# AIMMS publication report for: 2020-10-12

1. Scientific Perspectivism in Secondary-School Chemistry Educa (2020-8)
2. Performance of TDDFT Vertical Excitation Energies of Core-Su (2020-6)
3. Living with breakthrough: Two-dimensional liquid-chromatogra (2020-9)
4. Effect of Alkali Metal Cations on Length and Strength of Hyd (2020-9)
5. Kinetic analysis of the early signaling steps of the human c (2020-8)
6. Scientific Perspectivism in Secondary-School Chemistry Educa (2020-10)
7. Neurobehavioral effects of cyanobacterial biomass field extr (2020-9)
8. The atypical chemokine receptor 3 interacts with Connexin 43 (2020-9)
9. *N-Heterocyclic Silylenes as Ligands in Transition Metal Carb (2020-9)*
10. *Understanding the 1,3-Dipolar Cycloadditions of Allenes (2020-9)*
11. *Environmental Effects with Frozen-Density Embedding in Real- (2020-9)*
12. *Light-Matter Hybrid-Orbital-Based First-Principles Methods: (2020-9)*
13. *Neutralizing effects of small molecule inhibitors and metal (2020-9)*

### 1) Scientific Perspectivism in Secondary-School Chemistry Education: Integrating Concepts and Skills in Chemical Thinking

* Landa, I., Westbroek, H., Janssen, F., van Muijlwijk-Koezen, J. E., Meeter, M.
* LEARN! - Learning sciences, Team Secondary Education, Innovations in Human Health & Life Sciences, AIMMS, Educational and Family Studies, ICLON, Leiden University
* Science & Education
* https://doi.org/https://doi.org/10.1007/s11191-020-00145-3
* Corresponding author: Westbroek, H.
* Published 7 Aug 2020 (early online None)
* Processed: 2020-8

The importance of learning chemical ways of thinking is widely recognized. Various frameworks have been developed to address the essence of chemistry and chemical thinking. However, very few studies have focused on how chemical ways of thinking can be defined. To elaborate chemical ways of thinking, this paper draws on scientific perspectivism (Giere 2010; Wimsatt 2007; Thagard 2012). Scientific perspectivism states that, within each general domain, several broadly accepted theoretical models exist side by side. These general theoretical models, or theoretical perspectives, determine which research questions are generated, which types of models are developed, and which criteria are important for evaluating models. A theoretical perspective can be captured in a core reasoning that embodies the fundamental relationship between model and the “real world.” Starting with their most basic form, perspectives can be used in learning how to reason about all types of ill-structured problems, directing and organizing knowledge development, and integrating knowledge and skills. The study is part of a research project on how perspectivism can be applied to the design of secondary-school chemistry education. This particular study concerns the identification, elaboration, and validation of four chemical perspectives for secondary-school chemistry education. We use these perspectives to indicate the consequences of taking a perspectivism approach to a curriculum framework. We conclude with discussing the consequences for secondary chemistry curriculum.

### 2) Performance of TDDFT Vertical Excitation Energies of Core-Substituted Naphthalene Diimides

* Narsaria, A. K., Ruijter, J. D., Hamlin, T. A., Ehlers, A. W., Guerra, C. F., Lammertsma, K., Bickelhaupt, F. M.
* Theoretical Chemistry, AIMMS, Chemistry and Pharmaceutical Sciences, VU University
* Journal of Computational Chemistry
* https://doi.org/10.1002/jcc.26188
* Corresponding author: Lammertsma, K.
* Published 5 Jun 2020 (early online 6 Mar 2020)
* Processed: 2020-6

We have evaluated the performance of various density functionals, covering generalized gradient approximation (GGA), global hybrid (GH) and range-separated hybrid (RSH), using time dependent density functional theory (TDDFT) for computing vertical excitation energies against experimental absorption maximum (λmax) for a set of 10 different core-substituted naphthalene diimides (cNDI) recorded in dichloromethane. The computed excitation in case of GH PBE0 is most accurate while the trend is most systematic with RSH LCY-BLYP compared to λmax. We highlight the importance of including solvent effects for optimal agreement with the λmax. Increasing the basis set size from TZ2P to QZ4P has a negligible influence on the computed excitation energies. Notably, RSH CAMY-B3LYP gave the least error for charge-transfer excitation. The poorest agreement with λmax is obtained with semi-local GGA functionals. Use of the optimally-tuned RSH LCY-BLYP\* is not recommended because of the high computational cost and marginal improvement in results.

