# AIMMS publication report for: 2020-11-29

1. New approach methodologies (NAMs) for human-relevant biokine (2020-10)
2. Dynamic and Internal Longest Common Substring (2020-7)
3. Neutralising effects of small molecule toxin inhibitors on n (2020-10)
4. A Novel Method for Long-Term Analysis of Lactic Acid and Amm (2020-10)
5. Innovation in pharmaceutical R&D: mapping the research lands (2020-10)
6. Recent Advances in Palladium-Catalyzed Isocyanide Insertions (2020-10)
7. ROS networks: designs, aging, Parkinson’s disease and precis (2020-10)
8. Evaluation of the effects of acetylcholinesterase inhibitors (2020-10)
9. Efficient data structures for range shortest unique substrin (2020-11)
10. Bromo-cyclobutenaminones as new covalent udp-n-acetylglucosa (2020-11)
11. Stress-based high-throughput screening assays to identify in (2020-11)
12. Assessing the Legitimacy of Technological Innovation in the (2020-11)
13. *Scientific Perspectivism in Secondary-School Chemistry Educa (2020-10)*
14. *Innovation in pharmaceutical R&D: mapping the research lands (2020-10)*
15. *Shifting Towards αVβ6 Integrin Ligands Using Novel Aminoprol (2020-10)*
16. *Improving the Environmental Risk Assessment of Substances of (2020-11)*
17. *Exploring metal availability in the natural niche of Strepto (2020-10)*
18. *An Optimal Transport Approach for the Schrödinger Bridge Pro (2020-11)*
19. *A protein tertiary structure mimetic modulator of the Hippo (2020-11)*
20. *Is it worthwhile to go beyond the local-density approximatio (2020-11)*

### 1) New approach methodologies (NAMs) for human-relevant biokinetics predictions: Meeting the paradigm shift in toxicology towards an animal-free chemical risk assessment

* Punt, A., Bouwmeester, H., Blaauboer, B. J., Coecke, S., Hakkert, B., Hendriks, D. F. G., Jennings, P., Kramer, N. I., Neuhoff, S., Masereeuw, R., Paini, A., Peijnenburg, A. A. C. M., Rooseboom, M., Shuler, M. L., Sorrell, I., Spee, B., Strikwold, M., Van der Meer, A. D., Van der Zande, M., Vinken, M., Yang, H., Bos, P. M. J., Heringa, M. B.
* Molecular and Computational Toxicology, AIMMS, WFSR Wageningen Food Safety Research, Wageningen, The Netherlands., Division of Toxicology, Wageningen University and Research, Wageningen, The Netherlands., Institute for Risk Assessment Sciences, Utrecht University, Utrecht, The Netherlands. salome.scholtens@rivm.nl, Directorate F - Health, Consumers and Reference Materials, Joint Research Centre, European Commission, Ispra, Italy., National Institute for Public Health and the Environment (RIVM), Bilthoven, The Netherlands., Section of Pharmacogenetics, Department of Physiology and Pharmacology, Karolinska Institutet, Stockholm, Sweden., Certara UK Ltd, Simcyp Division, Sheffield, UK., Utrecht Institute for Pharmaceutical Sciences, Division Pharmacoepidemiology &Clinical Pharmacology, Utrecht University, Utrecht, 3508 TB, The Netherlands., Shell Health, Shell International B.V., The Hague, The Netherlands., Biomedical Engineering, Cornell University, Department of Biomedical Engineering, Ithaca, NY, USA., Unilever, Safety and Environmental Assurance Centre, Colworth Science Park, Sharnbrook, Bedfordshire MK44 1LQ, United Kingdom., Department of Clinical Sciences of Companion Animals, Faculty of Veterinary Medicine, Utrecht University, The Netherlands., Van Hall Larenstein University of Applied Sciences, Leeuwarden, The Netherlands., University of Twente, Department of Applied Stem Cell Technologies, Enschede, The Netherlands., Department of In Vitro Toxicology and Dermato-Cosmetology, Vrije Universiteit Brussel, Laarbeeklaan 103, 1090, Brussels, Belgium., Division of Drug Discovery and Safety, Leiden Academic Centre for Drug Research (LACDR)/Leiden University, Leiden, The Netherlands.
* Altex
* https://doi.org/10.14573/altex.2003242
* Corresponding author: None
* Published 20 Oct 2020 (early online 8 Jun 2020)
* Processed: 2020-10

