# AIMMS publication report for: 2021-02-22

1. Past, present, and future developments in enantioselective a (2021-1)
2. The CXCL12/CXCR4/ACKR3 Axis in the Tumor Microenvironment: S (2021-1)
3. Neurotoxicity and underlying cellular changes of 21 mitochon (2021-2)
4. Bioactivation of trichloroethylene to three regioisomeric gl (2021-2)
5. *A schematic sampling protocol for contaminant monitoring in (2021-1)*
6. *Receptor-based in vitro activities to assess human exposure (2021-1)*
7. *Asymmetrical flow field-flow fractionation to probe the dyna (2021-1)*
8. *Rapid Screening α-Glucosidase Inhibitors from Natural Produc (2021-1)*
9. *Reducing the influence of geometry-induced gradient deformat (2021-1)*
10. *Influence maximization in the presence of vulnerable nodes: (2021-1)*
11. *Dynamic co-culture metabolic models reveal the fermentation (2021-1)*
12. *Influence of short- And long-term exposure on the biodegrada (2021-1)*
13. *Critique of the “Comment” etitled “Pyrethroid exposure: Not (2021-1)*
14. *Serial propagation in water-in-oil emulsions selects for Sac (2021-1)*
15. *KLIFS: an overhaul after the first 5 years of supporting kin (2021-1)*
16. *Unlocking Elementary Conversion Modes: ecmtool Unveils All C (2021-1)*
17. *Hazardous compounds in recreational and urban recycled surfa (2021-2)*
18. *Circular pattern matching with k mismatches (2021-2)*
19. *G protein-coupled receptors as promising targets in cancer (2021-2)*
20. *Metabolic cooperation and spatiotemporal niche partitioning (2021-2)*

### 1) Past, present, and future developments in enantioselective analysis using capillary electromigration techniques

* de Koster, N., Clark, C. P., Kohler, I.
* BioAnalytical Chemistry, AIMMS, Leiden University
* Electrophoresis
* https://doi.org/10.1002/elps.202000151
* Corresponding author: Kohler, I.
* Published Jan 2021 (early online 11 Sep 2020)
* Processed: 2021-1

Enantioseparation of chiral products has become increasingly important in a large diversity of academic and industrial applications. The separation of chiral compounds is inherently challenging and thus requires a suitable analytical technique that can achieve high resolution and sensitivity. In this context, CE has shown remarkable results so far. Chiral CE offers an orthogonal enantioselectivity and is typically considered less costly than chromatographic techniques, since only minute amounts of chiral selectors are needed. Several CE approaches have been developed for chiral analysis, including chiral EKC and chiral CEC. Enantioseparations by EKC benefit from the wide variety of possible pseudostationary phases that can be employed. Chiral CEC, on the other hand, combines chromatographic separation principles with the bulk fluid movement of CE, benefitting from reduced band broadening as compared to pressure-driven systems. Although UV detection is conventionally used for these approaches, MS can also be considered. CE-MS represents a promising alternative due to the increased sensitivity and selectivity, enabling the chiral analysis of complex samples. The potential contamination of the MS ion source in EKC-MS can be overcome using partial-filling and counter-migration techniques. However, chiral analysis using monolithic and open-tubular CEC-MS awaits additional method validation and a dedicated commercial interface. Further efforts in chiral CE are expected toward the improvement of existing techniques, the development of novel pseudostationary phases, and establishing the use of chiral ionic liquids, molecular imprinted polymers, and metal-organic frameworks. These developments will certainly foster the adoption of CE(-MS) as a well-established technique in routine chiral analysis.