### 3) Living with breakthrough: Two-dimensional liquid-chromatography separations of a water-soluble synthetically grafted bio-polymer

* van de Ven, H. C., Purmova, J., Groeneveld, G., Bos, T. S., Gargano, A. F., van der Wal, S., Mengerink, Y., Schoenmakers, P. J.
* BioAnalytical Chemistry, AIMMS, Nouryon Chemicals, University of Amsterdam, DSM Food Specialties
* Separations
* https://doi.org/10.3390/separations7030041
* Corresponding author: van de Ven, H. C.
* Published Sep 2020 (early online 15 Jul 2020)
* Processed: 2020-9

In this study, we evaluate the use of various two-dimensional liquid chromatographic methods to characterize water-soluble, synthetically grafted bio-polymers, consisting of long poly(acrylic acid) chains and short maltodextrin grafts. The confirmation of the presence of grafting and the estimation of its extent is challenging. It is complicated by the limited solubility of polymers, their structural dispersity and chemical heterogeneity. Moreover, the starting materials (and other reagents, reaction products and additives) may be present in the product. Reversed-phase liquid chromatography (RPLC), hydrophilic-interaction liquid chromatography (HILIC) and size-exclusion chromatography (SEC) were used to characterize the product, as well as the starting materials. Additionally, fractions were collected for off-line characterization by infrared spectroscopy and mass spectrometry. The one-dimensional separation methods were found to be inconclusive regarding the grafting question. Breakthrough (the early elution of polymer fractions due to strong injection solvents) is shown to be a perpetual problem. This issue is not solved by comprehensive two-dimensional liquid chromatography (LC × LC), but information demonstrating the success of the grafting reaction could be obtained. SEC × RPLC and HILIC × RPLC separations are presented and discussed.

### 4) Effect of Alkali Metal Cations on Length and Strength of Hydrogen Bonds in DNA Base Pairs

* Stasyuk, O. A., Solà, M., Swart, M., Fonseca Guerra, C., Krygowski, T. M., Szatylowicz, H.
* AIMMS, Theoretical Chemistry, University of Girona, ICREA, University of Warsaw, Warsaw University of Technology
* ChemPhysChem
* https://doi.org/10.1002/cphc.202000434
* Corresponding author: Stasyuk, O. A.
* Published 15 Sep 2020 (early online 9 Jul 2020)
* Processed: 2020-9

For many years, non-covalently bonded complexes of nucleobases have attracted considerable interest. However, there is a lack of information about the nature of hydrogen bonding between nucleobases when the bonding is affected by metal coordination to one of the nucleobases, and how the individual hydrogen bonds and aromaticity of nucleobases respond to the presence of the metal cation. Here we report a DFT computational study of nucleobase pairs interacting with alkali metal cations. The metal cations contribute to the stabilization of the base pairs to varying degrees depending on their position. The energy decomposition analysis revealed that the nature of bonding between nucleobases does not change much upon metal coordination. The effect of the cations on individual hydrogen bonds were described by changes in VDD charges on frontier atoms, H-bond length, bond energy from NBO analysis, and the delocalization index from QTAIM calculations. The aromaticity changes were determined by a HOMA index.

### 5) Kinetic analysis of the early signaling steps of the human chemokine receptor CXCR4G protein–coupled receptors (GPCRs) are biologic switches that transduce extracellular stimuli into intracellular responses in the cell. Temporally resolving GPCR transduction pathways is key to understanding how cell signaling occurs. Here, we investigate the kinetics and dynamics of the activation and early signaling steps of the CXC chemokine receptor (CXCR) 4 in response to its natural ligands CXC chemokine ligand (CXCL) 12 and macrophage migration inhibitory factor (MIF), using Förster resonance energy transfer–based approaches. We show that CXCR4 presents a multifaceted response to CXCL12, with receptor activation (=0.6 seconds) followed by a rearrangement in the receptor/G protein complex (=1 seconds), a slower dimer rearrangement (=1.7 seconds), and prolonged G protein activation (=4 seconds). In comparison, MIF distinctly modulates every step of the transduction pathway, indicating distinct activation mechanisms and reflecting the different pharmacological properties of these two ligands. Our study also indicates that CXCR4 exhibits some degree of ligand-independent activity, a relevant feature for drug development.General information