For almost fifteen years, the availability and regulatory acceptance of new approach methodologies (NAMs) to assess the absorption, distribution, metabolism and excretion (ADME/biokinetics) in chemical risk evaluations are a bottleneck. To enhance the field, a team of 24 experts from science, industry, and regulatory bodies, including new generation toxicologists, met at the Lorentz Centre in Leiden, The Netherlands. A range of possibilities for the use of NAMs for biokinetics in risk evaluations were formulated (for example to define species differences and human variation or to perform quantitative in vitro-in vivo extrapolations). To increase the regulatory use and acceptance of NAMs for biokinetics for these ADME considerations within risk evaluations, the development of test guidelines (protocols) and of overarching guidance documents is considered a critical step. To this end, a need for an expert group on biokinetics within the Organisation of Economic Cooperation and Development (OECD) to supervise this process was formulated. The workshop discussions revealed that method development is still required, particularly to adequately capture transporter mediated processes as well as to obtain cell models that reflect the physiology and kinetic characteristics of relevant organs. Developments in the fields of stem cells, organoids and organ-on-a-chip models provide promising tools to meet these research needs in the future.

### 2) Dynamic and Internal Longest Common Substring

* Amir, A., Charalampopoulos, P., Pissis, S. P., Radoszewski, J.
* Bioinformatics, AIMMS, Bio Informatics (IBIVU), Bar-Ilan University, King's College London, University of Warsaw, Samsung R&D Institute Poland
* Algorithmica
* https://doi.org/10.1007/s00453-020-00744-0
* Corresponding author: Pissis, S. P.
* Published 1 Dec 2020 (early online 15 Jul 2020)
* Processed: 2020-7

Given two strings S and T, each of length at most n, the longest common substring (LCS) problem is to find a longest substring common to S and T. This is a classical problem in computer science with an O(n) -time solution. In the fully dynamic setting, edit operations are allowed in either of the two strings, and the problem is to find an LCS after each edit. We present the first solution to the fully dynamic LCS problem requiring sublinear time in n per edit operation. In particular, we show how to find an LCS after each edit operation in O~ (n2 / 3) time, after O~ (n) -time and space preprocessing. This line of research has been recently initiated in a somewhat restricted dynamic variant by Amir et al. [SPIRE 2017]. More specifically, the authors presented an O~ (n) -sized data structure that returns an LCS of the two strings after a single edit operation (that is reverted afterwards) in O~ (1) time. At CPM 2018, three papers (Abedin et al., Funakoshi et al., and Urabe et al.) studied analogously restricted dynamic variants of problems on strings; specifically, computing the longest palindrome and the Lyndon factorization of a string after a single edit operation. We develop dynamic sublinear-time algorithms for both of these problems as well. We also consider internal LCS queries, that is, queries in which we are to return an LCS of a pair of substrings of S and T. We show that answering such queries is hard in general and propose efficient data structures for several restricted cases.

### 3) Neutralising effects of small molecule toxin inhibitors on nanofractionated coagulopathic Crotalinae snake venoms

* Xie, C., Slagboom, J., Albulescu, L. O., Somsen, G. W., Vonk, F. J., Casewell, N. R., Kool, J.
* BioAnalytical Chemistry, AIMMS, Chemistry and Pharmaceutical Sciences, Liverpool School of Tropical Medicine
* Acta Pharmaceutica Sinica B
* https://doi.org/10.1016/j.apsb.2020.09.005
* Corresponding author: Kool, J.
* Published Oct 2020 (early online 15 Sep 2020)
* Processed: 2020-10

