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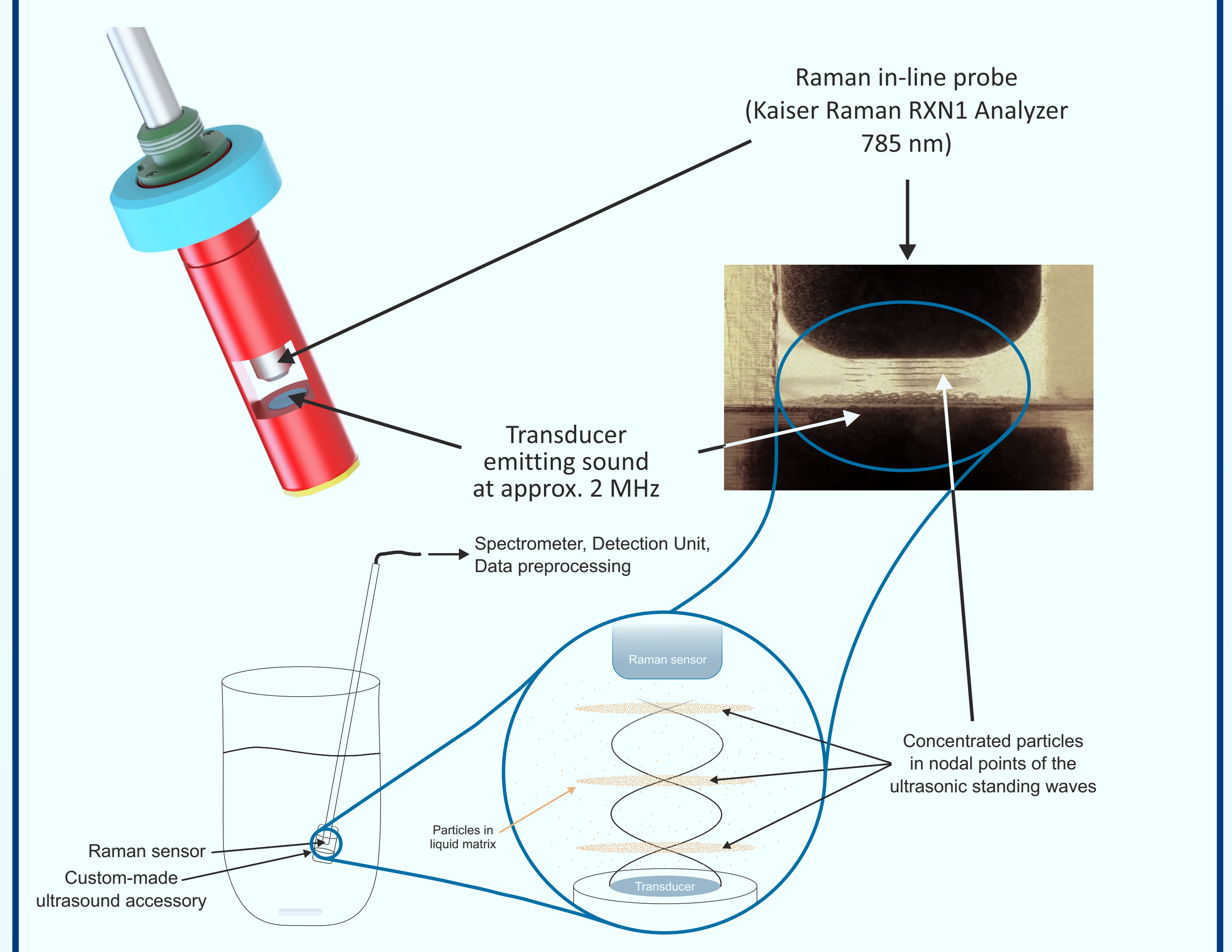
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## INTRODUCTION

Raman spectroscopy is a non-invasive method that offers analyte-specific information. Compared to Infrared spectroscopic techniques, it is less water sensitive and thus offers a very attractive tool for in-line monitoring of aqueous systems in process analytical technology (PAT). [1]

