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MICROCALORIMETER – ESSENTIAL ASPECTS OF MEASUREMENT

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This work describes the construction and calibration of a batch microcalorimeter designed for thermal characterization of liquid samples. The device consists of two fundamental parts — aluminium blocks and silicon chip NCM-9924. The main segment of the batch microcalorimeter includes a SiN membrane with Al-heater and thermopile in the centre of the membrane. This paper presents results on electrical and chemical calibration of the chip NCM-9924 and several details of the calibration and measurement processes. The sensitivity of the differing in the thickness of the SiN membrane was evaluated to be 2.29 V W^{-1} and 1.02 V W^{-1} for the thickness of 22 μm and 45 μm, respectively. Attention is paid also to the experimental conditions directly influencing the sensitivity of the chip — temperature and volume of the droplet on the chip.

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Introduction

Calorimetry is a scientific branch that studies and measures the heat released or consumed during various physical processes, e.g. chemical reactions. Nowadays the calorimetry is a powerful tool which enables precise investigation of chemical reactions and other chemical and physical properties of materials [1].

The term "nanocalorimeters", consistent with the current and accepted definition of microcalorimeter, is used to describe these calorimeters due to the low-power signals detected by the instrument rather than because of the dimensions of the object formed with integrated circuit technology. The advent of micro electromechanical systems (MEMS), also known as micro-system technology (MST), which has evolved from the methods used to manufacture integrated circuits (IC), has permitted the development of calorimeters that can operate with significantly smaller sample size. In our case we use a miniaturized batch heat-flow calorimeter (batch microcalorimeter; in literature also known as IC-calorimeter). Microcalorimeters have been used to measure thermodynamic properties of fluids for a long time. Sensitivity of the calorimetric chip is one of the most important properties of the entire device [2]. This main property of chip and heat of reaction of studied system was measured using a calorimeter chip NCM-9924. Two types of calibration were performed — chemical based on the reaction of tris-(hydroxymethyl)aminomethane (TRIS) with HCl and electrical calibration. In comparison with other chips, e.g. LCM-2506, the heavy-duty sensor NCM-9924 is available. This sensor features a membrane of 22-45 μm thickness which leads to indirectly proportional values of the power sensitivity 1.2-2.4 V W^{-1} [3]. The aim of this work was to provide an overview on this technique — to present several experimental results obtained for the calibration of the batch microcalorimeter and to provide a detailed description of the functions and manufacturing of calorimetric devices containing the NCM-9924 chip.

Theory

Sensor Description

Calorimeters with different types of chips (LCM-2506, LCM-2524 and NCM-9924) have been extensively investigated by Lerchner *et. al* from the TU Bergakademie Freiberg in collaboration with the Xensor Integration (Delft, Netherlands) company [4]. Two types of microcalorimeter chips are currently available from Xensor Integration: those based on thicker monocrystalline silicon membranes and those based on thin silicon-nitride membranes. The former have low thermal isolation but are very robust and well suited for use in liquids and generally for slow applications (LCM-2506, LCM-quad and NCM-9924 chips).

The latter type is more fragile but very well isolated and fast; these chips are better suited for application in gaseous environments and for fast measurements, such as scanning calorimetry (TCG-3880 and NCM-4000 chips) [3]. In this work we will focus on the chip NCM-9924 and its applications to liquid samples.

The microcalorimeter chip NCM-9924 consists of a 8.3 × 8.3 mm large and 22-45 μm thick monocrystalline silicon membrane in a thick silicon rim (Fig. 1). The sensitive area of 4 × 4 mm in the middle of the membrane contains three heater resistors. Two heaters are made of aluminium and galvanically isolated from thermopile by a dielectric layer. The third is a diffused resistor heater integrated in the membrane to measure the temperature increase of the sensitive centre with respect to the rim. The rim serves as a mechanical suspension and as a thermal reference (Fig. 2). Due to the thickness of the membrane, only a low thermal resistance is achieved, which makes this sensor especially well suited for liquid applications (droplet on the chip) where high thermal resistances are strongly decreased by the liquids. The thick membrane also makes this sensor suitable for repeated use with enzyme layers or coatings, which can be removed after the measurement without damaging or destroying the membrane [3].