Repurposing small molecule drugs and drug candidates is considered as a promising approach to revolutionise the treatment of snakebite envenoming. In this study, we investigated the inhibiting effects of the small molecules varespladib (nonspecific phospholipase A2 inhibitor), marimastat (broad spectrum matrix metalloprotease inhibitor) and dimercaprol (metal ion chelator) against coagulopathic toxins found in Crotalinae (pit vipers) snake venoms. Venoms from Bothrops asper, Bothrops jararaca, Calloselasma rhodostoma and Deinagkistrodon acutus were separated by liquid chromatography, followed by nanofractionation and mass spectrometry identification undertaken in parallel. Nanofractions of the venom toxins were then subjected to a high-throughput coagulation assay in the presence of different concentrations of the small molecules under study. Anticoagulant venom toxins were mostly identified as phospholipases A2, while procoagulant venom activities were mainly associated with snake venom metalloproteinases and snake venom serine proteases. Varespladib was found to effectively inhibit most anticoagulant venom effects, and also showed some inhibition against procoagulant toxins. Contrastingly, marimastat and dimercaprol were both effective inhibitors of procoagulant venom activities but showed little inhibitory capability against anticoagulant toxins. The information obtained from this study aids our understanding of the mechanisms of action of toxin inhibitor drug candidates, and highlights their potential as future snakebite treatments.

### 4) A Novel Method for Long-Term Analysis of Lactic Acid and Ammonium Production in Non-growing Lactococcus lactis Reveals Pre-culture and Strain Dependence

* Nugroho, A. D. W., Kleerebezem, M., Bachmann, H.
* Systems Bioinformatics, AIMMS, TI Food and Nutrition, NIZO food research, Wageningen University & Research
* Frontiers in Bioengineering and Biotechnology
* https://doi.org/10.3389/fbioe.2020.580090
* Corresponding author: Bachmann, H.
* Published Oct 2020 (early online 8 Oct 2020)
* Processed: 2020-10

In various (industrial) conditions, cells are in a non-growing but metabolically active state in which de novo protein synthesis capacity is limited. The production of a metabolite by such non-growing cells is dependent on the cellular condition and enzyme activities, such as the amount, stability, and degradation of the enzyme(s). For industrial fermentations in which the metabolites of interest are mainly formed after cells enter the stationary phase, the investigation of prolonged metabolite production is of great importance. However, current batch model systems do not allow prolonged measurements due to metabolite accumulation driving product-inhibition. Here we developed a protocol that allows high-throughput metabolic measurements to be followed in real-time over extended periods (weeks). As a validation model, sugar utilization and arginine consumption by a low density of translationally blocked Lactococcus lactis was designed in a defined medium. In this system L. lactis MG1363 was compared with its derivative HB60, a strain described to achieve higher metabolic yield through a shift toward heterofermentative metabolism. The results showed that in a non-growing state HB60 is able to utilize more arginine than MG1363, and for both strains the decay of the measured activities were dependent on pre-culture conditions. During the first 5 days of monitoring a ∼25-fold decrease in acidification rate was found for strain HB60 as compared to a ∼20-fold decrease for strain MG1363. Such measurements are relevant for the understanding of microbial metabolism and for optimizing applications in which cells are frequently exposed to long-term suboptimal conditions, such as microbial cell factories, fermentation ripening, and storage survival.

### 5) Innovation in pharmaceutical R&D: mapping the research landscape

* Romasanta, A. K. S., van der Sijde, P., van Muijlwijk-Koezen, J.
* Medicinal chemistry, Innovations in Human Health & Life Sciences, AIMMS, Organization Sciences, Network Institute, Organization & Processes of Organizing in Society (OPOS)
* None
* https://doi.org/10.1007/s11192-020-03707-y
* Corresponding author: Romasanta, A. K. S.
* Published 10 Oct 2020 (early online 10 Oct 2020)
* Processed: 2020-10

In response to the increasing number and breadth of innovation studies on the pharmaceutical industry, we mapped the literature to show the trends in recent research and to indicate areas for further research. In the first phase, we analyzed articles on the pharmaceutical industry published in innovation journals. We used these articles’ textual and citation data and applied hybrid cluster analysis. Three main clusters were produced basedon the level of analysis innovation scholars had used to investigate the industry: macro, meso and micro. We describe theresearch topics within these clusters and show that, overall, innovation scholars increasingly focus on the meso-level, analyzing the relationships across different firms. This shift in interest toward the collaborative nature of drug discovery and development was also apparent in macro- and micro-level studies. To explore how this literature is used by scientists in the industry, our second phase involved analysis of the citing articles published in pharmaceutical journals. Using our findings, we propose research areas that can be further explored in order to create an engaged and better-integrated literature on pharmaceutical innovation.

