Integrating Computational IR Spectroscopy and Principal Component Analysis for Monitoring Mechanoenzymatic Transformation of Glycolic Acid

Zrinka Pišonić, Jakov Borovec, Tomica Hrenar and Aleksandra Maršavelski

zpisonic@chem.pmf.hr

University of Zagreb, Faculty of Science, Department of Chemistry, Horvatovac 102a, Zagreb, Croatia

Poly(glycolic acid) (PGA) is a biodegradable and biocompatible polymer with growing importance in biomedical and environmentally sustainable applications [1]. Its synthetic pathway involves the esterification of glycolic acid to form linear oligomers, which then undergo cyclization to yield glycolide, a six-membered cyclic diester. Subsequently, glycolide is converted into PGA via ring-opening polymerization [2]. Traditional synthesis routes for glycolide and PGA typically require high temperatures, metal catalysts, and solvents. In contrast, mechanoenzymatic synthesis using *Candida antarctica* lipase B (CALB) under solvent-free conditions offers a greener and potentially more scalable alternative. However, real-time monitoring and product identification in such solid-state biocatalytic reactions remain challenging due to limited spectral resolution and overlapping vibrational features.

In this study, we combined attenuated total reflection infrared (ATR-FTIR) spectroscopy with density functional theory calculations and principal component analysis (PCA) to monitor and interpret the transformation of glycolic acid to glycolide under solvent-free conditions using CALB. Theoretical IR spectra of both glycolic acid and glycolide were computed at the B3LYP-D3BJ/6-311++g(d,p) level, showing good agreement with key experimental vibrational bands. PCA was applied to experimental IR data collected across different reaction time points, enabling clear separation of reactant and product phases and aiding in spectral assignment. This approach demonstrates how computational tools coupled with multivariate analysis can significantly improve the interpretation of complex spectral data and provide product identification in complex reaction mixtures.

References:

[1] D. J. A. Cameron, M. P. Shaver, *Chem. Soc. Rev.* **40** (2011) 1761-1776.

[2] S. W. Duchiron, E. Pollet, S. Givry, L. Avérous, *RSC Adv*. **5** (2015) 84627-84635.