Fig. 1 Back side of calorimeter chip NCM-9924 (Xensor Intrgration)

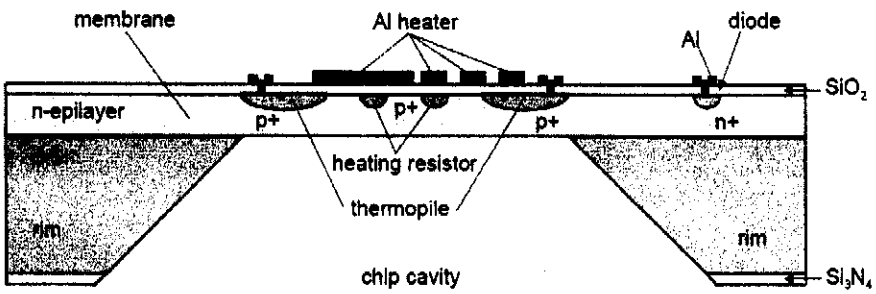

Fig. 2 Scheme of calorimeter chip with thermopile as temperature sensor

With MEMS technology, the microcalorimeter is manufactured as a single integrated structure including the heater, sensor and sample holder on Si base. MEMS is a technology used to manufacture three-dimensional silicon based structures with specific geometrical, mechanical and electrical properties to execute certain effects [2]. In the MEMS microcalorimeter the microstructure includes all the required components on one base: the heating resistor, temperature sensor, sensor for determining temperature differences, well-defined thermal conductor and a container. The resistor and thermopiles are formed atop of the silicon wafer by depositing specific substances that are subsequently shaped by a combination of photolithography and either wet or dry etching. The membrane with a heater in the centre serves as the sample holder. The heat flows laterally through the membrane to the support rim, which simultaneously works as a heat sink and creates a temperature difference across the membrane that is determined by the thermopile. The membrane is formed by removing the silicon beneath the thermopile with a process called back etching. Many microcalorimeters can be fabricated on one wafer and the individual devices are then separated from each other with a diamond cutting machine. Electrical connections to the MEMS are achieved by ultrasonically welding wires between the contact pads and external mount. MEMS usually require packaging that is specific to their end use and standard plastic IC packages are not usually used. Further details on MEMS and their processing can be found in Ref. [5].

Calorimeter Device

Miniaturised batch calorimeter (Fig. 3) was designed for the calorimetric monitoring of reactions in small samples of solutions. This type of microcalorimeter has been used at the department of inorganic technology of the University of Pardubice for three years now. The calorimeter consists of two axial connected cylindrical aluminium blocks. The thermopile chip is located in the centre of the arrangement. The silicon chip is fixed in a conventional integrated circuit chip carrier. The ceramic chip carrier is thermally connected to the lower aluminium cylinder *via* metallic pins. An axial hole in the upper cylinder serves for the mounting of the microsyringe which holds the second reactant before it is added. The wetting ring attached to the top of the interior calorimeter chamber is necessary for faster adjustment of the vapour pressure. This decreases the rate of vaporisation of the liquid sample placed at the surface of the silicon membrane and, therefore, leads to a faster stabilisation of the signal baseline. An accurately circular gauge with the diameter of 4 mm is used to ensure an exact positioning of the liquid droplet in the centre of the chip surface (bordered by the sensitive area of the chip). This also helps to increase the reproducibility of the size of the contacting area between the droplet and the membrane surface. The calorimeter

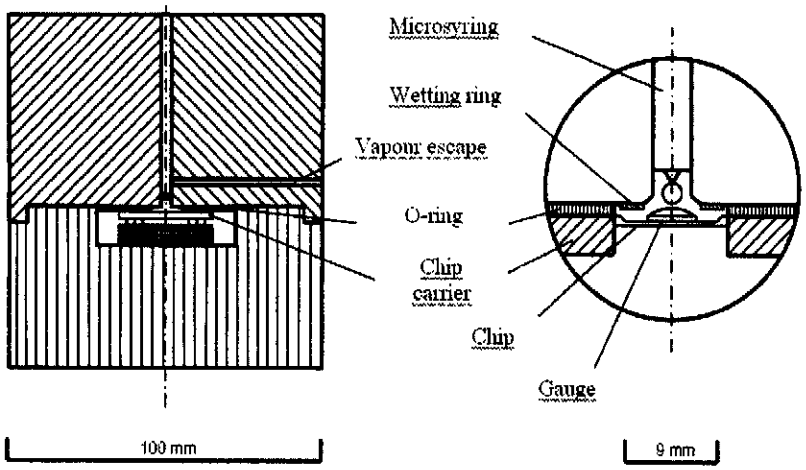

Fig. 3 Scheme of batch calorimeter [6]

