Summary

This thesis focuses on the development and application of an advanced mode of Raman spectroscopy, Time-Resolved Raman Spectroscopy (TRRS). Using a system with flexible instrumentation, depth-profiling measurements on a mm-scale were carried out in different kinds of analytically-challenging samples to solve practical research problems within a variety of fields.

Chapter 1 provides background information relevant to this thesis work, including a brief history of the discovery of Raman scattering, as well as an overview on many of the fundamental principles of Raman spectroscopy. This chapter provides a primer for the more applied studies in subsequent chapters. The technique of TRRS is also introduced here, and it is explained how this method is particularly useful for studying highly-scattering (translucent), heterogeneous samples that cannot be studied easily with conventional Raman spectroscopy.

Chapter 2 details the instrumentation used to implement TRRS in the work within this thesis. Additionally this chapter describes various settings, attributes and other optimization information regarding the TRRS approach, as supported by examples taken from my unpublished work. Many of these optimization settings are unique to this particular instrument, however the findings and measuring procedures may also be useful for future TRRS studies. These studied parameters include specific voltage settings of the intensified charge-coupled device (ICCD) detector used, as well as focusing aspects; For instance, it was observed that, in contrast to the behavior of the surface layer, focal distance to the surface of a sample is not critical for best signal collection from deeper layers.
Chapter 3 describes a proof of principle study of TRRS for depth analysis on multi-layered model systems. Different combinations of various polymer materials, cut into blocks of known dimensions, were combined into 2-layer systems, and depth profiles were determined using TRRS. From these exploratory measurements we were able to distinguish the Raman signal from the second layer from the much stronger signal of the first layer on the basis of the increased delay time of these photons to the detector. The results of this work are of importance as it allows us to establish typical delay times for photons traveling back and forth through different kinds of polymer materials with variable thicknesses and scattering properties. We determined that there is a measurable difference in this delay time among materials of different nature, indicating that the specific scattering properties have a significant effect on the random-walk pathlength the photons travel within these materials. As can be readily conceived, the time it takes to travel a certain net distance is increased with increased scattering. Establishing these delay times is valuable for future applications of this technique. Knowing the time delay is necessary in order to identify the depth and thickness of an unknown sample.

Chapter 4 describes an application of TRRS with relevance to the safety and security field. In this chapter, we demonstrate the use of this technique for detecting potentially harmful explosives and their derivatives, concealed behind strongly-scattering plastics. This experiment in part builds on the exploratory study in Chapter 3, where typical photon delay times within plastics were established. We now applied this information in order to detect dinitrotoluene and other derivatives and components of explosives as second layers behind such plastics. By changing the delay time of the detector in increments, we were able to perform a depth profile of these samples, and
acquire fairly clean spectra of the first and second layer materials. The advantage that we found for applying TRRS in such investigations was that by adjusting the delay time one could obtain a spectrum much more exclusively and discriminately from a particular depth than by an alternative Raman spectroscopy depth technique, Spatially-Offset Raman Spectroscopy (SORS), for example. This means that when using a short delay time, photons are collected from the surface of the sample, and the spectrum will be of only the first layer material. With a longer delay time one will get relatively more contribution of photons from deeper within the material. In this way, one can determine from what depth a signal is emanating, and also clearly distinguish the surface layer. Having a pure surface spectrum can be crucial for the analysis of unknown, potentially hazardous samples.

Chapter 5 provides an application of TRRS in the study of heterogeneous catalytic systems, for the non-invasive analysis of a modeled catalytic reaction, i.e., the synthesis of styrene from 1-phenylethanol occurring inside scattering alumina catalyst extrudate materials. Studying the chemistry within heterogeneous catalyst extrudates is a true analytical challenge in that these materials are translucent or highly scattering. Conventional analytical methods cannot penetrate the sample surface to find out what is occurring within the sample at depth. Additionally, fluorescence interference from contaminants and reaction byproducts is often a huge problem in such samples.

Using TRRS, we were able to overcome both the fluorescent background and the scattering nature of the sample in order to perform a depth analysis of a catalytic substrate. Using a modeled catalytic reaction within an alumina extrudate, we were able
to chemically distinguish the inside versus the outside of an extrudate pellet using TRRS, despite interference from an introduced fluorescent background.

The potential of TRRS for biomedical applications is also demonstrated. In Chapter 6 using a model tissue phantom material with synthetic biomineral inclusions, the technique is compared to other depth Raman techniques that are simultaneously being explored for use in this field, especially SORS. Previous unpublished work indicated that the tissue phantom material showed similar scattering behavior as porcine tissue ex vivo. Synthetic biomineral inclusions of varying depth, shape and composition were also embedded within the phantoms, and these were studied with TRRS, SORS, and their combination in order to gauge the limits of detection, and spatial/depth resolution of these techniques.

Future Perspectives

We have demonstrated the applicability of TRRS to various fields, and shown its advantages and disadvantages in tackling different analytically-challenging scenarios. TRRS is able to overcome various sources of fluorescence background from the sample surface and/or throughout the bulk of a material, and can be used to discriminate the surface Raman signal from signals emanating from deeper within a scattering material.

With all depth Raman techniques it remains a challenge to isolate the signal from a relatively low concentration analyte within a bulk scattering medium. Our preliminary experiments in Chapter 5 show the potential to enhance these lower concentrations through the use of SERS enhancement. Continuing studies in such combinations of depth Raman and SERS will prove to be promising.
An additional method of signal enhancement of low concentration analytes will be by means of RRS; i.e., utilizing a resonant excitation wavelength to selectively enhance the signal of interest in a bulk medium. This is the subject of current ongoing investigations (Hooijschuur and Iping Petterson, manuscript in prep).

The poorer S/N than in continuous wave measurements, as well as the lower NIR sensitivity of the ICCD camera remain the current bottleneck of the TRRS technique. Additionally, in its prototype state, this system is not yet practically commercially available or portable, as it requires advanced laser equipment and an optical table. With ongoing technological developments, a portable system can be developed with improved NIR sensitivity, which will open the door to field and other on-site applications.

To date, portable SORS and standoff time resolved (ns time scale) systems are already being tested in the field for the analysis of bulk chemicals inside unopened containers, for geological studies, and in a clinical setting as well. Handheld Raman spectrometers are also currently in production. The continuing development of this technology has potential applications for medical diagnostics, in the clinic and potentially in the field or in remote locations, as well as for geological and astrobiological studies.