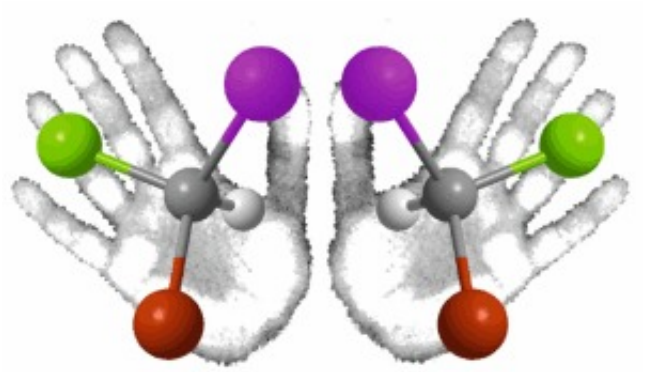
# Quantitative enantioselective Raman spectroscopy

A new approach for monitoring the production of chiral substances, e.g. pharmaceutically active ingredients, is proposed. Many biochemical and pharmaceutically active molecules are chiral. This means that two enantiomers exist exhibiting the same chemical structure without being identical. They are like mirror images, just like the left and right hand as indicated in Figure 1; hence, they are not superimposable. The two enantiomers of a chiral substance have identical physical properties, but their physiological effects may be very different. Thalidomide is probably the most prominent example. One enantiomer possesses the desired effect as a tranquilizer, while the other can cause birth defects in children.



The chemical synthesis of a chiral substance normally yields the racemate, which is a 50:50 mixture of both enantiomers. This mixture must then be processed in order to obtain the desired purified pharmaceutical agent. For an efficient production, the synthesis and processing must be monitored by suitable analytical methods. Existing technologies, however, have disadvantages such as being expensive and experimentally complicated, providing limited temporal resolution, or having the need for molecular labeling.

Raman spectroscopy is well established method for identification and quantification of molecular species. The Raman spectrum of a substance is a unique molecular fingerprint. Despite being a standard analytical tool, Raman spectroscopy has not been considered a suitable technique for monitoring the purification of enantiomers. The main reason was that conventional Raman spectroscopy of the different enantiomers yields identical signals. In other words, it does not provide the required enantioselective discrimination.

This paper presents an approach to overcome this problem by inserting a special optical component (a half-wave retarder) in the Raman signal produced inside a solution of chiral molecules. The method takes advantage of the optical activity of the solution and the half-wave retarder breaks the symmetry between the two enantiomers. An optically active solution rotates the polarization of the light as it propagates through the sample. One enantiomers causes a rotation clockwise and the other on counter-clockwise. As a consequence, both enantiomers exhibit slightly

different Raman spectra when the retarder is applied. A systematic investigation of the key experimental parameters is carried out in the paper. The results reveal that the new Raman technique is not only enantioselective but it is also capable of determining the enantiomer concentration and the enantiomer ratio. Hence, it represents an ideally suited tool for monitoring the production and processing of chiral substances, e.g. in the pharmaceutical industry. Further applications, for example, in the fields of biology and medicine, may be realized in the future.

## Publication

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*Analyst. 2015 Aug 7*