WILL THE FOURTH GENERATION OF FLOW INJECTION TECHNOLOGY COME FROM JAPAN ?

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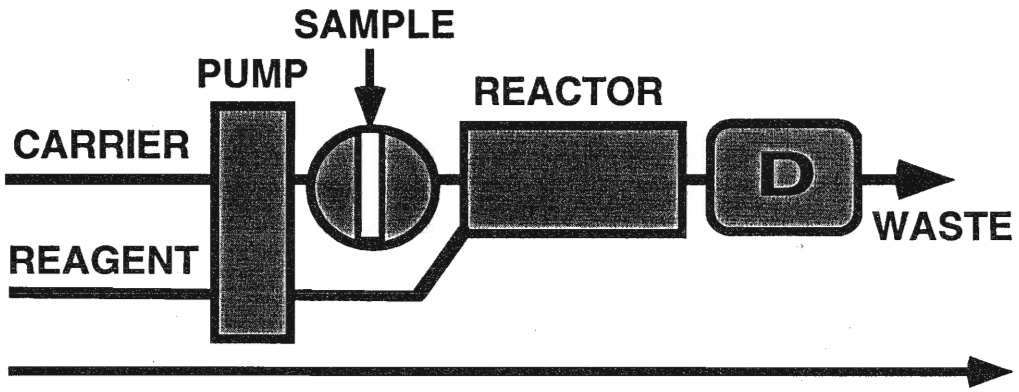
It seems to me to be only few years ago, when flow injection analysis was conceived - yet by the time this issue will be read, already twenty years will have passed since the first experiments confirming the feasibility of FIA had been conducted. Looking back at the evolution of this technique, which today has been described in perhaps more than 4000 papers, the strongest impression one gets is the versatility of this technique, its adaptability to challenges facing the analytical community, and the remarkable inventiveness of all scientists who became engaged in FIA research.

Yet the advance of knowledge and technology is not limited by national boundaries and flow injection was no different in that respect. Following the initial experiments in Denmark and proof of practicability in Brazil, it soon proliferated to Sweden, Netherlands, Britain and South Africa, while being simultaneously pursued in the United States. In Japan, the first paper was co-authored by N. Ishibashi in whose honor this issue of the Journal of Flow Injection Analysis is being dedicated.

Science and technology devours itself through perpetual critical revision and innovation. What was an advanced tool of yesterday will be, at best, a museum piece of tomorrow. What lasts, however, are the principles of those techniques which are adaptable by remaining useful and intellectually challenging. Flow injection seems to fit this mould, since it has changed its form and mission several times already.

The first generation of flow injection (Fig.1), which developed during the first ten years was based on a concept, which in retrospect can be recognized as somewhat narrow: the emphasis had been placed almost entirely on the speed, with which sample solutions could be processed, with the sole purpose of increasing the sampling frequency of serial assays. In that period of discovery, as well as of competition with air segmented continuous flow analysis (AutoAnalyzer), flow injection was much influenced by the goals



CONTINUOUS FLOW

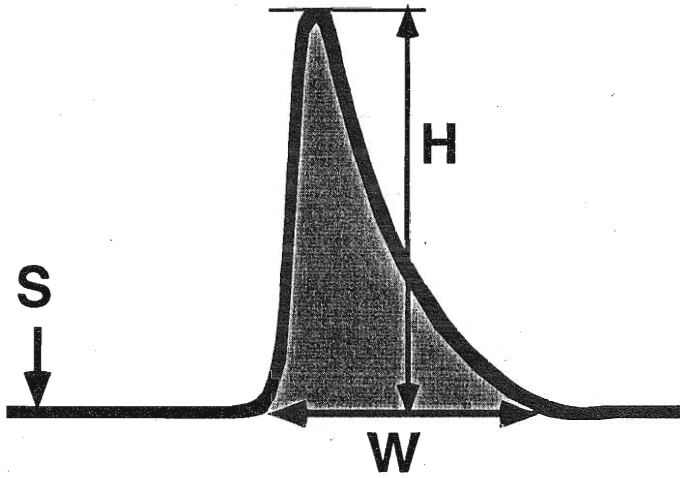


Fig.1.