### 2) The CXCL12/CXCR4/ACKR3 Axis in the Tumor Microenvironment: Signaling, Crosstalk, and Therapeutic Targeting

* Smit, M. J., Schlecht-Louf, G., Neves, M., Van Den Bor, J., Penela, P., Siderius, M., Bachelerie, F., Mayor, F.
* Medicinal chemistry, AIMMS, ComUE Paris-Saclay, Universidad Autónoma de Madrid, University of Valencia, Instituto de Salud Carlos III
* Annual Review of Pharmacology and Toxicology
* https://doi.org/10.1146/annurev-pharmtox-010919-023340
* Corresponding author: Smit, M. J.
* Published 6 Jan 2021 (early online 21 Sep 2020)
* Processed: 2021-1

Elevated expression of the chemokine receptors CXCR4 and ACKR3 and of their cognate ligand CXCL12 is detected in a wide range of tumors and the tumor microenvironment (TME). Yet, the molecular mechanisms by which the CXCL12/CXCR4/ACKR3 axis contributes to the pathogenesis are complex and not fully understood. To dissect the role of this axis in cancer, we discuss its ability to impinge on canonical and less conventional signaling networks in different cancer cell types; its bidirectional crosstalk, notably with receptor tyrosine kinase (RTK) and other factors present in the TME; and the infiltration of immune cells that supporttumor progression. We discuss current and emerging avenues that target the CXCL12/CXCR4/ACKR3 axis. Coordinately targeting both RTKs and CXCR4/ACKR3 and/or CXCL12 is an attractive approach to consider in multitargeted cancer therapies. In addition, inhibiting infiltrating immune cells or reactivating the immune system along with modulating the CXCL12/CXCR4/ACKR3 axis in the TME has therapeutic promise.

### 3) Neurotoxicity and underlying cellular changes of 21 mitochondrial respiratory chain inhibitors

* Delp, J., Cediel-Ulloa, A., Suciu, I., Kranaster, P., van Vugt-Lussenburg, B. M., Munic Kos, V., van der Stel, W., Carta, G., Bennekou, S. H., Jennings, P., van de Water, B., Forsby, A., Leist, M.
* Molecular and Computational Toxicology, AIMMS, University of Konstanz, Karolinska Institutet, Uppsala University, BioDetection Systems B.V., Leiden University, Technical University of Denmark, Stockholm University
* Archives of Toxicology
* https://doi.org/10.1007/s00204-020-02970-5
* Corresponding author: Leist, M.
* Published Feb 2021 (early online 29 Jan 2021)
* Processed: 2021-2

Inhibition of complex I of the mitochondrial respiratory chain (cI) by rotenone and methyl-phenylpyridinium (MPP +) leads to the degeneration of dopaminergic neurons in man and rodents. To formally describe this mechanism of toxicity, an adverse outcome pathway (AOP:3) has been developed that implies that any inhibitor of cI, or possibly of other parts of the respiratory chain, would have the potential to trigger parkinsonian motor deficits. We used here 21 pesticides, all of which are described in the literature as mitochondrial inhibitors, to study the general applicability of AOP:3 or of in vitro assays that are assessing its activation. Five cI, three complex II (cII), and five complex III (cIII) inhibitors were characterized in detail in human dopaminergic neuronal cell cultures. The NeuriTox assay, examining neurite damage in LUHMES cells, was used as in vitro proxy of the adverse outcome (AO), i.e., of dopaminergic neurodegeneration. This test provided data on whether test compounds were unspecific cytotoxicants or specifically neurotoxic, and it yielded potency data with respect to neurite degeneration. The pesticide panel was also examined in assays for the sequential key events (KE) leading to the AO, i.e., mitochondrial respiratory chain inhibition, mitochondrial dysfunction, and disturbed proteostasis. Data from KE assays were compared to the NeuriTox data (AO). The cII-inhibitory pesticides tested here did not appear to trigger the AOP:3 at all. Some of the cI/cIII inhibitors showed a consistent AOP activation response in all assays, while others did not. In general, there was a clear hierarchy of assay sensitivity: changes of gene expression (biomarker of neuronal stress) correlated well with NeuriTox data; mitochondrial failure (measured both by a mitochondrial membrane potential-sensitive dye and a respirometric assay) was about 10-260 times more sensitive than neurite damage (AO); cI/cIII activity was sometimes affected at > 1000 times lower concentrations than the neurites. These data suggest that the use of AOP:3 for hazard assessment has a number of caveats: (i) specific parkinsonian neurodegeneration cannot be easily predicted from assays of mitochondrial dysfunction; (ii) deriving a point-of-departure for risk assessment from early KE assays may overestimate toxicant potency.

