

mary drying, is a powerful tool for maintaining product quality, as product temperature affects the structure of the dry cake which in turn affects product residual moisture content, reconstitution time, product shelf life and potentially product efficacy. Thus, a TDLAS sensor can provide real-time processing information that can be directly linked to critical product quality attributes.

TDLAS sensors utilize the unique characteristics of diode lasers (narrow spectral linewidth and rapid wavelength tunability) combined with ultrasensitive detection techniques (e.g., frequency modulation, FM, spectroscopy [45–47] or balanced radiometric detection, BRD [48, 49]) to accurately and sensitively measure gas phase analytes using the Beer–Lambert law shown in Eq. 7:

$$I_v = I_{o,v} \exp[-S(T)g(v - v_o)N\ell] \quad (7)$$

where $I_{o,v}$ is the initial laser intensity at frequency v , I_v is the intensity recorded after traversing a path length, ℓ , across the measurement volume, $S(T)$ is the temperature dependent absorption line strength, $g(v - v_o)$ is the spectral line shape function, and N is the number density of absorbers (the water concentration). The lineshape function describes the temperature—and pressure-dependent broadening mechanisms of the fundamental line strength. Measurements within the low-pressure (~ 100 mTorr) conditions present during lyophilization, with limited gas collisions, result in $g(v - v_o)$ described by a Gaussian function. Using the BRD technique [50] and scanning the diode laser frequency across the entire absorption lineshape from baseline to baseline removes any pressure dependency of the lineshape function from the number density measurement, $\int g(v - v_o) dv = 1$. Scanning the fully resolved absorption lineshape also reduces the effect of broadband absorbers in the background gas and nonresonant scattering from any aerosols or particulates that may be present in the flow.

The water concentration, $[H_2O]$, in molecules cm^{-3} is calculated using Eq. 8:

$$N = \frac{\int \ln \left[\frac{I(v)}{I_o(v)} \right] dv}{S(T)\ell} \quad (8)$$

where dv is the laser frequency scan rate per data point ($\text{cm}^{-1}/\text{point}$).

The gas temperature is determined by analyzing the water vapor absorption lineshape using Eq. 9, where Δv_D is the absorption lineshape full width at half maximum (FWHM) frequency (cm^{-1}), v_o is the line center frequency (7181 cm^{-1}), T is the gas temperature (K), and M is the molecular weight (g/mole) of the absorbing species (water vapor):

$$\Delta v_D = 7.162 \times 10^{-7} v_o \sqrt{(T/M)} \quad (9)$$

Real-time measurement of the gas temperature is required to calculate the temperature-dependent water absorption line strength and properly determine the water vapor concentration. The isolated, near-infrared (IR), 7181 cm^{-1} , ($3_{03} \leftarrow 2_{02}$ rotational