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and means of this older, well established technique. This is why the initial work on FIA focused towards a high speed serial assay, since this was considered a crucial aspect. The first generation also relied on continuous unidirectional flow, which was counterproductive, since it imposed limitations on the reaction time reagent consumption and critical dimensions of the flow channel. Curiously, this misconception seems to linger on, as flow injection is still considered by some as a *continuous flow* technique while the body of flow injection theory, being derived either from chromatography or flow-trough reactor engineering, supports this notion by dealing mainly with models based on continuous unidirectional flow.

The second generation of flow injection(Fig.2) is based on two principles: the *stopped-flow* technique and exploitation of a concentration gradient formed from the dispersed sample zone. By stopping the flow when a selected section of a dispersed sample zone is in the observation field of the detector three advantages were gained. First, the reaction rate of the interaction of the reagent with the analyte can be monitored, thus yielding additional information and higher selectivity. Secondly, an optimum sample/reagent ratio can be selected by means of a computer. Thirdly, reaction time can be extended without need to consume reagents, since the solutions are no any longer continuously pumped.

The third generation of flow injection (Fig.3.) the *sequential injection* technique, is based on three principles: flow reversal, stopped-flow and mutual penetration of sample and reagent concentration gradients. In addition to advantages of reaction rate measurement, sequential injection is mechanically simple, since it uses only one valve and one pump, its saves reagents and creates a minimum amount of waste, as it consumes microliter amounts of reagent per assay. Since reaction times are adjusted by stopping the flow and the analyte reagent ratio can be adjusted by combination of flow reversal and of the stop delay time, the optimization of assay parameters can be achieved from the computer keyboard rather than by changing the coil length, pumping rate or size of the injection loop - as must be done for earlier generations of flow injection techniques.

Anyone familiar with flow injection literature must ask at this point, why the majority of flow injection methods published so far are based on the first generation - the continuous flow technique - if the stopped flow or sequential injection techniques are clearly superior? And, especially since stopped flow injection has been around for more than ten years, and sequential for nearly three years? The most likely answer is that the more advanced FIA

