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to those who may be concerned,
in particular the committee responsible for the academic promotion procedure at the
Faculty of Pharmacy of the Charles University in Hradec Kralove

review of dr Burkhard Horstkotte's habilitation thesis

The reviewed habilitation thesis, written by Burkhard Horstkotte, is a study of a monothematic set of publications in prestigious journals from the Philadelphia list. The number of publications included in the study, as well as the time in which these publications were created, is impressive. Doctor Horstkotte's achievements include over 60 publications, almost half of which are the subject of his habilitation thesis and illustrate the author's effort in the development of the Lab-in-Syringe analytical technique. The reviewed work shows both the development of the technique and the successive development of the author, although even before taking up the subject of Lab-in-Syringe, Dr. Horstkotte was a scientist with high recognition and reputation in the family of people dealing with analytical flow techniques. Quoting the author: "11 years after its invention, in 9 research groups (...) in 7 different countries" proves that Dr. Horstkotte is an devoted, creative, visionary, determined and hardworking scientist. This is also the impression get when reading the habilitation thesis.

The dissertation has a standard layout, it is divided into a literature part and a part related to own research. In the thesis, as many as 354 literature items were correctly quoted, which makes the literature part a extraordinary study, an almost ready literature review or a



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book with current information in the field. In this part, the author describes issues related to both the basic concepts of flow analysis and introduces the instrumentation of most of the techniques. It is difficult for me to assess whether such an extensive introduction was necessary, because it is only from page 37 that the author begins to address topics closely related to the monothematic collection of publications, which is the basis of the habilitation process. Nevertheless, this is not an objection that could reduce the quality of the description of the state of the art in flow analytics. The introduction, although extensive, contains only basic information and, as I understand it, the author's intention was to prove that the analytical technique developed by him is unique against the background of those already known and developed since the 1950s.

As mentioned, it is entirely reasonable to include chapter 3.3 in the reviewed thesis, which introduces the reader to the subject of extraction processes necessary in some analytical procedures, i.e. de facto provides information why the Author undertook the development of the Lab-in-Syringe technique as one of the potential ways to solve the problem of automating analytical procedures involving such a stage as extractions from solids or liquids. It seems correct to conclude here that among the various published analytical techniques, lab-in-syringe may be a solution to the problems related to the automation of extraction procedures.

In the introduction to the chapter on automating the idea of lab-in-syringe, Dr. Horskotte honestly divides the credit for the invention of this technique between Dr. Fernando Maya and himself, emphasizing that LIS as a concept has already proven its genius, efficiency and universality, and I would add also its effectiveness. It is undeniable that the first attempts to automate the lab-in-syringe concept are Dr Horskotte personal achievement due to his postdoctoral stays, mirrored his first authorships of the cited publications. This chapter ends the literature part and in the summary of my evaluation of this part of the dissertation, I would like to emphasize the ease of formulating thoughts and conclusions by the habilitation candidate. For a reader unfamiliar with the subject, it may be difficult to follow the story, but for a person familiar with the issues of flow analysis, it is a coherent and logical introduction to the proper topic of the dissertation.



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In the next chapter, the personal contribution of the postdoctoral researcher to the development of the strategies for automating extraction procedures with the use of Lab-in-Syringe setup is described. After a cursory reading of the content of this chapter, it turns out why the literature introduction had to be so extensive. The description of the content of 28 papers, both original and review, by Dr. Horstkotte had to be made in a concise manner so that the reader would not miss the most important features of subsequent modifications, applications and advantages of automatic lab-in-syringe systems.

The next chapter is a discussion, and it is indeed a discussion. The author tries to decide whether the methodologies he develops deserve to be called new, "pure"-flow analysis, groundbreaking and so on. The author concludes that LIS is new, unorthodoxly flow analysis and may be a breakthrough technique. Allow me to comment more extensively here:

With the current development of technology in general and the mechanization of analytical procedures in particular, it is difficult to come up with a new concept that has not yet been discovered and tested. All of us, every day, try to come up with something new, and as time passes, we come to the conclusion that the definition of Elo Hansen (that Dr. Horstkotte quotes: *"The ultimate test for an analytical method is not that it can do better what can be done by other means, but that it permits us to do something that we cannot do in any other way."*) is not entirely correct because most of us will not find the Holy Grail of mechanization in analytics. Dr. Horstkotte's achievements can be evaluated in two ways, and it is prove of his maturity that he raises both of them in the discussion. The first way of evaluating LIS as an innovative technique is in line with Elo Hansen's philosophy. In fact, what Burkhard Horstkotte presents in his works is difficult to achieve in any other way. The second way of evaluating LIS is openly admitting that making flow systems more complicated and overcoming the resulting technical problems by making them even more complicated is a dead end path. Burkhard, as he himself emphasizes, postulates that a step back is needed, some technical procedure that will reset these tendencies to more and more complications in order to achieve a meager improvement in the analytical parameters of a given analytical method. In my opinion, this proves the uniqueness of Dr. Horstkotte that he develops something unquestionably new, while showing that the simplest solution is also the best.



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Dr. Horstkotte also discusses whether his solution can be called "pure flow analysis". In my opinion, his doubts are unfounded. First of all, "pure" in the sense of "orthodox" will always impose boundary conditions on the inventor, which will bind him in a completely unnecessary way and force him to compromise, which will certainly not be the optimal solution to the problem. The philosophy of thinking outside-the-box is also necessary in the field of analytical chemistry and especially in flow analysis instrumentation's development. Such a philosophy may be considered impertinent by the older ones, considered confusing by the very young - in the end, in my opinion, it will turn out to be the only appropriate approach to solving any scientific problems.

I agree with the thesis that perhaps as a relatively young analytical technique, LIS, is in the early part of the Gartner hype cycle. Time will tell how it really is, but the author of the reviewed dissertation certainly contributes to ensuring that at least this initial growth, aimed at seeding the technology in many scientific groups, will last for a long time. The long-term effort of the habilitation candidate, showing both successes and dead ends, perfectly described in original papers, reviews and reviewed dissertations is one side of the coin. The second is the fact that Dr. Horstkotte deliberately uses tools such as rapid prototyping, showing that any modification nowadays can be carried out by any subsequent scientist, if only he has even the simplest 3D printer.

I completely agree with the conclusions of the work and my final conclusion is that I had a honour to review an outstanding study, completely deserving of a scientific promotion, which could take place even a few years earlier. The dissertation could summarize the achievements predestining for the title of professor due to: the time that has elapsed since obtaining doctorate, the experience of Dr. Horstkotte collected and described, the quality of research and the prestige of scientific journals in which his research results were published, and his creative inventive activity.