* Perpiñá-Viciano, C., Işbilir, A., Zarca, A., Caspar, B., Kilpatrick, L. E., Hill, S. J., Smit, M. J., Lohse, M. J., Hoffmann, C.
* Medicinal chemistry, AIMMS, Friedrich Schiller University Jena, University of Würzburg, Max Delbrück Center for Molecular Medicine in the Helmholtz Association, University of Nottingham, University of Birmingham
* Molecular Pharmacology
* https://doi.org/10.1124/MOL.119.118448
* Corresponding author: Hoffmann, C.
* Published 1 Aug 2020 (early online None)
* Processed: 2020-8

Kinetic analysis of the early signaling steps of the human chemokine receptor CXCR4G protein–coupled receptors (GPCRs) are biologic switches that transduce extracellular stimuli into intracellular responses in the cell. Temporally resolving GPCR transduction pathways is key to understanding how cell signaling occurs. Here, we investigate the kinetics and dynamics of the activation and early signaling steps of the CXC chemokine receptor (CXCR) 4 in response to its natural ligands CXC chemokine ligand (CXCL) 12 and macrophage migration inhibitory factor (MIF), using Förster resonance energy transfer–based approaches. We show that CXCR4 presents a multifaceted response to CXCL12, with receptor activation (=0.6 seconds) followed by a rearrangement in the receptor/G protein complex (=1 seconds), a slower dimer rearrangement (=1.7 seconds), and prolonged G protein activation (=4 seconds). In comparison, MIF distinctly modulates every step of the transduction pathway, indicating distinct activation mechanisms and reflecting the different pharmacological properties of these two ligands. Our study also indicates that CXCR4 exhibits some degree of ligand-independent activity, a relevant feature for drug development.

### 6) Scientific Perspectivism in Secondary-School Chemistry Education: Integrating Concepts and Skills in Chemical Thinking

* Landa, I., Westbroek, H., Janssen, F., van Muijlwijk, J., Meeter, M.
* Team Secondary Education, LEARN! - Learning sciences, Innovations in Human Health & Life Sciences, AIMMS, Educational and Family Studies, VU University, Leiden University
* Science and Education
* https://doi.org/10.1007/s11191-020-00145-3
* Corresponding author: Westbroek, H.
* Published 1 Oct 2020 (early online 7 Aug 2020)
* Processed: 2020-10

The importance of learning chemical ways of thinking is widely recognized. Various frameworks have been developed to address the essence of chemistry and chemical thinking. However, very few studies have focused on how chemical ways of thinking can be defined. To elaborate chemical ways of thinking, this paper draws on scientific perspectivism (Giere 2010; Wimsatt 2007; Thagard 2012). Scientific perspectivism states that, within each general domain, several broadly accepted theoretical models exist side by side. These general theoretical models, or theoretical perspectives, determine which research questions are generated, which types of models are developed, and which criteria are important for evaluating models. A theoretical perspective can be captured in a core reasoning that embodies the fundamental relationship between model and the “real world.” Starting with their most basic form, perspectives can be used in learning how to reason about all types of ill-structured problems, directing and organizing knowledge development, and integrating knowledge and skills. The study is part of a research project on how perspectivism can be applied to the design of secondary-school chemistry education. This particular study concerns the identification, elaboration, and validation of four chemical perspectives for secondary-school chemistry education. We use these perspectives to indicate the consequences of taking a perspectivism approach to a curriculum framework. We conclude with discussing the consequences for secondary chemistry curriculum.