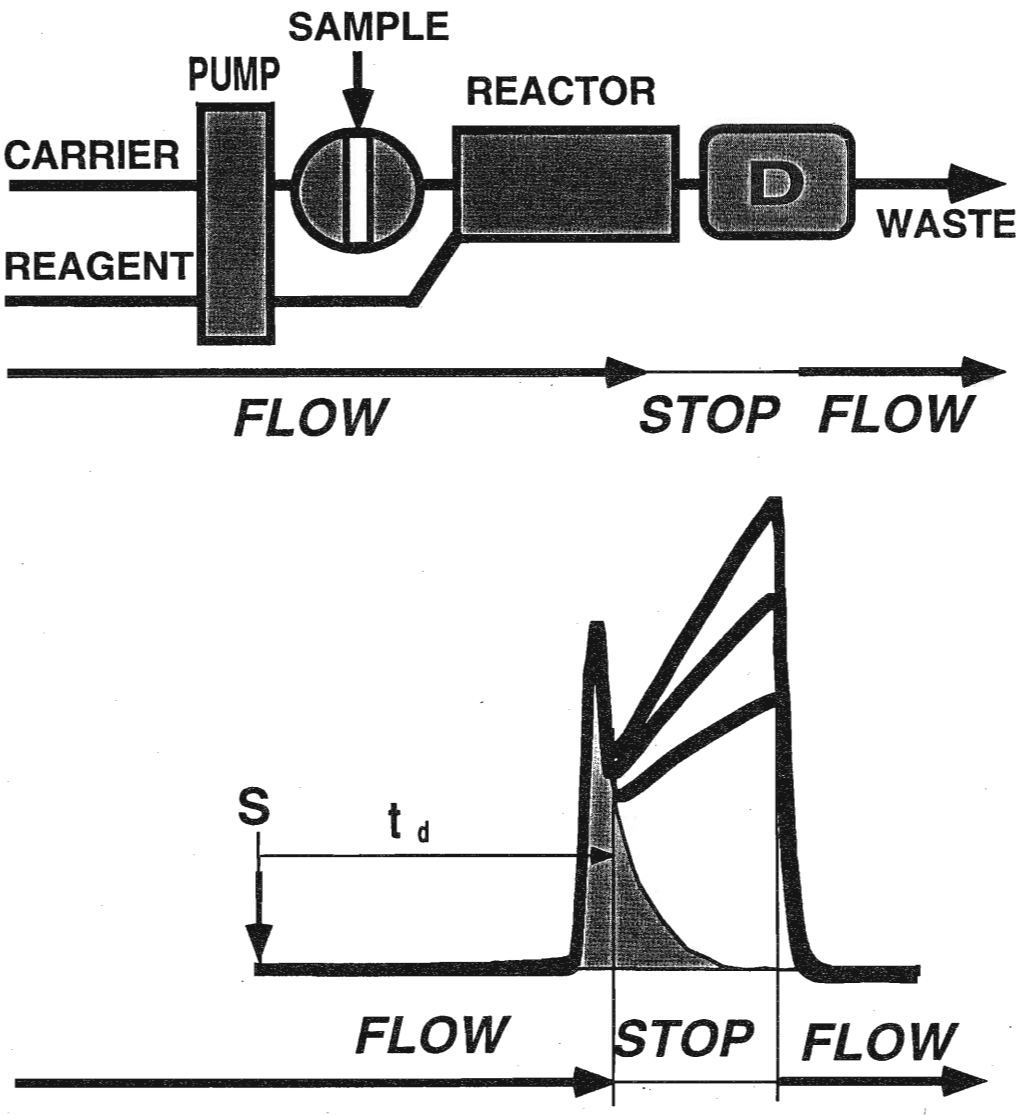

Fig.2.

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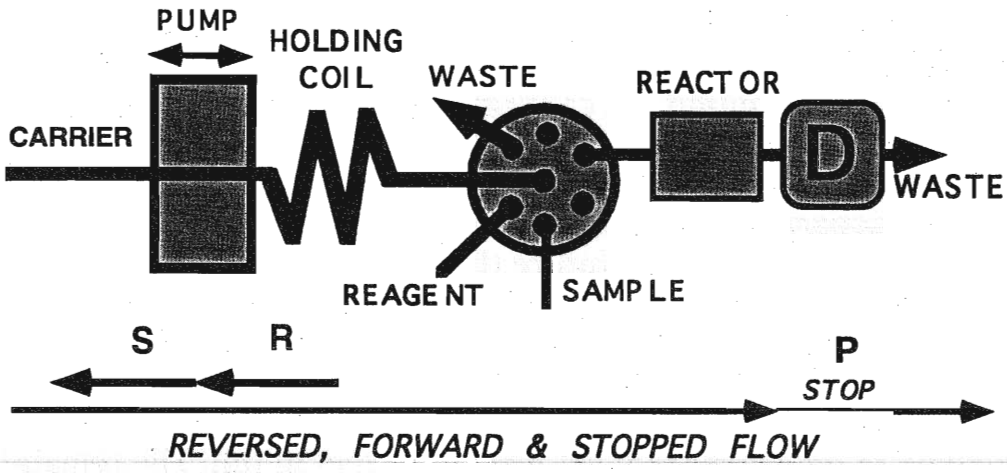