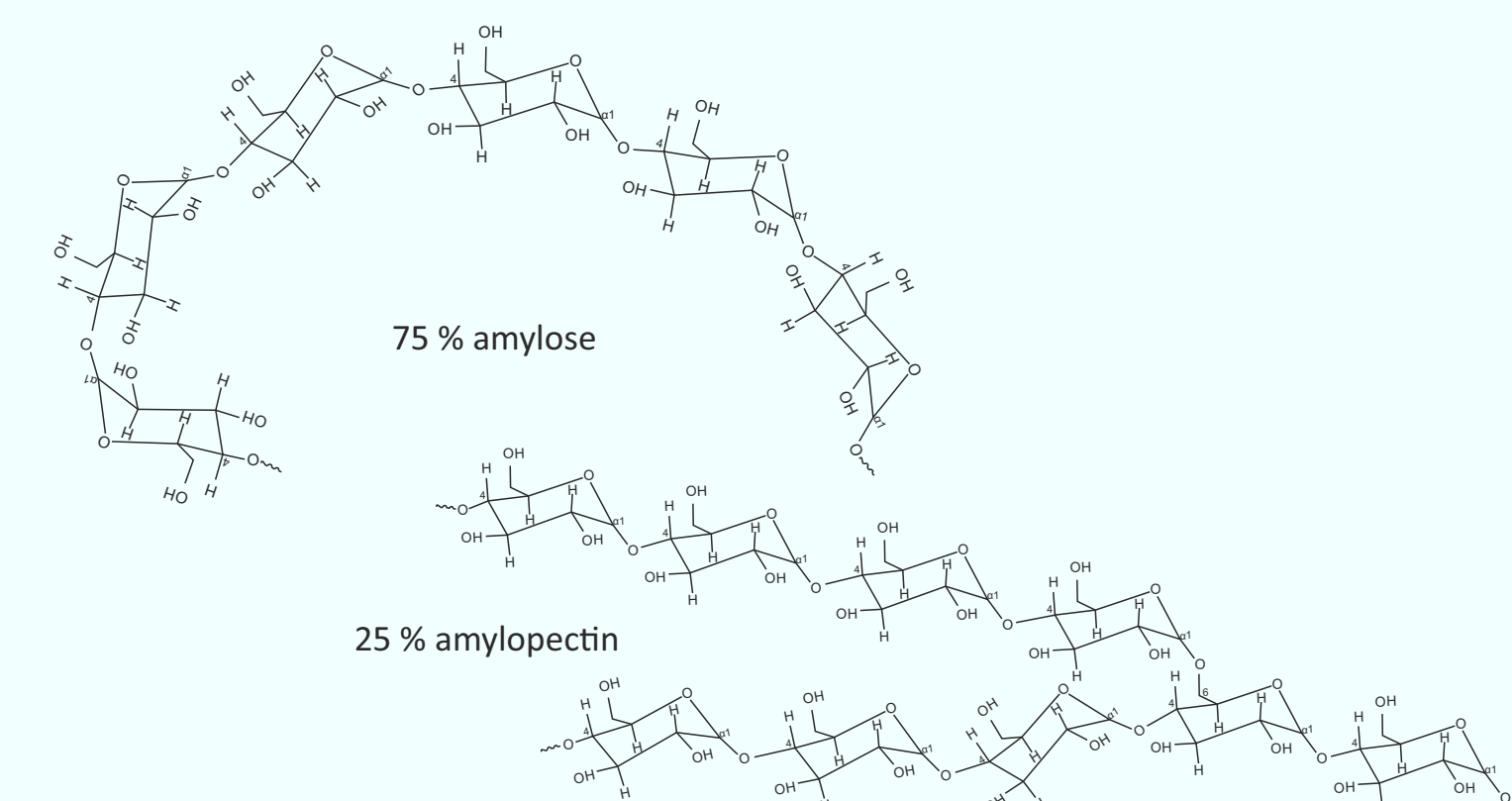
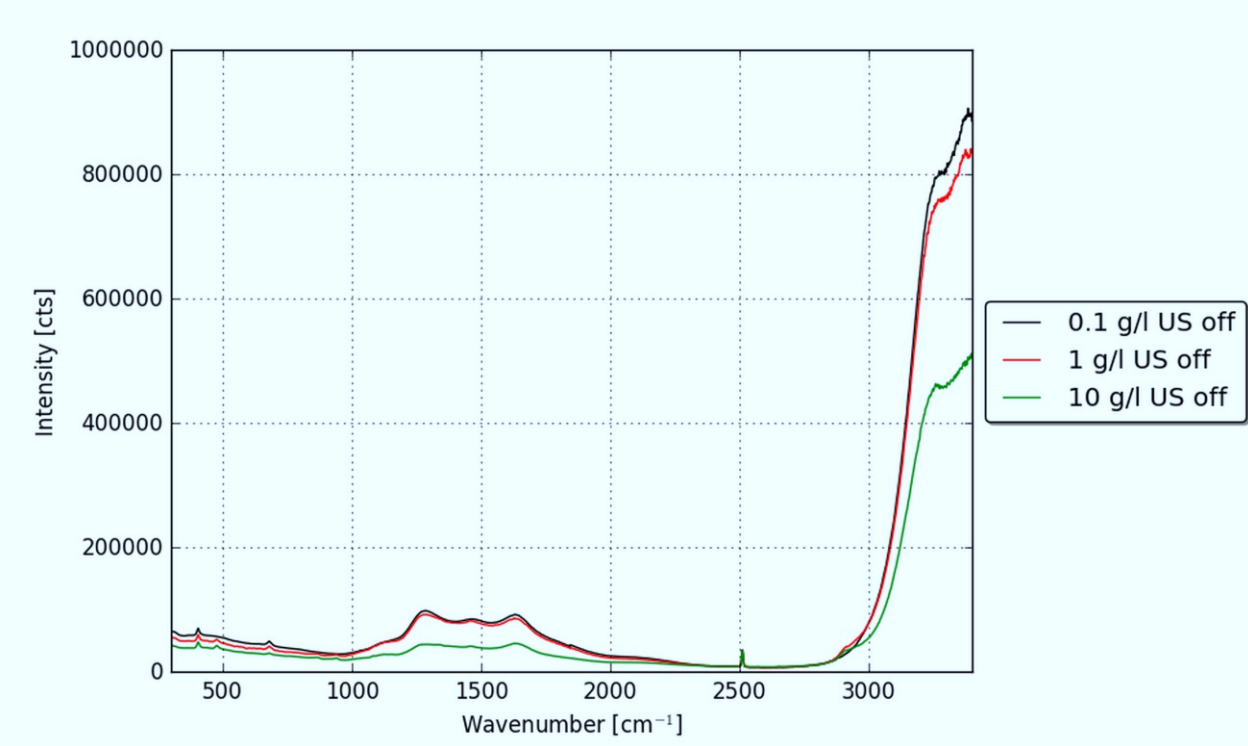
Ultrasonic standing wave fields have been used for particle manipulation in ultrasound-enhanced attenuated total reflection mid-infrared spectroscopy as in-line probing method in bioreactors. The axial acoustic radiation force acting on the particles is applied to push the analyte against the surface of the ATR element and thus into the evanescent field. [2] Here, we go one step further by combining the Raman probe with a custom-made ultrasound accessory to improve the limit of detection (LOD) compared to conventional Raman spectroscopy. Therefore, three different starch concentrations in aqueous solution (0.1, 1.0 and 10.0 g/l) were investigated and compared, respectively. Subsequently, the crystallization process in H<sub>2</sub>O:C<sub>2</sub>H<sub>6</sub>O 80:20 solution as a more complex chemical system was chosen for detailed investigation.

