## Chip calorimetry of aggregated biological samples in segmented flow

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In contrast to batch calorimeters, devices operated in flow-through mode allow the long-term maintenance of well-defined cultivation conditions (e. g. pH, oxygen tension, carbon source) to biological materials. Therefore, they are well suited for the study of transient effects caused by drug treatment [1, 2]. However, usual flow-through calorimeters require the fixation of aggregated samples in the measuring chamber which drastically reduces the sample throughput. Applying the segmented-flow technology [3], we present for the first time a calorimeter for the study of solid and aggregated biological materials in flow-through.

In the newly developed segmented-flow calorimeter, solid particles or biological aggregates up to 1.5 mm are immersed in segments of aqueous solutions. The segments are transported to the heat flow detector of the calorimeter by a carrier liquid. The interfacial tension between the aqueous segments and the water immiscible carrier liquid ensures plug flow and prevents sample dispersion. At a typical segment volume of 11  $\mu$ L, a volume specific calorimetric resolution of 2 mW L<sup>-1</sup> was achieved.

The proper functioning of the new calorimeter was proved by measuring the metabolic heat production of biofilms cultivated on glass beads and sulfidic ore particles. For the first time, the heat production of cellular spheroids, pieces of cancer tissue, and human hair follicles could be analyzed in flow-through. The measurement of the basal microbial activity of small soils samples demonstrates the capability of the device to measure solid samples with quite coarse texture. With the successful implementation of the segmented-flow technology, the application range of chip calorimetry is considerably extended.

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