODERN LABORATORY

First developed in the late 1980s, capillary electrophoresis (CE) has long been the go-to separation method of choice for scientists around the world. Today, the technique's importance has grown exponentially as a precise and straightforward method for the quality control of biologics, including biotherapeutic antibodies. As such, over the past decade capillary electrophoresis technology has seen considerable development.

In this article, we talk to Prof. Dr. Hermann Wätzig, a capillary electrophoresis industry leader based at the Technical University of Braunschweig in Germany, where he leads at the Institute of Medicinal and Pharmaceutical Chemistry a research group focussing on the fields of pharmaceutical analytics and medicinal chemistry. Since 2001, he has chaired the pharmaceutical analysis and quality control division of the German Pharmaceutical Society. Wätzig has a long-standing interest in the interface between sciences and mathematical statistics – having studied pharmacy where he would actively seek out research projects combining both disciplines.

Here, we learn how he has worked to qualify the broad range of capillary electrophoresis instrumentation available, and the benefits he sees it bringing to researchers today. His vast array of application knowledge bridges all modes of capillary electrophoresis from traditional set-ups to CE-MS, CE-SDS and more recently automated solutions such as Maurice™, from ProteinSimple, a Bio-Techne brand.

### WHAT KEY BENEFITS OF CE DO YOU SEE FOR RESEARCHERS TODAY?

This needs to be discussed in the context with gel electrophoresis and chromatography. I think since the beginning there has been a need for separation sciences within biosciences and this will never change. It's just that the techniques that can be used progress, and I think that capillary electrophoresis progressed in parallel to chromatography and both actually gained compared to the gel electrophoresis. So, gel electrophoresis, whilst we still see a lot of important work using this technique, it will be kind of replaced by capillary electrophoresis one by one, step by step over the next few decades.

### HOW HAVE YOU SEEN MICROCHIP CE HELPING RESEARCHERS?

I think that we might see more microchip separations in the next few years. It's still not as robust or reliable as I would like to have it, but it's improved a lot. We see more and more suitable applications and so there's a steady growth in this field, the small ranges and the fast analyses. It's still difficult to say which role it will play in the next few years, but I think it's an important topic.

### HOW HAS THE HISTORICAL USE OF CE INFLUENCED ITS IMPACT ON BIOPHARMACEUTICAL DEVELOPMENT TODAY?

Capillary electrophoresis has had a changeable history. In the 1980s there was a lot of enthusiasm about all the benefits of capillary electrophoresis, high separation efficiencies, and independence of central equipment and so on; however, then a number of drawbacks were observed. I think the most important one missing was the reliability of the instrumentation. So, we saw that people shifted back to liquid chromatography in many cases.

Whereas now we are seeing the renaissance of capillary electrophoresis within biopharma, as you need all the information you can get, to characterize biopharmaceuticals properly. In biopharma, it is much better to use capillary electrophoresis than gel electrophoresis, even though people are actually still using both techniques in parallel to get as much information as possible. But you cannot properly guarantee the quality of biopharmaceuticals without the use of capillary electrophoresis.

## AS WE SEE SCIENTISTS SHIFT FROM GEL ELECTROPHORESIS TO CE, WHAT ARE THE KEY CHALLENGES THEY MIGHT FACE?

I think that the main point is that you have a lot of historic data, beta data, for example, from your development or from further production lots. And if you would like to switch to the superior technique, you still need to be able to compare your newer results with the historic results. That's of crucial importance. So, actually, you need proper rules to be able to do that: How many bridging samples can be recommended? How can we make sure that the bridging samples properly represent the whole data sets, including data expected in the future? How can we properly consider analytical uncertainty? These are the topics to be addressed next, to allow a smooth transition from SDS-PAGE to CE-SDS.

## HOW DO TECHNOLOGICAL DEVELOPMENTS IN CE ENSURE RELIABILITY & HIGH-QUALITY DATA?

The reliability is generally related to the making and the design of the instrument they are using. When using the Maurice charge separation mode, it's really very nice that you can monitor in real time the cIEF separation process. I think that the data we produced [on Maurice] shows excellent quality, due to the precise and reliable Maurice instrument.

In general, the quality of the software, which makes it easier for someone who's actually not an expert in capillary electrophoresis to start working, as well as the reliability of an instrument, the support in maintenance and training and so on, are also a very important aspect which needs to be mentioned.

## WOULD YOU CONSIDER THE MAURICE TO BE AN INSTRUMENT THAT YOU COULD GIVE TO, SAY, A PHD STUDENT JUST STARTING OUT, AND THEY'D BE ABLE TO PICK IT UP RELATIVELY EASILY?

Yes, I think, also for the Maurice, it requires some training, but maybe less effort than for some of the other instruments.

## WHAT DO YOU THINK ARE THE TOP THINGS TO CONSIDER WHEN CHOOSING INSTRUMENTATION?

There is price to performance ratio as well, and then reliability, also precision and speed. And apart from that, of course, always, usability with straightforward access to an instrument and a quick start after one day of training, that's of course also great.

## WHAT DO YOU SEE FOR THE FUTURE OF CE?

I think that at least some of the future goes in the direction of two-dimensional or multi-dimensional separation, maybe also involving microchip separations. And I also think that ligand-binding assays, might shift to affinity capillary electrophoresis as well, in particular, in the beginning of a drug development process, where have you rather weakly binding systems and you have to distinguish between non-binding and weakly binding systems. For this affinity capillary electrophoresis is the best choice for, to still distinguish between differently weakly binding systems.

## SUGGESTED ADDITIONAL READING:


Determination of protein charge variants with (imaged) capillary isoelectric focusing and capillary zone electrophoresis, J Kahle, H Wätzig, *Electrophoresis,* 2018; 39(20):2492-2511.

The next generation of capillary electrophoresis instruments: Performance of CE-SDS protein analysis, J Kahle, K Maul, H Wätzig, *Electrophoresis,* 2018; 39(2):311–325.

Recent advances in capillary electrophoretic migration techniques for pharmaceutical analysis (2013–2015), S El Deeb, H Wätzig, D Abd El-Hady, C Sänger-van de Griend, G Scriba, *Electrophoresis,* 2016; 37(12):1591–1608.

The transfer of analytical procedures, J Ermer, M Limberger, K Lis, H Wätzig, *Journal of Pharmaceutical and Biomedical Analysis,* 2013; 86:262–276.