### 6) Recent Advances in Palladium-Catalyzed Isocyanide Insertions

* Collet, J. W., Roose, T. R., Weijers, B., Maes, B. U., Ruijter, E., Orru, R. V.
* Organic Chemistry, AIMMS, Chemistry and Pharmaceutical Sciences, Vrije Universiteit Amsterdam, University of Antwerp
* Molecules (Basel, Switzerland)
* https://doi.org/10.3390/molecules25214906
* Corresponding author: None
* Published 23 Oct 2020 (early online None)
* Processed: 2020-10

Isocyanides have long been known as versatile chemical reagents in organic synthesis. Their ambivalent nature also allows them to function as a CO-substitute in palladium-catalyzed cross couplings. Over the past decades, isocyanides have emerged as practical and versatile C1 building blocks, whose inherent N-substitution allows for the rapid incorporation of nitrogeneous fragments in a wide variety of products. Recent developments in palladium catalyzed isocyanide insertion reactions have significantly expanded the scope and applicability of these imidoylative cross-couplings. This review highlights the advances made in this field over the past eight years.

### 7) ROS networks: designs, aging, Parkinson’s disease and precision therapies

* N. Kolodkin, A., Sharma, R. P., Colangelo, A. M., Ignatenko, A., Martorana, F., Jennen, D., Briedé, J. J., Brady, N., Barberis, M., Mondeel, T. D., Papa, M., Kumar, V., Peters, B., Skupin, A., Alberghina, L., Balling, R., Westerhoff, H. V.
* AIMMS, Systems Bioinformatics, Molecular Cell Biology, Infrastructure for Systems Biology Europe (ISBE.NL), University of Luxembourg, Vrije Universiteit Amsterdam, University of Amsterdam, Infrastructure for Systems Biology Europe (ISBE.IT), University of Milan - Bicocca, Luxembourg Institute of Science and Technology, Maastricht University, Johns Hopkins University, University of Surrey, Infrastructure for Systems Biology Europe (ISBE.IT), University of Campania Luigi Vanvitelli, Universidad Rovira i Virgili, Pere Virgili Health Research Institute
* NPJ systems biology and applications
* https://doi.org/10.1038/s41540-020-00150-w
* Corresponding author: N. Kolodkin, A.
* Published 1 Dec 2020 (early online 26 Oct 2020)
* Processed: 2020-10

How the network around ROS protects against oxidative stress and Parkinson’s disease (PD), and how processes at the minutes timescale cause disease and aging after decades, remains enigmatic. Challenging whether the ROS network is as complex as it seems, we built a fairly comprehensive version thereof which we disentangled into a hierarchy of only five simpler subnetworks each delivering one type of robustness. The comprehensive dynamic model described in vitro data sets from two independent laboratories. Notwithstanding its five-fold robustness, it exhibited a relatively sudden breakdown, after some 80 years of virtually steady performance: it predicted aging. PD-related conditions such as lack of DJ-1 protein or increased α-synuclein accelerated the collapse, while antioxidants or caffeine retarded it. Introducing a new concept (aging-time-control coefficient), we found that as many as 25 out of 57 molecular processes controlled aging. We identified new targets for “life-extending interventions”: mitochondrial synthesis, KEAP1 degradation, and p62 metabolism.