is closed after placing the first reactant on the chip. Then the microsyringe is filled with the second component and put into the hole in the upper block of the calorimeter. Good thermal contact between the blocks, chip and capillary ensures insignificant temperature differences between both reactants [7]. About 20 min after preparing the calorimeter, the reaction can be started by emptying the microsyringe.

Experimental

Batch microcalorimeter can be used to study solid-liquid or liquid-liquid reactions. One reactant (solid or liquid) is placed on the surface of the chip and the other one (liquid) is put into the microsyringe, as is illustrated in Fig. 3. After establishing thermal equilibrium (ca 20 min), the reaction is started by addition of a droplet from microsyringe. The measurement is stopped ca 10 min after the addition of the second reactant when the output signal turns again into a horizontal line.

The following substances were used for chemical calibration: 0.1 mol l^{-1} solution of tris-(hydroxymethyl)aminomethane (Sigma Aldrich); 0.025 and 0.05 mol l^{-1} solutions of hydrochloric acid (Lach-ner).

Distilled water was used to study how the sensitivity of the chip is influenced by the temperature of measurement and by the volume of the droplet on chip. The temperature was changed stepwise in the range of 20-45 °C; 5 measurements were performed at each temperature. The amount of the distilled water on the chip was 8 μl. Additionally, the influence of the droplet volume on the sensitivity of the calorimetric signal was studied. Droplets of different volumes

(varying from 0 to 14 μl) were placed on the sensor, and for each volume 5 measurements were performed at the temperature of 25 °C. The last effect influencing the output signal was investigated by keeping the total volume of water equal to 8 μl while changing the ratio between the volumes of reactant on chip and reactant in the microsyringe (as is described in Table I). For each ratio 5 measurements were performed at the temperature of 25 °C. Since 5 experiments were carried out for each of the conditions, the result is their mean value and also the standard deviation was determined.

Table I Specification and designation of experiments determining addition effect

Reaction system		
Volume on chip, μl	Volume in microsyringe, μl	Designation
7	1	7 + 1
6	2	6 + 2
5	3	5 + 3
4	4	4 + 4
3	5	3 + 5

In all the experiments the moisture ring was impregnated with 8 μl water. In the case of chemical calibration the solution of hydrochloric acid (of the same concentration as that of the droplet on chip) was used for wetting of the ring. The wetting was necessary for saturation of the vapour chamber.

Results and Discussion

This paper focuses on main aspects of the measurements performed by means of batch microcalorimeter. The calibration, chemical as well as electrical, is described in detail. Then the factors influencing the accuracy of measurement — temperature, volume of the droplet on chip and effect of the liquid added from microsyringe — are discussed.

Calibration Procedure

In calorimetry the observed peak is proportional to the heat of reaction. Well known materials or reactions with published values of reaction enthalpies are used to calibrate the calorimeter. In the case of a batch microcalorimeter, chemical or electrical calibration can be performed. The calibration process for the batch

microcalorimeter was mainly done in order to correctly determine the up-to-date sensitivity of the NCM-9924 chip. In the case of chemical calibration a protonization reaction of 0.1 mol l^{-1} tris-(hydroxymethyl)aminomethane with hydrochloric acid (the concentration range of 0-0.05 mol l^{-1}) was applied (Fig. 4). The calorimetric sensitivity data were derived from the slope shown in Fig. 5 using the protonization enthalpy of –47.4 kJ mol^{-1} [8]. The electrical calibration was based on a comparison of the output and input signals.