### 4) Bioactivation of trichloroethylene to three regioisomeric glutathione conjugates by liver fractions and recombinant human glutathione transferases: species differences and implications for human risk assessment

* Capinha, L., Jennings, P., Commandeur, J. N.
* Molecular and Computational Toxicology, AIMMS
* Toxicology Letters
* https://doi.org/10.1016/j.toxlet.2021.01.021
* Corresponding author: None
* Published 1 Feb 2021 (early online None)
* Processed: 2021-2

Enzymatic conjugation of glutathione (GSH) to trichloroethylene (TCE) followed by catabolism to the corresponding cysteine-conjugate, S-(dichlorovinyl)-L-cysteine (DCVC), and subsequent bioactivation by renal cysteine conjugate beta-lyases is considered to play an important role in the nephrotoxic effects observed in TCE-exposed rat and human. In this study, it is shown for the first time that three regioisomers of GSH-conjugates of TCE are formed by rat and human liver fractions, namely S-(1,2-trans-dichlorovinyl)-glutathione (1,2-trans-DCVG), S-(1,2-cis-dichlorovinyl)-glutathione (1,2-cis-DCVG) and S-2,2-dichlorovinyl-glutathione (2,2-DCVG). In incubations of TCE with rat liver fractions their amounts decreased in order of 1,2-cis-DCVG > 1,2-trans-DCVG > 2,2-DCVG. Human liver cytosol showed a more than 10-fold lower activity of GSH-conjugation, with amounts of regioisomers decreasing in order 2,2-DCVG > 1,2-trans-DCVG > 1,2-cis-DCVG. Incubations with recombinant human GSTs suggest that GSTA1-1 and GSTA2-2 play the most important role in human liver cytosol. GSTP1-1, which produces regioisomers in order 1,2-trans-DCVG > 2,2-cis-DCVG > 1,2-cis-DCVG, is likely to contribute to extrahepatic GSH-conjugation of TCE. Analysis of the products formed by a beta-lyase mimetic model showed that both 1,2-trans-DCVC and 1,2-cis-DCVC are converted to reactive products that form cross-links between the model nucleophile 4-(4-nitrobenzyl)-pyridine (NBP) and thiol-species. No NBP-alkylation was observed with 2,2-DCVC corresponding to its low cytotoxicity and mutagenicity. The lower activity of GSH-conjugation of TCE by human liver fractions, in combination with the lower fraction of potential nephrotoxic and mutagenic 1,2-DCVG-isomers, suggest that humans are at much lower risk for TCE-associated nephrotoxic effects than rats.

### *5) A schematic sampling protocol for contaminant monitoring in raptors*

* Espín, S., Andevski, J., Duke, G., Eulaers, I., Gómez-Ramírez, P., Hallgrimsson, G. T., Helander, B., Herzke, D., Jaspers, V. L., Krone, O., Lourenço, R., María-Mojica, P., Martínez-López, E., Mateo, R., Movalli, P., Sánchez-Virosta, P., Shore, R. F., Sonne, C., van den Brink, N. W., van Hattum, B., Vrezec, A., Wernham, C., García-Fernández, A. J.
* AIMMS, Environment and Health, University of Murcia, Vulture Conservation Foundation, Oxford University Centre for the Environment, Aarhus University, University of Iceland, Swedish Museum of Natural History, Norwegian Institute for Air Research, Norwegian University of Science and Technology, Leibniz Institute for Zoo and Wildlife Research, University of Evora, Santa Faz” Wildlife Rehabilitation Centre, CSIC, Naturalis National Museum of Natural History, Lancaster University, Wageningen University & Research, National Institute of Biology Ljubljana, Slovenian Museum of Natural History, University of Stirling
* Ambio
* https://doi.org/10.1007/s13280-020-01341-9
* Corresponding author: Espín, S.
* Published Jan 2021 (early online 12 May 2020)
* Processed: 2021-1

Birds of prey, owls and falcons are widely used as sentinel species in raptor biomonitoring programmes. A major current challenge is to facilitate large-scale biomonitoring by coordinating contaminant ...

