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Noninvasive and Continuous *in vivo* Monitoring of Physiological Parameter Variations Based on CW-Photoacoustic Protocol: Application to Body Temperature Measurements

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Noninvasive *in vivo* measurements of blood glucose level (BGL) are so challenging that despite the huge needs and several detection techniques tried over the last few decades, none of the proposed approaches reaches the market place despite *in vitro* promising results. Over the last few years, we developed protocols based on continuous wave photoacoustic (CW-PA) technique and dedicated to the noninvasive and continuous monitoring of BGLs. So far, all the experiments were performed *in vitro* and showed promising characteristics. However, before further developing our sensor, we tested the approach *in vivo* with a dedicated custom-made detection cell. The CW-PA protocols rely on the presence of acoustic resonant peaks at certain frequencies that depend on the local environment, or cavity dimensions. Several test-sites of the human body were tested, including the hand (near the hand web between the thumb and fore-finger), the ear-lob and the belly. Every time, we could get acoustic resonance at several frequencies despite huge variations of the amplitude levels. The results from the hand are consistent with the 3D cavity due to the presence of lateral reflecting surfaces from the flesh/bones and flesh/air interfaces. On the contrary, when using the ear-lobe or belly, the results are consistent with the 1D-cavity *in vitro* measurements. Then, we applied the previously developed frequency-shift [1] (FS) protocol to continuously monitor changes of one physiological parameter. However, the precise control of BGL (level, delay) is difficult to achieve, so that we used the temperature dependence of FS protocol to monitor the body temperature change induced by placing an ice-pack close to the measurement site for few minutes. Figure 1 shows the results with both amplitude and phase signals varying in good agreement with expected change of body temperature in real time. Despite measuring one potential interferents to BGL monitoring, these qualitative results demonstrate the potential use of CW-PA protocol for noninvasive and continuous monitoring of physiological parameters.

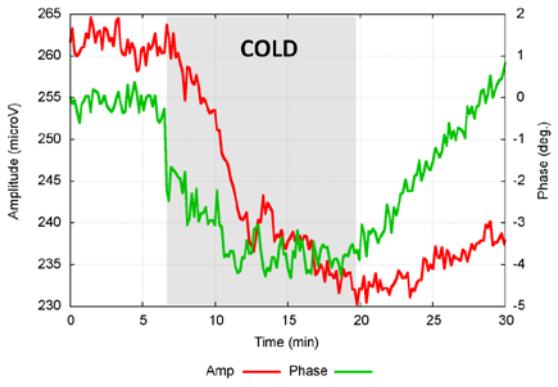

Fig. 1 Continuous monitoring of FS-based sensor response (amplitude and phase) along time while ice-pack is applied close to the test-site (Cold, area in light grey) to locally lower the temperature. Experiments done from the belly.

[1] S. Camou *et al.*, Anal. Chem. 2012, 84, 4718-4724.