### 7) Neurobehavioral effects of cyanobacterial biomass field extracts on zebrafish embryos and potential role of retinoids

* Pípal, M., Legradi, J., Smutná, M., Kočí, T., Priebojová, J., Bláhová, L., Krauss, M., Hilscherová, K.
* E&H: Environmental Health and Toxicology, AIMMS, Masaryk University, Helmholtz Centre for Environmental Research
* Aquatic Toxicology
* https://doi.org/10.1016/j.aquatox.2020.105613
* Corresponding author: Hilscherová, K.
* Published Nov 2020 (early online 6 Sep 2020)
* Processed: 2020-9

Cyanobacteria are known for their ability to produce and release mixtures of up to thousands of compounds into the environment. Recently, the production of novel metabolites, retinoids, was reported for some cyanobacterial species along with teratogenic effects of samples containing these compounds. Retinoids are natural endogenous substances derived from vitamin A that play a crucial role in early vertebrate development. Disruption of retinoid signalling- especially during the early development of the nervous system- might lead to major malfunctions and malformations. In this study, the toxicity of cyanobacterial biomass samples from the field containing retinoids was characterized by in vivo and in vitro bioassays with a focus on the potential hazards towards nervous system development and function. Additionally, in order to identify the compounds responsible for the observed in vitro and in vivo effects the complex cyanobacterial extracts were fractionated (C18 column, water-methanol gradient) and the twelve obtained fractions were tested in bioassays. In all bioassays, all-trans retinoic acid (ATRA) was tested along with the environmental samples as a positive control. Retinoid-like activity (mediated via the retinoic acid receptor, RAR) was measured in the transgenic cell line p19/A15. The in vitro assay showed retinoid-like activity by specific interaction with RAR for the biomass samples. Neurotoxic effects of selected samples were studied on zebrafish (Danio rerio) embryos using the light/dark transition test (Viewpoint, ZebraLab system) with 120 hpf larvae. In the behavioural assay, the cyanobacterial extracts caused significant hyperactivity in zebrafish at 120 hpf after acute exposure (3 h prior to the measurement) at concentrations below the teratogenicity LOEC (0.2 g dw L−1). Similar effect was observed after exposure to fractions of the extracts with detected retinoid-like activity and additive effect was observed after combining the fractions. However, the effect on behaviour was not observed after exposure to ATRA only. To provide additional insight into the behavioural effects and describe the underlying mechanism gene expression of selected biomarkers was measured. We evaluated an array of 28 genes related to general toxicity, neurodevelopment, retinoid and thyroid signalling. We detected several affected genes, most notably, the Cyp26 enzymes that control endogenous ATRA concentration, which documents an effect on retinoid signalling.

### 8) The atypical chemokine receptor 3 interacts with Connexin 43 inhibiting astrocytic gap junctional intercellular communication

* Fumagalli, A., Heuninck, J., Pizzoccaro, A., Moutin, E., Koenen, J., Séveno, M., Durroux, T., Junier, M. P., Schlecht-Louf, G., Bachelerie, F., Schütz, D., Stumm, R., Smit, M. J., Guérineau, N. C., Chaumont-Dubel, S., Marin, P.
* Medicinal chemistry, AIMMS, Université de Montpellier, Sorbonne Université, ComUE Paris-Saclay, Friedrich Schiller University Jena
* Nature Communications
* https://doi.org/10.1038/s41467-020-18634-y
* Corresponding author: Marin, P.
* Published 1 Dec 2020 (early online 25 Sep 2020)
* Processed: 2020-9

The atypical chemokine receptor 3 (ACKR3) plays a pivotal role in directing the migration of various cellular populations and its over-expression in tumors promotes cell proliferation and invasiveness. The intracellular signaling pathways transducing ACKR3-dependent effects remain poorly characterized, an issue we addressed by identifying the interactome of ACKR3. Here, we report that recombinant ACKR3 expressed in HEK293T cells recruits the gap junction protein Connexin 43 (Cx43). Cx43 and ACKR3 are co-expressed in mouse brain astrocytes and human glioblastoma cells and form a complex in embryonic mouse brain. Functional in vitro studies show enhanced ACKR3 interaction with Cx43 upon ACKR3 agonist stimulation. Furthermore, ACKR3 activation promotes β-arrestin2- and dynamin-dependent Cx43 internalization to inhibit gap junctional intercellular communication in primary astrocytes. These results demonstrate a functional link between ACKR3 and gap junctions that might be of pathophysiological relevance.

