Gas Phase Analysis of Water using Fourier Transform Infrared Spectroscopy

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Design of Medical Devices Conference
Minneapolis, Minnesota
April 18, 2007
Absorption of Infrared Radiation
Fourier Transform
(Time Domain to Frequency)

Interferogram (Time Domain Spectrum)
Transformed Interferogram

- Frequency Domain
- Photon intensity at the detector (Y-axis) at each wavenumber cm\(^{-1}\) (X-axis)
  - Single beam spectrum

Single Beam \(\text{SB}_{\text{BKG}}\)

Water Absorbance (specific frequencies)

Single Beam \(\text{SB}_{\text{Sample}}\)
Transmission Spectrum of Water

- Simple intensity ratio ($SB_{sample}/SB_{bg}$)
- Scales logarithmically with concentration

Transmittance:

$$T = \frac{I}{I_0}$$
Absorbance Spectrum

- Absorbance of Spectrum of Water
  - Absorbance = \log_{10} \frac{1}{\text{Transmission}}
  - Scales linearly with concentration

\[ A = \log \frac{I_0}{I} \]
Beer's Law Summary

\[ A_i = a_i \times b \times c_i \]

- **A_i**: Absorption at a given frequency of the \( i^{th} \) sample component
- **a_i**: Absorption coefficient (absorptivity) of the \( i^{th} \) sample component
- **b**: Pathlength of cell
- **c_i**: Concentration of \( i^{th} \) sample

**A** = \( \log_{10} \left( \frac{1}{T} \right) = -\log_{10} T \)

- **A**: Absorbance
- **T**: Transmittance
Absorption Coefficient & Pathlength

Certified gases are used to generate single component reference standards.

The absorption coefficient is a property of a material and it defines the extent to which a material absorbs energy.

- Affected by Temperature
- Affected by Pressure

Path length is fixed and calibrated.
# Calibration Reference Spectra

*(Prediction Model)*

<table>
<thead>
<tr>
<th>Filename</th>
<th>Actual Conc (ppm)</th>
<th>Predicted Conc (ppm)</th>
<th>SEC (ppm)</th>
<th>Prediction %Error (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>7_93H2O</td>
<td>7.93</td>
<td>7.93</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>12_5H2O</td>
<td>12.54</td>
<td>12.069</td>
<td>0.056</td>
<td>-3.76</td>
</tr>
<tr>
<td>17_3H2O</td>
<td>17.32</td>
<td>16.874</td>
<td>0.070</td>
<td>-2.575</td>
</tr>
<tr>
<td>23_9H2O</td>
<td>23.89</td>
<td>24.593</td>
<td>0.207</td>
<td>2.943</td>
</tr>
<tr>
<td>39_4H2O</td>
<td>39.44</td>
<td>39.774</td>
<td>0.094</td>
<td>0.848</td>
</tr>
<tr>
<td>52_2H2O</td>
<td>52.22</td>
<td>50.788</td>
<td>0.182</td>
<td>-2.741</td>
</tr>
<tr>
<td>58_9H2O</td>
<td>58.9</td>
<td>58.073</td>
<td>0.194</td>
<td>-1.404</td>
</tr>
<tr>
<td>71_4H2O</td>
<td>71.41</td>
<td>74.851</td>
<td>0.285</td>
<td>4.819</td>
</tr>
</tbody>
</table>
CLS Prediction Model Linearity

\[ y = 1.0099x \]

\[ R^2 = 0.9965 \]
Drivers for Alternative Test Methods

- Seek method that minimizes product consumption with increased sensitivity
- Test methods which can meet multiple regulations (e.g. ISO 10993-7 & 10993-18)
- Determine compliant, cost effective “One Shot Analysis”
Innovative New Alternative to Existing Technologies 

Static Headspace with Fourier Transform Infrared (FTIR) Detection

- Detection of Acids, Bases, and Volatiles
- Identification and Quantitation
- Fast collection and analysis time – Get Product to Market Faster
- Provides Low Limits of Detection required by Guidelines
FTIR Static Headspace (SHS): Outgassing Profile

FTIR Static HS Gas Cell

IR Source

IR Detector

Total Cumulative Outgassing vs Time

SAMPLE

FITR Spectra

Absorbance Units

Concentration

Time

PaceAnalytical
FTIR Static Headspace (SHS): Outgassing Profile

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Concentration

Time

Absorbance Units

PaceAnalytical
Controlled Testing

Environment

- Dry Box Purged with house nitrogen
- Independent nitrogen purge ports
  - Located at opposing points on the box to enhance mixing.
  - Controlled flow (20 LPM) at each point.
  - 9 Volume exchanges per Hour
- Added independent measured and controlled flow to ante chamber.
  - Measurable volume exchanges
- Mounted fan inside Dry Box
  - Improved mixing.
- Added independent exhaust to Dry box.
FTIR Technologies

Gas Phase FTIR

Typical Bench Top FTIR

Absorbance / Wavenumber (cm⁻¹)
File # 2 : 71_4H2O
Water in G.5 N2, Cosameter 74.57 ppm -3.16 ppm BG= 71.41 ppm, 10m,0.981 atm, 121C,Avg files 34-36  BAL

Y-Zoom CURSOR
High Resolution vs. Low Resolution

Absorbance / Wavenumber (cm⁻¹)

High Resolution (0.5 cm⁻¹)

Low Resolution (4 cm⁻¹)
Analysis

- Reference spectra
  - Prepared on the instrument used for analysis but can be transferred to other instruments
  - Recorded at the experimental temperature / conditions
  - Concentration is measured using second technique or certified standard
  - Multiple concentrations are prepared to bracket the experiment range

- Reference spectra are implemented into a Classical Least Squares (CLS) fit routine

