Towards high throughput chip calorimetry by use of segmented-flow technology

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The adaptation of the segmented-flow technology (SFT) to chip calorimetry extends its application range considerably, in particular for the study of (micro-)biological materials. Primarily, the SFT was developed to handle samples of picoliters or nanoliters in micro-fluidic systems [1]. Samples dissolved or suspended in aqueous droplets are forced through the fluidic channels by a water-immiscible carrier liquid. Due to the interface tension, plug flow characteristic is achieved which is the precondition for an increased throughput. Moreover, the formation of spatially limited plugs enables the defined transport of solid or aggregated samples through the measuring device. As an effect of the viscous entrainment of the carrier liquid and the capillary pressure inside the droplets, a thin lubricant film is present between the droplets and the walls. The thin film protects the walls against contamination by the sample (e. g. biofilm formation) and prevents cross-talking.

The adaptation of the SFT to calorimetry is not a trivial task. The design of calorimeter components like measuring chambers, heat-exchangers, injection ports, and transport channels is a particular challenge if they should meet the requirements of the SFT. Thus, all components of the fluidics must be highly hydrophobic to prevent attachment of the aqueous sample to the channel walls. Furthermore, only moderate changes in the cross-sections of the fluid pathway can be tolerated to avoid fragmentation of the droplets. Consequently, the adaptation of the SFT to calorimetry is reasonable only for miniaturized, chip-based calorimeters.

We present new chip calorimeters for liquid and solid samples which fit the requirements of SFT. They are based on prototype chip calorimeters [2, 3, 4] which have been routinely used for biological investigations. By use of these calorimeters, solid and aggregated biological materials can be investigated in flow-through which enables the design of fully automated monitoring systems. Based on numerical simulations, the calorimeter components were optimized with respect to calorimetric sensitivity and heat exchange efficiency. The dynamics of the signal generation under segmented-flow conditions was analyzed to find optimal settings of the operation parameters for maximum throughput and requested signal-to-noise ratio. Furthermore, it was proved that thin films of carrier liquid suppress undesirable biofilm formation in the measuring chamber. The proper work of the segmented-flow chip calorimeters was demonstrated by monitoring of the growth kinetics of bacterial cultures and by the measurement of the metabolic heat production of mammalian cells. For the first time, the heat production of artificial micro-tissues (spheroids), pieces of cancer tissue, and human hair follicles could be continuously analyzed in flow-through.

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