## WORKING PRINCIPLE



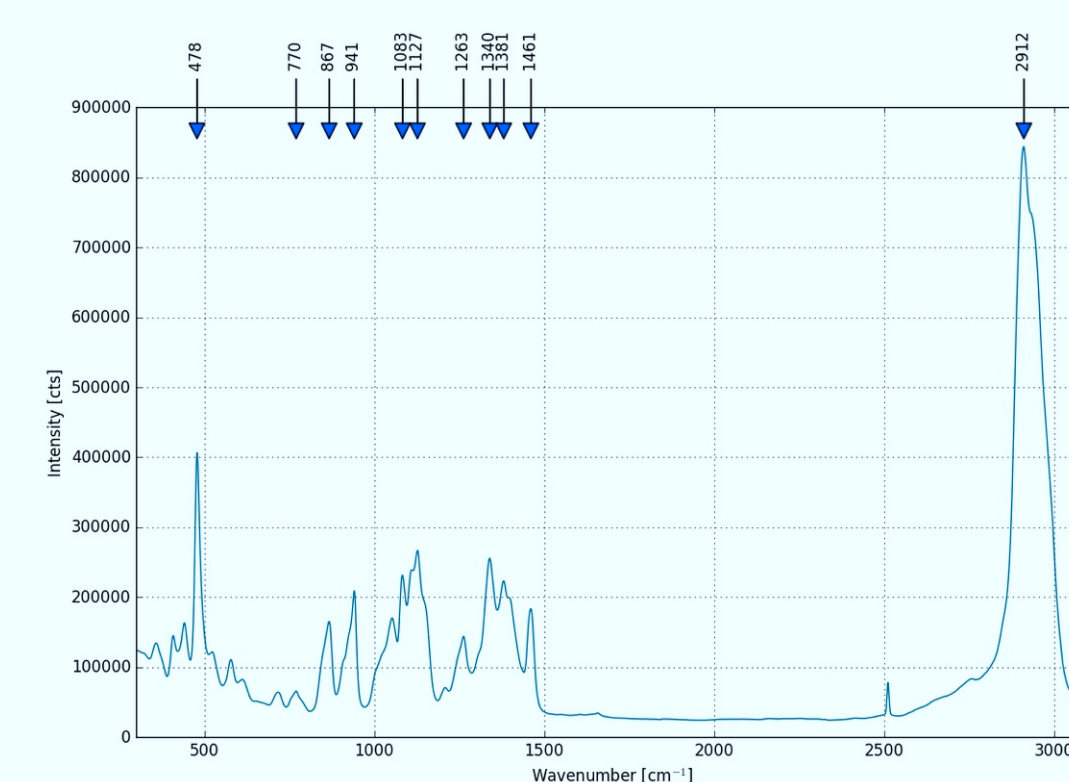
## STARCH PARTICLES IN AQUEOUS SOLUTION

### Conventional Raman Spectroscopy



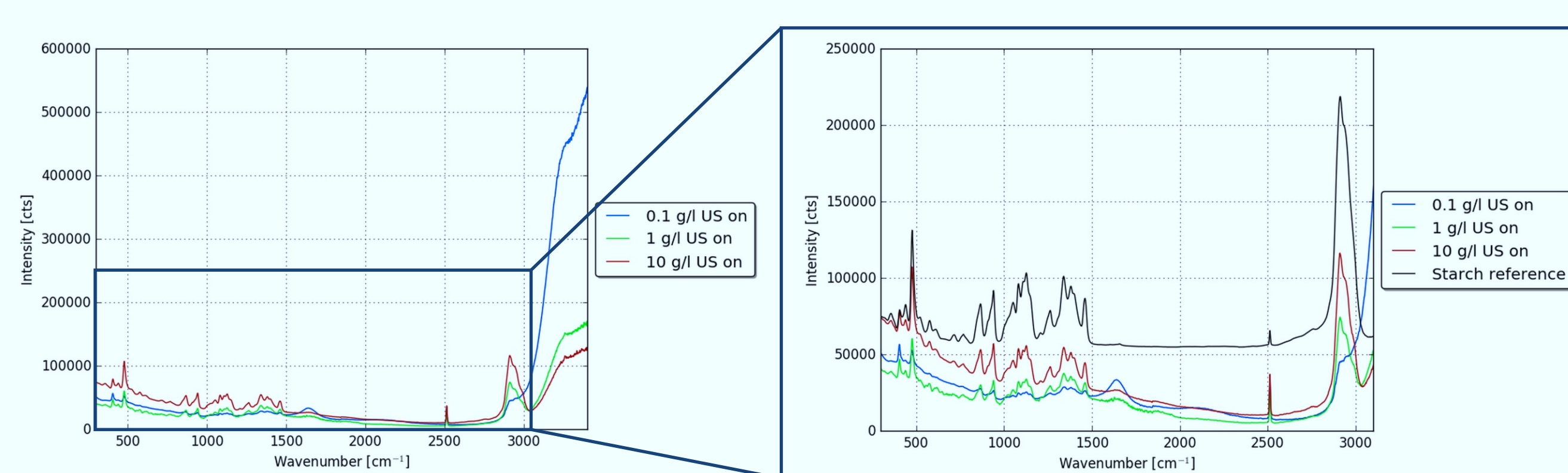
While there are hardly any Raman bands of starch visible in the spectra obtained with conventional Raman spectroscopy (see figure above) the spectroscopic fingerprint of the starch particles are perfectly visible once the ultrasound has been turned on (see figures below).

