**APPLICATION NOTE 5**

**Bubble pressure tensiometry for pharmaceutical applications**

This application note illustrates how the Attension BPA-800P can be used to determine dynamic surface tension and presents an example of pharmaceutical application.

**Introduction**

The maximum bubble pressure tensiometry is the only technique allowing dynamic surface tension measurements in the short time range down to milliseconds. It was invented already mid of the 19th century by Simon [1]; however development of the theory and technique has been continued until these days resulting commercially available tensiometers based on the technology [2].

The main principle of the maximum bubble pressure technique is to generate continuously bubbles at the tip of the capillary and to determine the pressure in the bubble.

The bubble formation from the capillary is shown schematically in Figure 1. Bubble pressure (P) reaches its maximum at the hemispherical size (Figure 1 C). The surface tension (γ) can be calculated according to Laplace equation \( \gamma = Pr / 2 \), when the capillary radius (r) is known. The time interval from bubble generation to the hemispherical size is called bubble lifetime and from the hemispherical size until the bubble detaches is called bubble deadtime. The bubbles are generated at different frequencies allowing to characterize a dependency of surface tension on time [3].

![Figure 1. Bubble radius is at first large (A), then decreases to a minimum when the radius is the same as that of the capillary (C) and then increases again (E).](image-url)
Even if the main principle is the same in all bubble pressure tensiometers, the technical principle to measure the lifetime can be different.

Attension BPA-800P is equipped with a gas flow oscillation analyzer. When the air is delivered in the system by compressor, the air flow rate (L) and internal system pressure (Pₛ) against time (t) can be determined by pressure sensors. The internal system pressure, Pₛ, varies as a function of bubble life time and the maximum pressure can be calculated from the peak values of the Pₛ(t) dependence. The maximum pressure correlates to the hemispherical bubble.

However, gravity causes distortion to the spherical bubble shape, which needs to be corrected when capillary radius is larger than 0.1 mm. The correction is done by a factor f (Equation 1). Since the pressure is not measure directly from the bubble, but in the system connected to the capillary, the measured pressure Pₛ exceeds the pressure in the bubble. The excess pressure is mainly caused by the aerodynamic resistance of the capillary and viscosity of the probe liquid, which effects need to be subtracted from the measured surface tension. In addition, hydrostatic pressure of the liquid at the capillary tip, Pₕ, needs to be subtracted from the Pₛ. Therefore, dynamic surface tension can be expressed according to following equation [2]:

\[ \gamma = f \left( \frac{P_s - P_h}{2} - \Delta \gamma_a - \Delta \gamma_v \right) \]  

(Equation 1)

The \( \Delta \gamma_a \) and \( \Delta \gamma_v \) represents the effects caused by the aerodynamic resistance and the viscosity of the probe liquid, respectively. All the corrections are performed automatically by the instrument.

Bubble pressure tensiometry is widely utilized to study various dynamic surface phenomena including industrial and biological applications. Many industrial processes, such as coating, printing and flotation, operate under dynamic conditions and therefore surface tension determined within short life spans provides often more relevant information than equilibrium state values. Under dynamic conditions surface active components might not have time to reach surface and therefore their influence on surface tension might be significantly different compared to the equilibrium state value. In Figure 2 is shown a typical dynamic surface tension curve: surface tension of an UV based inkjet ink decreases as a function of bubble life time.

**Case study: Investigation of the dynamic process during spray-drying to improve aerodynamic performance of inhalation particles.**

Inhalation therapy has been regarded as a promising method for systematic drug delivery as well as treatment of pulmonary diseases, for example asthma. However, the inhalation technology needs still significant improvements in terms of devices and formulation to achieve wider use. Particle size has been recognized to be one of the most important factors influencing on the drug delivery in the lungs. The most common manufacturing method for inhalation particles is the dynamic particle formation process called spray-drying. In the process, particle size is controlled by varying instrumental conditions and solution concentration. Kawakami et al. [4] studied how the surface tension affects the particle formation in spray-drying technology. Even if it is easily assumed that surface tension should have influence on the particle size formation, no clear correlation has been presented. Previous researches have frequently been performed by using equilibrium surface tensions, which do not apply well to dynamic process characterization.

Kawakami et al. [4] used bubble pressure tensiometer BPA-800P (Attension, previously KSV Instruments) to study dynamic surface tension of the inhalation feed solutions. They were able to show that no equilibrium values can be obtained in the time scale used in the particle formation, even if the surfactants were added at a concentration higher than the critical micelle concentration (CMC). The surface tension at 10 ms was found to correlate well with both size of the droplet produced from the spray nozzle and that of the solid particle, as shown in Figure 3.
Conclusion

The maximum bubble pressure tensiometry is a unique technique to measure dynamic surface tensions in short time ranges. Dynamic surface phenomena take place in many fields of applications, when equilibrium state surface tension values do not apply well for characterization. Dynamic surface tension is able to demonstrate surfactant kinetics and how it influences on the surface tension under dynamic conditions.

References