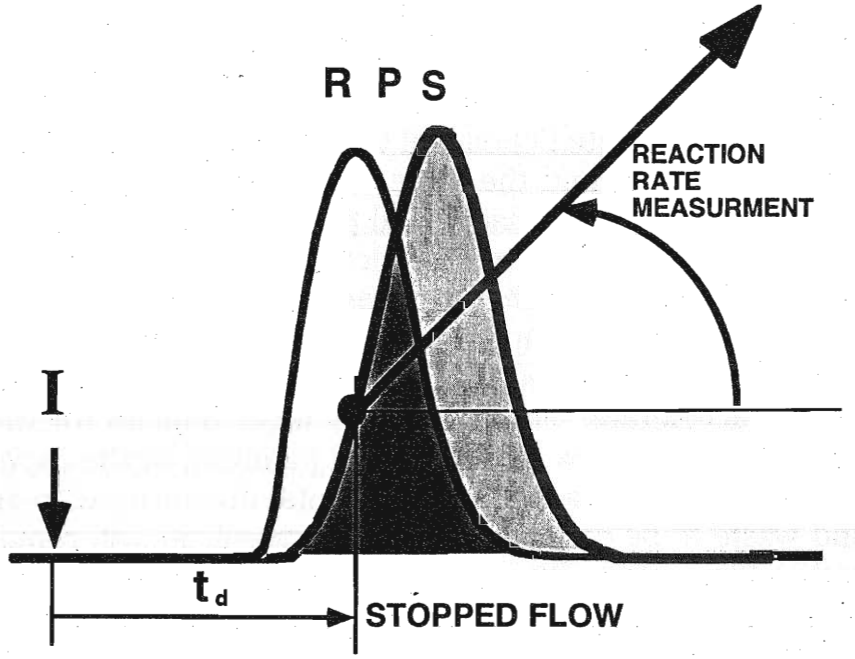

Fig.3. Ruzicka

techniques require precise hardware and sophisticated software. While continuous FIA could easy borrow components from either Autoanalyzer technology , chromatography or even from everyday life (aquarium pumps as well as pressurized air from automobile tubes have reportedly been used to propel the carrier stream), this is no longer so for more advanced techniques, as anyone who tried to carryout even a simple stopped flow measurment with a chromatographic pump will confirm. Thus while in the past, a functional, however crude FIA system could be compiled from components pilfered from surplus or the outcasts of any sizable chemical department - a situation which put off many professional instrument makers - in the future this will not be likely. The old pumps are not capable of precise stop and reversed flow - even if they are computer compatible. Mutiposition valves for SIA need to be fast, with minimized internal volume and computer compatible. The requirements on software, its timing, ease of programming and reliabilty of data collection yet need to be met in full. The remaining question is , whether stopped flow or sequential injection are worth this additional effort. The answer is that they are, since new requirements of the ever changing world are already at our doorstep.

The rising price of chemicals - more sophisticated as well as of simple organic solvents, the crucial need to drastically reduce the volume of generated chemical waste, the price of labor and laboratory space and the increasing need to improve quality control of chemical and pharmaceutical production, will lead to micro miniaturization of all wet chemical assays to the scale far below the test tube and beaker chemistry as we know today. The requirement for full computer compatibility of analytical instrumentation - a trend keenly embraced by the young generations of chemists, will further accelerate. FIA and SIA are ideal vehicles for this purpose since they will allow computerized planning of the experiment, its execution, optimization and even total inventory of reagents used and waste to be produced, while all chemicals will remain enclosed within the system. We can never quite eliminate the use of poisonous, potentially dangerous or carcinogenic substances in a chemical laboratory, but we can minimize the risk by reducing their consumption to microlitre volumes and by containing them. This ability of flow injection, its adaptability to a wide range of detectors and sensors, and the identified need for a miniaturized, precise and sophisticated instrument will inevitably lead to a fourth generation of flow injection, which will become mass produced as much as today's pH meters or spectrophotometers.

Reviewing the present field of instrument makers and considering the wide acceptance of flow injection in Japan, where the first Society for Flow Injection has been founded, and where the only Journal for Flow Injection Analysis is being published, it is likely that the fourth generation of flow injection technology will be conceived and manufactured there. When it happens, it will be a most fitting acknowledgment of the outstanding contribution of Nobuhiko Ishibashi, of his colleagues and of his students.

Acknowledgment. I wish to express my gratitude to my colleagues and students at the University of Washington for cooperation in development of flow injection methodology and to J. Breen from the Environmental Protection Agency for focusing my attention at the importance of chemical waste reduction.