### Raman spectrum of highly concentrated starch suspension



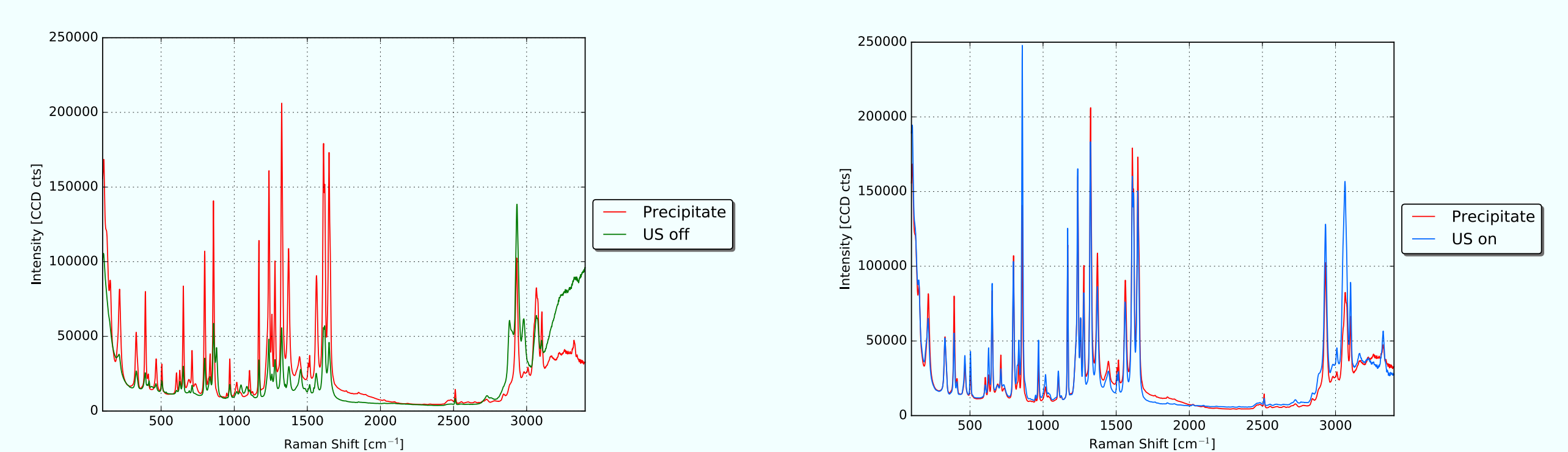
Raman Shift [cm <sup>-1</sup> ]	Band assignment [3]
478	C-C bend; C-O torsion
770	C-C-O bend
867	C-C-H, C-O-C bend.
941	C-O-C, C-O-H bend; C-O str.
1083	C-O, C-C str; C-O-H bend.
1127	C-O, C-C str; C-O-H bend.
1263	C-C-H, O-C-H, C-O-H bend.
1340	CO str, O-C-H, C-O-H bend.
1381	C-O-H bend.
1461	CH, CH <sub>2</sub> , C-O-H bend.
2912	CH str.