### *6) Receptor-based in vitro activities to assess human exposure to chemical mixtures and related health impacts*

* Vinggaard, A. M., Bonefeld-Jørgensen, E. C., Jensen, T. K., Fernandez, M. F., Rosenmai, A. K., Taxvig, C., Rodriguez-Carrillo, A., Wielsøe, M., Long, M., Olea, N., Antignac, J. P., Hamers, T., Lamoree, M.
* E&H: Environmental Health and Toxicology, AIMMS, E&H: Environmental Chemistry and Toxicology, Technical University of Denmark, Aarhus University, University of Greenland, University of Southern Denmark, University of Granada, Consortium for Biomedical Research in Epidemiology & Public Health (CIBERESP), École nationale vétérinaire, agroalimentaire et de l'alimentation, Nantes-Atlantique
* Environment International
* https://doi.org/10.1016/j.envint.2020.106191
* Corresponding author: Vinggaard, A. M.
* Published Jan 2021 (early online 14 Oct 2020)
* Processed: 2021-1

Humans are exposed to a large number of chemicals from sources such as the environment, food, and consumer products. There is growing concern that human exposure to chemical mixtures, especially durin ...

### *7) Asymmetrical flow field-flow fractionation to probe the dynamic association equilibria of β-D-galactosidase*

* Ventouri, I. K., Astefanei, A., Kaal, E. R., Haselberg, R., Somsen, G. W., Schoenmakers, P. J.
* BioAnalytical Chemistry, AIMMS, University of Amsterdam, Center for Analytical Sciences Amsterdam, DSM Food Specialties
* Journal of Chromatography A
* https://doi.org/10.1016/j.chroma.2020.461719
* Corresponding author: Ventouri, I. K.
* Published 4 Jan 2021 (early online 13 Nov 2020)
* Processed: 2021-1

Protein dynamics play a significant role in many aspects of enzyme activity. Monitoring of structural changes and aggregation of biotechnological enzymes under native conditions is important to safegu ...

### *8) Rapid Screening α-Glucosidase Inhibitors from Natural Products by At-Line Nanofractionation with Parallel Mass Spectrometry and Bioactivity Assessment*

* Liu, R., Kool, J., Jian, J., Wang, J., Zhao, X., Jiang, Z., Zhang, T.
* BioAnalytical Chemistry, AIMMS, Jinan University, SCIEX (China) Co., Ltd.
* Journal of Chromatography A
* https://doi.org/10.1016/j.chroma.2020.461740
* Corresponding author: Jiang, Z.
* Published 4 Jan 2021 (early online 23 Nov 2020)
* Processed: 2021-1

In this study, a novel at-line nanofractionation screening platform was successfully developed for the rapid screening and identification of α-glucosidase inhibitors from natural products. A time-cour ...

### *9) Reducing the influence of geometry-induced gradient deformation in liquid chromatographic retention modelling*

* Bos, T. S., Niezen, L. E., den Uijl, M. J., Molenaar, S. R., Lege, S., Schoenmakers, P. J., Somsen, G. W., Pirok, B. W.
* BioAnalytical Chemistry, AIMMS, University of Amsterdam, Centre for Analytical Sciences Amsterdam (CASA), Agilent Technologies
* Journal of Chromatography A
* https://doi.org/10.1016/j.chroma.2020.461714
* Corresponding author: Bos, T. S.
* Published 4 Jan 2021 (early online 13 Nov 2020)
* Processed: 2021-1

Rapid optimization of gradient liquid chromatographic (LC) separations often utilizes analyte retention modelling to predict retention times as function of eluent composition. However, due to the dwel ...

### *10) Influence maximization in the presence of vulnerable nodes: A ratio perspective*

* Chen, H., Loukides, G., Pissis, S. P., Chan, H.
* Bioinformatics, AIMMS, Bio Informatics (IBIVU), King's College London, University of Nebraska-Lincoln
* Theoretical Computer Science
* https://doi.org/10.1016/j.tcs.2020.11.020
* Corresponding author: Loukides, G.
* Published 8 Jan 2021 (early online 20 Nov 2020)
* Processed: 2021-1

Influence maximization is a key problem seeking to identify users who will diffuse information to influence the largest number of other users in a social network. A drawback of the influence maximizat ...