### *9) N-Heterocyclic Silylenes as Ligands in Transition Metal Carbonyl Chemistry: Nature of Their Bonding and Supposed Innocence*

* Krahfuß, M. J., Nitsch, J., Bickelhaupt, F. M., Marder, T. B., Radius, U.
* Chemistry and Pharmaceutical Sciences, AIMMS, University of Würzburg, VU Amsterdam, University of Würzburg
* Chemistry - A European Journal
* https://doi.org/10.1002/chem.202001062
* Corresponding author: Radius, U.
* Published 1 Sep 2020 (early online 31 Mar 2020)
* Processed: 2020-9

A study on the reactivity of the N-heterocyclic silylene Dipp2NHSi (1,3-bis(diisopropylphenyl)-1,3-diaza-2-silacyclopent-4-en-2-yliden) with the transition metal complexes [Ni(CO)4], [M(CO)6] (M=Cr, M ...

### *10) Understanding the 1,3-Dipolar Cycloadditions of Allenes*

* Yu, S., Vermeeren, P., van Dommelen, K., Bickelhaupt, F. M., Hamlin, T. A.
* Theoretical Chemistry, AIMMS, Chemistry and Pharmaceutical Sciences, VU University
* Chemistry - A European Journal
* https://doi.org/10.1002/chem.202000857
* Corresponding author: Bickelhaupt, F. M.
* Published 4 Sep 2020 (early online 27 Mar 2020)
* Processed: 2020-9

We have quantum chemically studied the reactivity, site-, and regioselectivity of the 1,3-dipolar cycloaddition between methyl azide and various allenes, including the archetypal allene propadiene, he ...

### *11) Environmental Effects with Frozen-Density Embedding in Real-Time Time-Dependent Density Functional Theory Using Localized Basis Functions*

* De Santis, M., Belpassi, L., Jacob, C. R., Severo Pereira Gomes, A., Tarantelli, F., Visscher, L., Storchi, L.
* Theoretical Chemistry, AIMMS, University of Perugia, Technical University of Braunschweig, Universite de Lille 2, Gabriele d’Annunzio University
* Journal of chemical theory and computation
* https://doi.org/10.1021/acs.jctc.0c00603
* Corresponding author: None
* Published 8 Sep 2020 (early online 27 Jul 2020)
* Processed: 2020-9

Frozen-density embedding (FDE) represents a versatile embedding scheme to describe the environmental effect on electron dynamics in molecular systems. The extension of the general theory of FDE to the ...

### *12) Light-Matter Hybrid-Orbital-Based First-Principles Methods: The Influence of Polariton Statistics*

* Buchholz, F., Theophilou, I., Giesbertz, K. J., Ruggenthaler, M., Rubio, A.
* Theoretical Chemistry, AIMMS, Max Planck Institute for the Structure and Dynamics of Matter, Simons Foundation
* Journal of chemical theory and computation
* https://doi.org/10.1021/acs.jctc.0c00469
* Corresponding author: None
* Published 8 Sep 2020 (early online 21 Jul 2020)
* Processed: 2020-9

A detailed understanding of strong matter-photon interactions requires first-principle methods that can solve the fundamental Pauli-Fierz Hamiltonian of nonrelativistic quantum electrodynamics efficie ...

### *13) Neutralizing effects of small molecule inhibitors and metal chelators on coagulopathic Viperinae snake venom toxins*

* Xie, C., Albulescu, L. O., Bittenbinder, M. A., Somsen, G. W., Vonk, F. J., Casewell, N. R., Kool, J.
* AIMMS, BioAnalytical Chemistry, Liverpool School of Tropical Medicine, VU University, Centre for Analytical Sciences Amsterdam (CASA), Naturalis Biodiversity Center
* Biomedicines
* https://doi.org/10.3390/BIOMEDICINES8090297
* Corresponding author: Kool, J.
* Published Sep 2020 (early online 20 Aug 2020)
* Processed: 2020-9

Animal-derived antivenoms are the only specific therapies currently available for the treatment of snake envenoming, but these products have a number of limitations associated with their efficacy, saf ...