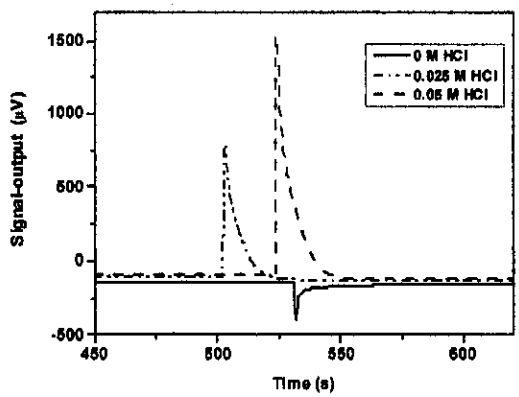

Fig. 4 Illustration of peak height change with concentration of hydrochloric acid

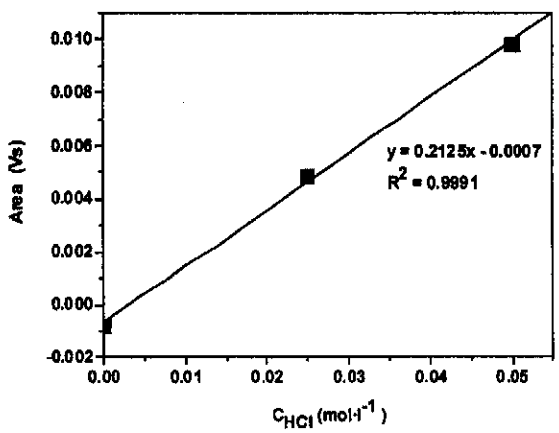

Fig. 5 Evaluation of chip sensitivity (45 μm thin membrane)

Chemical Calibration

For the chemical calibration we used the protonization reaction of TRIS with hydrochloric acid running according the following scheme:

$$(HOCH_2)_3C\text{-}NH_2 + H^+ \rightarrow (HOCH_2)_3C\text{-}NH_3^+ \quad (1)$$

Compared to the electrical calibration, the chemical calibration is more complicated and time consuming. Therefore it is performed only in the case when the chip is new or tested for being damaged.

On the surface of the chip 3 μl of the first reactant was placed — this reactant was hydrochloric acid with the following concentrations: 0; 0.025 and 0.05 mol l^{-1}. The Hamilton microsyringe was filled with the second component — 4.4 μl 0.1 mol l^{-1} TRIS. After placing the first reactant on the chip, the calorimeter was closed. When the thermal equilibrium was established, the reaction was started by the addition of TRIS solution from the Hamilton microsyringe. For the calculation of the chip sensitivity, the area under the peaks observed for various HCl concentrations was used. The sensitivity (S) was then evaluated from the slope of the HCl concentration dependence of the peak area

$$S = \frac{k(x)}{\Delta H_r^{25\,°C} V_{HCl}} \quad (2)$$

where $k(x)$ is the slope of the dependence of peak area on HCl concentration (Fig. 4), $\Delta H_r^{25\,°C}$ is enthalpy of the protonization reaction of HCl with TRIS, and V_{HCl} is the volume of HCl. So, in Eq. (2) the concentration reflected in the value of the slope $k(x)$. The unit of the slope is Vs mol^{-1} l (peak area/concentration) and that of enthalpy W s mol^{-1}, the resulting sensitivity being in V W^{-1}. The sensitivity of the chip with membrane of 45 μm thickness was evaluated to be 1.02 V W^{-1}.

Electrical Calibration

The electrical calibration is based on comparison of output and input signals. The chip is not dry during calibration (as supposed from classical calorimetry) but the hot area is covered with liquid. During electrical calibration, first a water droplet (volume 8 μl) was placed on the sensor, the moisture ring was impregnated with water (6 μl) and the calorimeter was closed. Then an empty Hamilton microsyringe was introduced into the hole of the upper block of the calorimeter. The resulting sensitivity of the chip was obtained from the comparison of output and input signals as the mean value from 5 calibration cycles (see Figs 6 and 7). This procedure is faster than chemical calibration while also being predicative concerning the actual state of the microchip. Figures 6 and 7 show the measured signals used for determination of the mean sensitivity of the 22 μm thick membrane at the temperature of 25 °C. The value of sensitivity 2.29 V W^{-1} was calculated as dU/dP where dU is output signal and dP is the input signal.