### *11) Dynamic co-culture metabolic models reveal the fermentation dynamics, metabolic capacities and interplays of cheese starter cultures*

* Özcan, E., Seven, M., Şirin, B., Çakır, T., Nikerel, E., Teusink, B., Toksoy Öner, E.
* Systems Bioinformatics, AIMMS, Systems Bioinformatics, Vrije Universiteit Amsterdam, Marmara University, Yeditepe University, Gebze Technical University
* Biotechnology and Bioengineering
* https://doi.org/10.1002/bit.27565
* Corresponding author: Teusink, B.
* Published Jan 2021 (early online 14 Sep 2020)
* Processed: 2021-1

In this study, we have investigated the cheese starter culture as a microbial community through a question: can the metabolic behaviour of a co-culture be explained by the characterized individual org ...

### *12) Influence of short- And long-term exposure on the biodegradation capacity of activated sludge microbial communities in ready biodegradability tests*

* Dalmijn, J. A., Poursat, B. A., Van Spanning, R. J., Brandt, B. W., De Voogt, P., Parsons, J. R.
* Systems Bioinformatics, AIMMS, Bioinformatics, University of Amsterdam, Wageningen University & Research, KWR Water Research Institute
* Environmental Science: Water Research and Technology
* https://doi.org/10.1039/d0ew00776e
* Corresponding author: Poursat, B. A.
* Published Jan 2021 (early online None)
* Processed: 2021-1

Ready biodegradability tests (RBTs) are extensively used to screen the potential of chemicals to be biodegraded. The use of RBT protocols often results in large variations of test results that may lea ...

### *13) Critique of the “Comment” etitled “Pyrethroid exposure: Not so harmless after all” by Demeneix et al. (2020) published in the lancet diabetes endocrinology*

* Barile, F. A., Berry, S. C., Blaauboer, B., Boobis, A., Bolt, H., Borgert, C. J., Dekant, W., Dietrich, D., Domingo, J. L., Gori, G. B., Greim, H., Hengstler, J., Kacew, S., Marquardt, H., Pelkonen, O., Savolainen, K., Heslop-Harrison, P., Tsatsakis, A., Vermeulen, N. P.
* Chemistry and Pharmaceutical Sciences, AIMMS, St. John's University, Queen Mary University of London, Utrecht University, Imperial College London, Dortmund University, Applied Pharmacology and Toxicology, Inc. Gainesville, University of Würzburg, University of Konstanz, Pere Virgili Health Research Institute, The Health Policy Center, Technical University of Munich, University of Ottawa, Toxicology, University of Oulu, Finnish Institute of Occupational Health, University of Leicester, University of Crete
* Toxicology Letters
* https://doi.org/10.1016/j.toxlet.2020.12.020
* Corresponding author: Greim, H.
* Published 1 Apr 2021 (early online 4 Jan 2021)
* Processed: 2021-1

...

### *14) Serial propagation in water-in-oil emulsions selects for Saccharomyces cerevisiae strains with a reduced cell size or an increased biomass yield on glucose*

* van Tatenhove-Pel, R. J., Zwering, E., Boreel, D. F., Falk, M., van Heerden, J. H., Kes, M. B., Kranenburg, C. I., Botman, D., Teusink, B., Bachmann, H.
* AIMMS, Systems Bioinformatics, Systems Bioinformatics, Vrije Universiteit Amsterdam
* Metabolic Engineering
* https://doi.org/10.1016/j.ymben.2020.12.005
* Corresponding author: Bachmann, H.
* Published Mar 2021 (early online 5 Jan 2021)
* Processed: 2021-1

In S. cerevisiae and many other micro-organisms an increase in metabolic efficiency (i.e. ATP yield on carbon) is accompanied by a decrease in growth rate. From a fundamental point of view, studying t ...

### *15) KLIFS: an overhaul after the first 5 years of supporting kinase research*

* Kanev, G. K., de Graaf, C., Westerman, B. A., de Esch, I. J., Kooistra, A. J.
* Chemistry and Pharmaceutical Sciences, AIMMS, Vrije Universiteit Amsterdam, Amsterdam, Department of Neurosurgery, Amsterdam University Medical Centers, Sosei Heptares, University of Copenhagen
* Nucleic acids research
* https://doi.org/10.1093/nar/gkaa895
* Corresponding author: None
* Published 8 Jan 2021 (early online None)
* Processed: 2021-1

Kinases are a prime target of drug development efforts with >60 drug approvals in the past two decades. Due to the research into this protein family, a wealth of data has been accumulated that keeps o ...

