International Conference on Advanced Optical Technologies
University of Erlangen-Nürnberg, March 13th – 15th 2019

Enantioselective interactions: basis for differentiation between D- and L-enantiomers using Raman spectroscopy

Hanna Koch[1], **Stefan Will**[1]

[1]Lehrstuhl für Technische Thermodynamik (LTT), Friedrich-Alexander-Universität Erlangen-Nürnberg, Am Weichselgarten 8, D-91058 Erlangen and Erlangen Graduate School in Advanced Optical Technologies (SAOT), Paul-Gordan-Str. 6, D-91052 Erlangen
hanna.koch@fau.de

Enantiomers possess identical chemical formula but opposite configurations. As they are relevant in pharmacy and may exhibit also different bioactivities, it is of utmost importance to produce enantiopure drugs. One well-known example is thalidomide, where D-thalidomide acts as a sedative while L-thalidomide is teratogenic. To receive enantiopure drugs enantioseparation has to be performed. Based on the fact that enantiomers have the same physiochemical properties separation is quite demanding. Common enantioseparation techniques are chromatography, crystallization, enzymatic resolution, diastereomer separation, membrane processes or a combination of these techniques[1]. These methods allow the separation of D- and L-enantiomers. Optical measurement techniques enable the determination of the purity of the enantiomers. Optical rotary dispersion (ORD), circular dichroism (CD) and Raman optical activity (ROA)[2] are common used optical measurement techniques for the optical differentiation of enantiomers. Nevertheless, these methods exhibit long measurement periods, a low sensitivity or the analysis of only one enantiomer instead of several ones. Contrary to the common belief, Raman spectroscopy can also be used to optical separate D- and L-enantiomers. This works due to the enantioselective interactions which is shown in two recent studies.[3] Raman spectroscopy allows for fast measurements with a high sensitivity. Moreover, more than one enantiomer in a solution or as a solid can be investigated.
In this study we want to show that Raman spectroscopy offers the possibility to optical separate between enantiomers by principal component analysis (PCA). Besides, we reveal that also a determination of the mixing ratio of D- to L-enantiomer is possible by using the multivariate data analysis method partial least squares regression (PLSLR). The basis of the optical separation are enantioselective interactions between D-D-, L-L- and D-L-enantiomers. We also show that the addition of a chiral agent leads to the formation of enantioselective interactions between the enantiomer and the chiral agent which also allows an optical separation. As Raman spectroscopy can also be used for online- and inline-measurements, the results indicate that an online optical separation of enantiomers using this optical measurement technique could be possible.

References

[1] M. Kaspereit, S. Swernath and A. Kienle, *Org. Process Res. Dev.* **16**, 353-363 (2012).
[2] C. Johannessen, E. W. Blanch, C. Villani, S. Abbate, G. Longhi, N. R. Agarwal, M. Tommasini and D. A. Lightner, *J. Phys. Chem. B* **117**, 2221-2230 (2013).
[3] H. Koch, S. Polepil, K. Eisen and S. Will, *Phys. Chem. Chem. Phys.* **19**, 30533-30539 (2017).