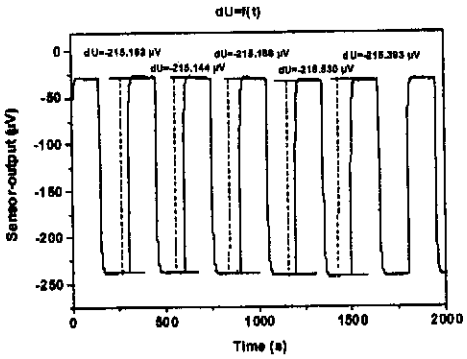

Fig. 6 Dependence of output signal on time

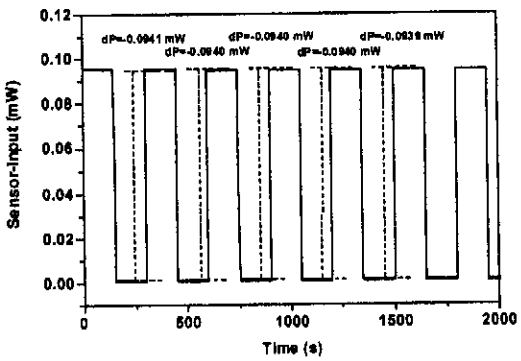

Fig. 7 Dependence of intput signal on time

Factors Influencing Accuracy of Measurement

Temperature

Most calorimetric measurements are usually investigated at the temperature of 25 °C; however, there is a large group of biologically or enzymatically catalyzed reactions that are measured at the temperature of 37 °C. Therefore, every calorimeter designed for studying both these groups of reactions must be checked with regard to the temperature influence on sensitivity and accuracy of measurement. The results of sensitivity determined at selected temperatures are given in Fig. 8. It is evident that sensitivity is significantly influenced by changing the temperature of measurement: with increasing temperature the sensitivity decreases.

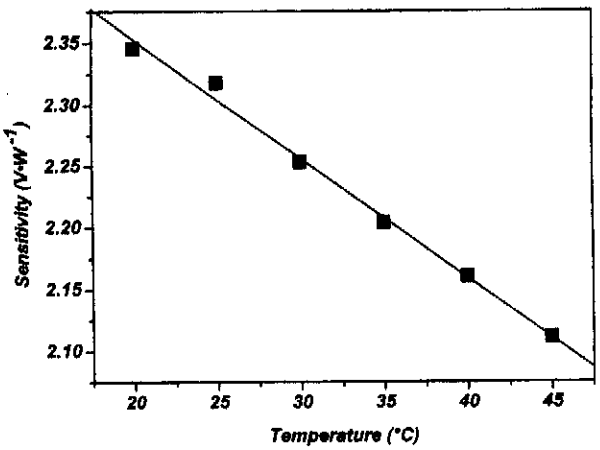

Fig. 8 Dependence of sensitivity on temperature during measurement (points); line is to guide eye

Volume of Droplet

The hot area of the chip is the zone which is surrounded by the thermopiles. We applied the sensor with the surface area of 4 × 4 mm^2 and a thinner (22 μm) membrane for which the sensitivity was determined to be 2.4 VW^{-1}. This parameter depends on the droplet volume. The influence of the droplet volume on sensitivity was tested using water as a sample. A given volume of water was placed on the chip and the empty microsyringe was introduced into the hole of the upper block of batch microcalorimeter. Figure 9 shows the calculated values of sensitivity for the droplet volumes ranging from 0 to 14 ml. From the graph it is evident that with increasing droplet volume the sensitivity of the membrane decre-

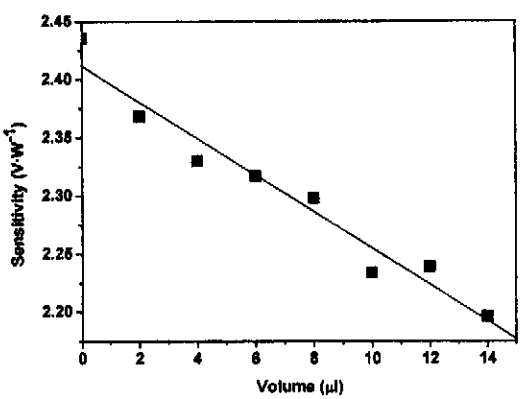

Fig. 9 Dependence of sensitivity on volume of droplet on chip (points); line is to guide eye

ases. Similar results were also previously mentioned by Lerchner *et al.* [7]. The volumes of 12 and 14 μl were considered to be critical because in such case the droplet can already extend beyond the edges of the hot "area". The volume ranging from 8 to10 μl was found to be optimal; however, the sensitivity of the chip is not highest but the volumes of both reactants are optimal for better mixing.