### *16) Unlocking Elementary Conversion Modes: ecmtool Unveils All Capabilities of Metabolic Networks*

* Clement, T. J., Baalhuis, E. B., Teusink, B., Bruggeman, F. J., Planqué, R., de Groot, D. H.
* Systems Bioinformatics, AIMMS, Systems Bioinformatics, Mathematics, Vrije Universiteit Amsterdam
* Patterns
* https://doi.org/10.1016/j.patter.2020.100177
* Corresponding author: Clement, T. J.
* Published 8 Jan 2021 (early online None)
* Processed: 2021-1

The metabolic capabilities of cells determine their biotechnological potential, fitness in ecosystems, pathogenic threat levels, and function in multicellular organisms. Their comprehensive experiment ...

### *17) Hazardous compounds in recreational and urban recycled surfaces made from crumb rubber. Compliance with current regulation and future perspectives*

* Celeiro, M., Armada, D., Dagnac, T., de Boer, J., Llompart, M.
* Environment and Health, AIMMS, University of Santiago de Compostela, Agronomic Research Centre (AGACAL-CIAM) – Unit of Organic Contaminants
* Science of the Total Environment
* https://doi.org/10.1016/j.scitotenv.2020.142566
* Corresponding author: Llompart, M.
* Published 10 Feb 2021 (early online 29 Sep 2020)
* Processed: 2021-2

Crumb rubber obtained from scrap tires is greatly employed for the construction of different facilities for sport, recreational and other uses. However, in recent years the concern about their safety ...

### *18) Circular pattern matching with k mismatches*

* Charalampopoulos, P., Kociumaka, T., Pissis, S. P., Radoszewski, J., Rytter, W., Straszyński, J., Waleń, T., Zuba, W.
* Bioinformatics, AIMMS, Bio Informatics (IBIVU), King's College London, University of Warsaw, Bar-Ilan University
* Journal of Computer and System Sciences
* https://doi.org/10.1016/j.jcss.2020.07.003
* Corresponding author: Pissis, S. P.
* Published Feb 2021 (early online 29 Jul 2020)
* Processed: 2021-2

We consider the circular pattern matching with k mismatches (k-CPM) problem in which one is to compute the minimal Hamming distance of every length-m substring of T and any cyclic rotation of P, if th ...

### *19) G protein-coupled receptors as promising targets in cancer*

* Perez Almeria, C. V., Setiawan, I. M., Siderius, M., Smit, M. J.
* AIMMS, Medicinal chemistry
* Current Opinion in Endocrine and Metabolic Research
* https://doi.org/10.1016/j.coemr.2020.10.005
* Corresponding author: Smit, M. J.
* Published Feb 2021 (early online 26 Oct 2020)
* Processed: 2021-2

G protein-coupled receptors (GPCRs) control diverse cellular functions, and their dysregulation is involved in a plethora of diseases including tumorigenesis. In the last decade, the association of GP ...

### *20) Metabolic cooperation and spatiotemporal niche partitioning in a kefir microbial community*

* Blasche, S., Kim, Y., Mars, R. A., Machado, D., Maansson, M., Kafkia, E., Milanese, A., Zeller, G., Teusink, B., Nielsen, J., Benes, V., Neves, R., Sauer, U., Patil, K. R.
* Systems Bioinformatics, AIMMS, Systems Bioinformatics, European Molecular Biology Laboratory, Swiss Federal Institute of Technology Zurich, Chr. Hansen AS, University of Cambridge, Chalmers University of Technology
* NATURE MICROBIOLOGY
* https://doi.org/10.1038/s41564-020-00816-5
* Corresponding author: Patil, K. R.
* Published Feb 2021 (early online None)
* Processed: 2021-2

Microbial communities often undergo intricate compositional changes yet also maintain stable coexistence of diverse species. The mechanisms underlying long-term coexistence remain unclear as system-wi ...