- Sample Spectra are quantified by comparison to Single Component Reference spectra using CLS

- Multiple Species can be quantified simultaneously
  - Analysis regions can be chosen to avoid interferences
  - Multiple regions can be chosen to circumvent saturated absorbance bands that may deviate from Beer’s Law
IDEAL GAS LAW
PV = nRT

Cell Volume = 5.7 L
Pressure = 1 atm
Molecular Weight = 18 g/mol
Cell Temperature = 121 °C
Water Contribution from System

- Dry Box Air
  - Rate: 0.041 PPMv / Minute

- Grade 5 Nitrogen
  - Rate: 0.041 PPMv / Minute

Concentration vs. Elapsed Time Graph
Dry Box Air Static Blank Data

Concentration (PPMv) vs. Elapsed Time (min)

Graph showing the concentration over time.
## System Suitability

**Contribution of FTIR Gas Cell to Water Vapor Concentration**

<table>
<thead>
<tr>
<th>Trial</th>
<th>Elapsed Time</th>
<th>PPM increase</th>
<th>PPMv / Minute</th>
<th>µg / minute</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>29.8</td>
<td>1.414</td>
<td>0.0474</td>
<td>0.151</td>
</tr>
<tr>
<td>2</td>
<td>39.1</td>
<td>1.851</td>
<td>0.0473</td>
<td>0.150</td>
</tr>
<tr>
<td>3</td>
<td>109.3</td>
<td>4.434</td>
<td>0.0406</td>
<td>0.129</td>
</tr>
<tr>
<td>4</td>
<td>758.3</td>
<td>31.189</td>
<td>0.0411</td>
<td>0.131</td>
</tr>
<tr>
<td>Average</td>
<td></td>
<td>0.0441</td>
<td>0.0441</td>
<td>0.140</td>
</tr>
<tr>
<td>% RSD</td>
<td></td>
<td>8.6 %</td>
<td>8.6 %</td>
<td>8.6 %</td>
</tr>
</tbody>
</table>
# Table of Recoveries

Percent Recovery of Liquid Water Injected in the FTIR Gas Cell

<table>
<thead>
<tr>
<th>Spike</th>
<th>µl of Water Spiked</th>
<th>% Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.2</td>
<td>87</td>
</tr>
<tr>
<td>2</td>
<td>0.2</td>
<td>75</td>
</tr>
<tr>
<td>3</td>
<td>0.2</td>
<td>101</td>
</tr>
<tr>
<td>4</td>
<td>0.2</td>
<td>92</td>
</tr>
</tbody>
</table>

Average % Recovery: 89

% RSD: 13%
## Gas Standard Recoveries

<table>
<thead>
<tr>
<th>Delivered Concentration (PPMv)</th>
<th>Percent Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>28.4</td>
<td>94%</td>
</tr>
<tr>
<td>38.6</td>
<td>106%</td>
</tr>
<tr>
<td>49.2</td>
<td>95%</td>
</tr>
<tr>
<td>51.0</td>
<td>102%</td>
</tr>
<tr>
<td>68.1</td>
<td>99%</td>
</tr>
</tbody>
</table>
Biodegradable Polymer
Lot 1 (125 mg vs. 25 mg)

Outgassing Concentration (PPMv) – ~125 mg of Material
Cell Baseline (PPMv) – Sept ‘06

Outgassing Concentration (PPMv) – ~25 mg of Material
Cell Baseline (PPMv) - Jan ‘07

Elapsed Time (minutes)
Outgassing Profile

25mg of Biodegradable Polymer

- Grade 5.0 Nitrogen Purge
- Dry Box Air Purge
- Dry Box Air Static
- Static Cell Blank 0.41 PPMv
- Increase Over 25min.

Concentration (PPMv) vs. Time (Min.)

25 mg Biodegradable Polymer

1300 µg/g Difference
Lot 1 Matrix Spike

Spike 0.1 ul water
% Recovery = 91

Purge Cell with Nitrogen

Spike Additional 0.1ul water
% Recovery = 105

5 Parts Outgassed Static

Spike 0.1ul water
% Recovery = 88
## Table Recoveries

<table>
<thead>
<tr>
<th>Spike Volume (µL)</th>
<th>5 – Lot 1 Spike (% Recovery)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial 2 Spike 1</td>
<td>91</td>
</tr>
<tr>
<td>Trial 2 Spike 2</td>
<td>88</td>
</tr>
<tr>
<td>Trial 2 Spike 3</td>
<td>105</td>
</tr>
<tr>
<td>Trial 3 Spike 1</td>
<td>89</td>
</tr>
<tr>
<td>Trial 3 Spike 2</td>
<td>114</td>
</tr>
<tr>
<td>Trial 3 Spike 3</td>
<td>117</td>
</tr>
<tr>
<td>Trial 4 Spike 1</td>
<td>99</td>
</tr>
<tr>
<td><strong>Average</strong></td>
<td>99</td>
</tr>
<tr>
<td><strong>% RSD</strong></td>
<td>12%</td>
</tr>
</tbody>
</table>
Specificity

Water Spectrum

Bio-degradable Polymer Spectrum

Absorbance / Wavenumber (cm⁻¹)
Method Advantages

- Real-time data collection allows calculation of release rates, formation of compounds, & outgassing endpoints
- FTIR method allows simultaneous data collection for materials characterization (ISO 10993-18)
Method Advantages

- FTIR is additive, interferences can be subtracted
- Multiple compounds can be detected in a single test using fewer devices for testing
- Limits of Detection can be lower than GC methods
Method Advantages

- Broad range of selectivity for detection of compounds (organic and inorganic)
- Multiple spectral regions can be used to quantify compounds
- Recent ASTM, NIOSH & EPA approvals
- Methods have been validated