Addition effect

Batch microcalorimeters are usually used to study liquid-liquid reactions at constant temperature. At the beginning of experiment a droplet of one reactant is placed on the chip and the second reactive liquid is in the microsyringe. When the temperature in calorimeter is equilibrated the reaction starts by emptying the

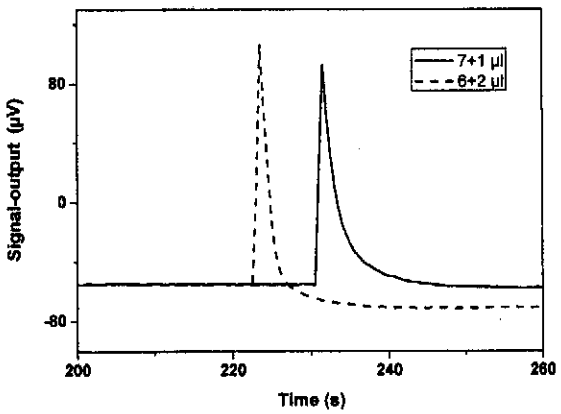

Fig. 10 Time dependence of signal output for reaction systems 7+1; 6+2 μl (see Table I)

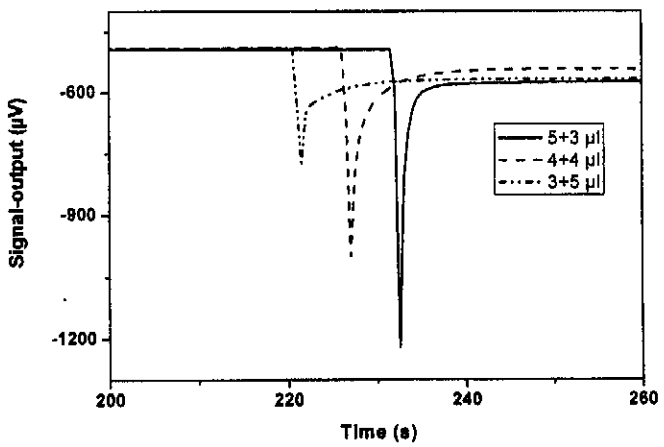

Fig. 11 Time dependence of signal output for reaction systems 5+3; 4+4; 3+5 μl (see Table I)

microsyringe. This addition of the second liquid to the droplet on the chip and its possible effect on sensitivity was also studied in this work. All the measurements were carried out in the same way, and in all the cases the total volume of both liquids was 8 μl. Graphs in Figs 10 and 11 depict signals for reaction ratios from Table I and describe the addition effect for the water-water system. It is evident that the first two ratios provide an exo-effect, while the others (Fig. 11) show an endo-effect. This exo-endo effect with volume ratio change was also observed for solutions other than water. Comparison Figs 10 and 11 indicates a certain baseline drift. The measured peak corresponds to the remaining temperature difference between both droplets due to the addition effect. The baseline is shifted because of the change of the droplet surface which results in an increase of the vaporisation rate [9]. Generally, the baseline drift for this type of batch calorimeter is lower than 0.003 $\mu W\ s^{-1}$, and the noise varies in the range of 0.2 μV [9].

Although the peak of the addition effect seems to be relatively high and broad, it is negligible compared to the effect of any measured reaction.

Conclusion

In this paper we present a batch microcalorimeter with the chip NCM-9924 which is suitable for measuring thermal properties of liquid samples. The first part of this paper describes the microcalorimeter device and the chip. Furthermore, several details on the calibration methods and factors influencing the sensitivity of the chip are given. The device was calibrated by using chemical reaction between TRIS and hydrochloric acid; moreover, also the electrical calibration was carried out. From the study of possible influences of experimental conditions on the chip sensitivity is apparent that statistically remarkable factors are the temperature and the volume of the droplet placed on the chip. The sensitivity of the chip decreases with increasing temperature and also with increasing volume of the droplet. In the last part of the paper the effect of addition on the observed calorimetric signal is discussed.

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