Biodegradation of Water-Soluble Polymers – Reviewing In-Silico Methods (Interim state)

D. Skodras[1], M. Hüben[1], J. Klein[1]

[1] Fraunhofer Institute for Molecular Biology and Applied Ecology IME, Schmallenberg, Germany

Fraunhofer IME

QSAR/Read-Across

- Derive substance properties based on regression or similarity
- Use descriptors/similarity indices to characterize substances
- Fit models (MLR, RF, SVM, kNN, ANN) to consistent datasets
- Examples: BIOWIN[1], VEGA[2]

Motivation:

- Water soluble polymers are exempt from REACH.
- If they become subject, assessing biodegradability is obliged
- In-silico are cost-effective methods used for risk assessment
- Hence, the current landscape of models is examined

Pathway Prediction System

- Predict pathways based on rules mapping functional groups onto products
- Assign likelihood to rules based on expert knowledge or probability calculations
- Discriminate reactions and apply recursively to final degradation products
- Examples: CATABOL[3], enviPath[4], BESS[5]

Predicting Biodegradability of Polymers

Data, Descriptors

- Crucial for reliable predictions but sufficiently large and consistent set of water soluble polymer degradation data is lacking
- Polymers need to be characterized and discriminatory descriptors identified also encompassing macroscopic properties

Pathways, Rules

- To establish pathways, rules for polymer degradation need to be identified and probabilities assigned.
- Due to their variability and macroscopic properties, rules need to include patterns beyond functional groups

Connection, Complexity

- While the degradation process may be modelled at this level a derivation of biodegradability is not established
- Modelling specific polymers in itself is a non-trivial task. Including their stochastic nature increases the complexity considerably

Molecular Modelling

- Model substances explicitly on the atomic/molecular level
- Compute energy minima, normal modes, binding-sites for enzymes, interaction strength
- Examples: GROMACS[6], AUTODOCK[7], CHARMM[8]

Outlook:

- Adaptations of the approaches are needed to predict biodegradability of polymers
- PPS might be most promising
- Establish degradation rules and assign interdependent likelihoods
- Determine set of descriptors suited or polymer characterization

Dimitrios Skodras

Modelling & Bioinformatics
Tel. +49 2972 302-282
dimitrios.Skodras@ime.fraunhofer.de

[1] Howard P H, Stiteler W M, Meylan W M, Hueber A E, Beauman J A, Larosche M Eand Boethling R S 1992 *Environmental toxicology and chemistry* **11** 593
[2] Benfenati E, Roncaglioni A, Lombardo Aand Manganaro A 2019 *Advances in Computational Toxicology* vol 30 ed H Hong (Cham: Springer International Publishing) pp 365–81.
[3] Jaworska J, Dimitrov S, Nikolova Nand Mekenyan O 2002 *SAR and QSAR in environmental research* 307.
[4] Wicker J, Lorsbach T, Gütlein M, Schmid E, Latino D, Kramer Sand Fenner K 2016 *Nucleic acids research* **44** D502-8.
[5] Punch B, Patton A, Wight K, Larson B, Masscheleyn Pand Forney L 1996 *Biodegradability Prediction* eds W J G M Peijnenburg and J Damborský (Dordrecht: Springer Netherlands) pp 65–73.
[6] Berendsen H, van der Spoel Dand van Drunen R 1995 *Computer Physics Communications* **91** 43.
[7] Morris G M, Huey R, Lindstrom W, Sanner M F, Belew R K, Goodsell D Sand Olson A J 2009 *Journal of computational chemistry* **30** 2785.
[8] Brooks B R, Bruccoleri R E, Olafson B D, States D J, Swaminathan Sand Karplus M 1983 *Journal of computational chemistry* **4** 187.

ICCS INTERNATIONAL COLLABORATION ON COSMETICS SAFETY

This research work was funded by ICCS