### Ultrasound-Enhanced Raman Spectroscopy



## CRYSTALLIZATION OF ACETAMINOPHEN

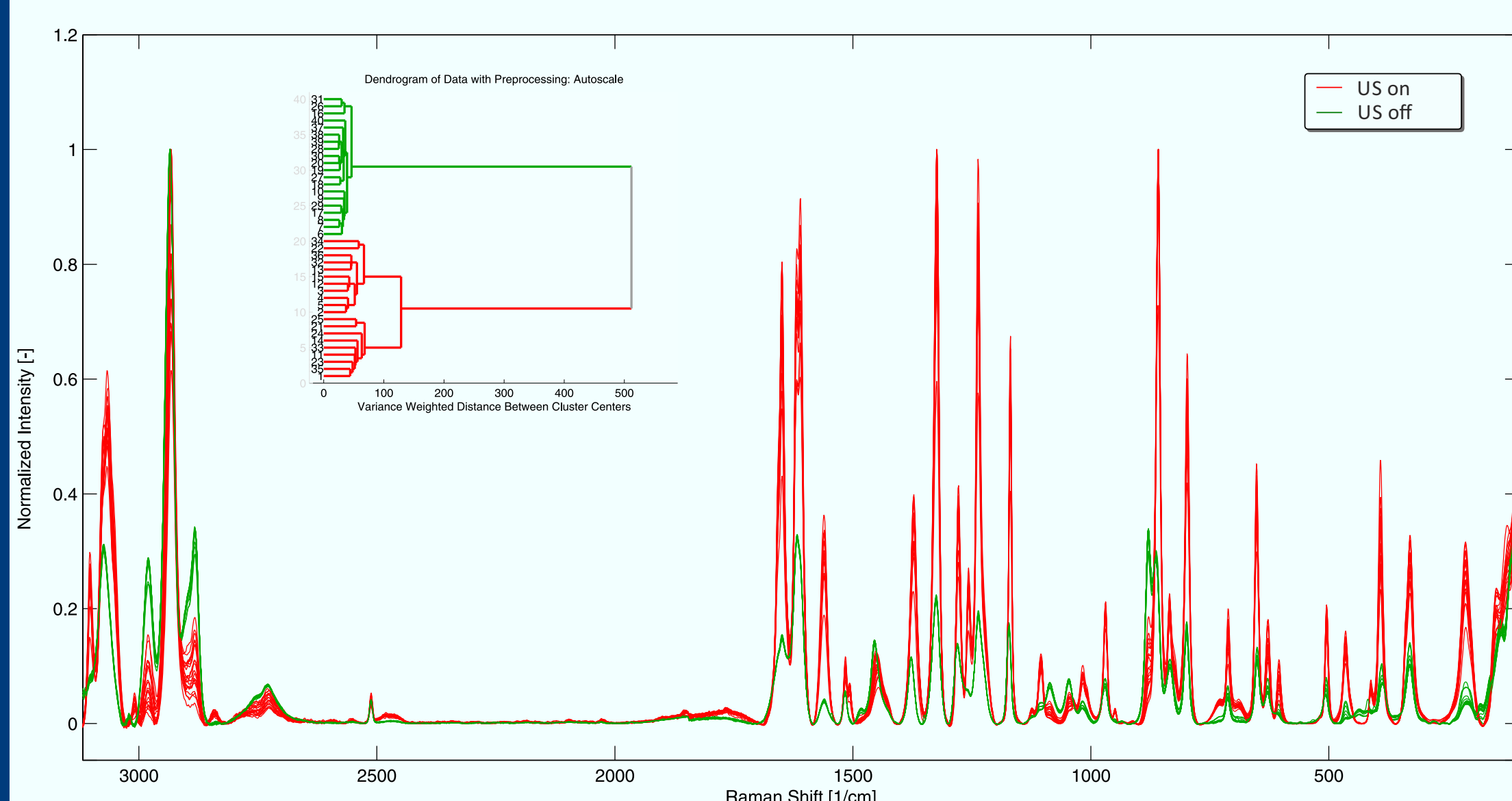
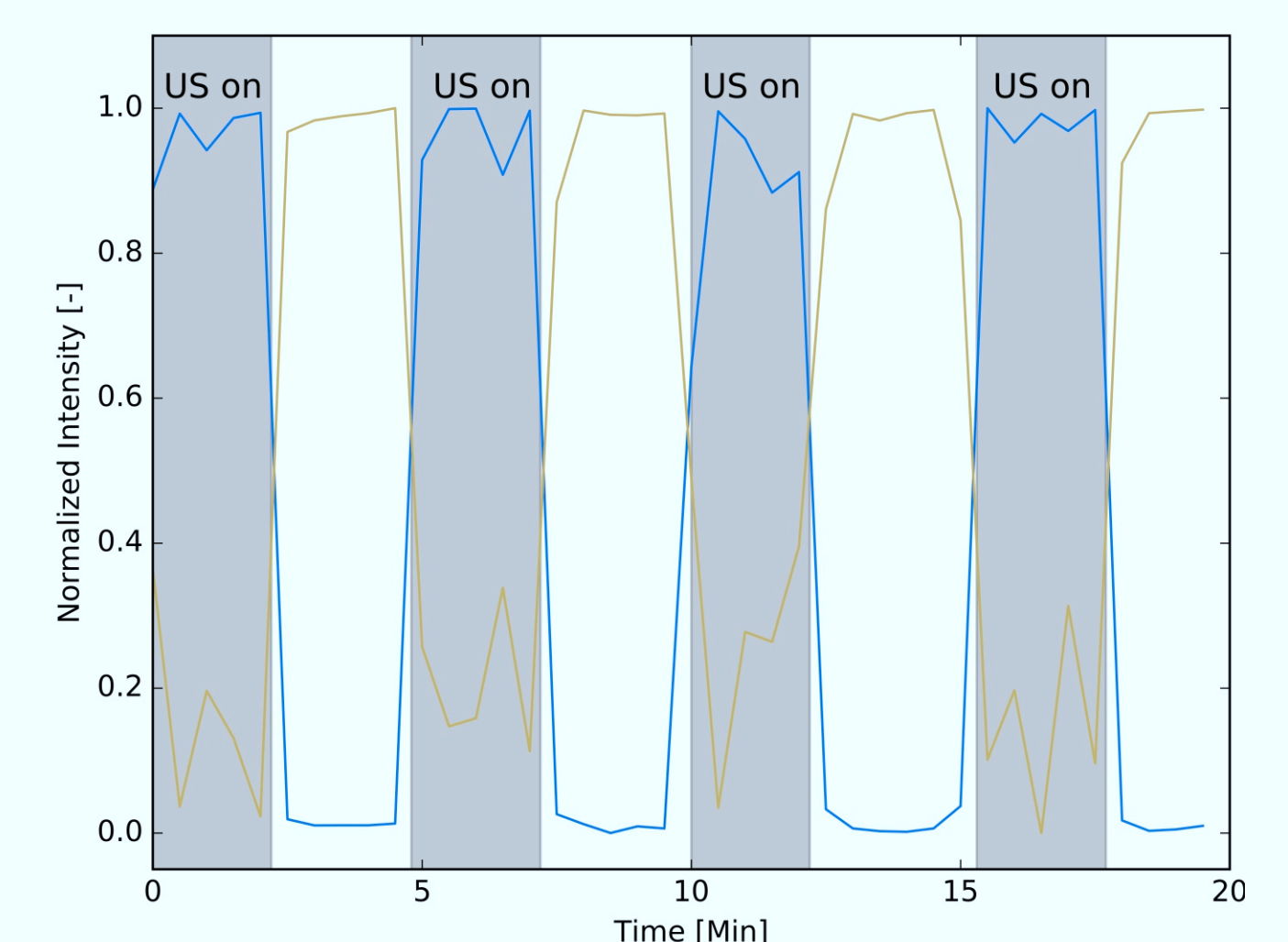
### Conventional vs. Ultrasound-Enhanced Raman Spectroscopy



### The effect of US-Enhanced Raman spectroscopy

- 110 g/l Acetaminophen in H<sub>2</sub>O:C<sub>2</sub>H<sub>6</sub>O 80:20
- Turning ultrasound on and off at constant temperature
- Single spectrum recorded every 5 seconds

Intensity changes with ultrasound on and off:  
- Aromatic ring bending of **Acetaminophen**  
- C-C-O stretching vibration of **Ethanol**



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