### 8) Evaluation of the effects of acetylcholinesterase inhibitors in the zebrafish touch-evoked response: quantitative vs. qualitative assessment

* Guzman, L., Besa, G., Linares, D., González, L., Pont, C., Bartolini, M., Haigis, A. C., Legradi, J., Muñoz-Torrero, D., Gómez-Catalán, J., Barenys, M.
* E&H: Environmental Health and Toxicology, AIMMS, University of Barcelona, University of Bologna, RWTH Aachen University
* Environmental Sciences Europe
* https://doi.org/10.1186/s12302-020-00421-7
* Corresponding author: Barenys, M.
* Published 1 Dec 2020 (early online 28 Oct 2020)
* Processed: 2020-10

Background: The difficulty of finding new treatments for neurological diseases with great impact in our society like Alzheimer’s disease can be ascribed in part to the complexity of the nervous system and the lack of quick and cost-effective screening tools. Such tools could not only help to identify potential novel treatments, but could also be used to test environmental contaminants for their potential to cause neurotoxicity. It has been estimated that 5–10% of the anthropogenic chemicals are developmental neurotoxic (DNT) and exposure to DNT compounds has been linked to several neurological diseases. Within this study we were testing the applicability of a quick and cost-effective behavioural test using zebrafish embryos: the touch-evoked response assay, in this case, an assay evaluating the swimming response to a tap in the tail. Two acetylcholinesterase (AChE) inhibitors positive controls (paraoxon and huprine Y), as well as 10 huprine-derivative compounds were tested and the results were evaluated using 2 different methods, a quantitative and a qualitative one. Results: We could show that the methodology presented is able to detect behavioural effects of AChE inhibitors. A good correlation between the results obtained with the quantitative and the qualitative method was obtained (R2 = 0.84). Conclusions: Our proposed method enables combination of screening for new drugs with toxicity screening in a whole embryo model alternative to animal experimentation, thereby merging 2 drug development steps into one.

### 9) Efficient data structures for range shortest unique substring queries†Let T[1, n] be a string of length n and T[i, j] be the substring of T starting at position i and ending at position j. A substring T[i, j] of T is a repeat if it occurs more than once in T; otherwise, it is a unique substring of T. Repeats and unique substrings are of great interest in computational biology and information retrieval. Given string T as input, the Shortest Unique Substring problem is to find a shortest substring of T that does not occur elsewhere in T. In this paper, we introduce the range variant of this problem, which we call the Range Shortest Unique Substring problem. The task is to construct a data structure over T answering the following type of online queries efficiently. Given a range [α, β], return a shortest substring T[i, j] of T with exactly one occurrence in [α, β]. We present an O(n log n)-word data structure with O(logw n) query time, where w = Ω(log n) is the word size. Our construction is based on a non-trivial reduction allowing for us to apply a recently introduced optimal geometric data structure [Chan et al., ICALP 2018]. Additionally, we present an O(n)-word data structure with O(√ n logɛ n) query time, where ɛ > 0 is an arbitrarily small constant. The latter data structure relies heavily on another geometric data structure [Nekrich and Navarro, SWAT 2012].General information

* Abedin, P., Ganguly, A., Pissis, S. P., Thankachan, S. V.
* Bioinformatics, AIMMS, Bio Informatics (IBIVU), University of Central Florida, University of Wisconsin-Whitewater
* Algorithms
* https://doi.org/10.3390/a13110276
* Corresponding author: Pissis, S. P.
* Published Nov 2020 (early online 30 Oct 2020)
* Processed: 2020-11

Efficient data structures for range shortest unique substring queries†Let T[1, n] be a string of length n and T[i, j] be the substring of T starting at position i and ending at position j. A substring T[i, j] of T is a repeat if it occurs more than once in T; otherwise, it is a unique substring of T. Repeats and unique substrings are of great interest in computational biology and information retrieval. Given string T as input, the Shortest Unique Substring problem is to find a shortest substring of T that does not occur elsewhere in T. In this paper, we introduce the range variant of this problem, which we call the Range Shortest Unique Substring problem. The task is to construct a data structure over T answering the following type of online queries efficiently. Given a range [α, β], return a shortest substring T[i, j] of T with exactly one occurrence in [α, β]. We present an O(n log n)-word data structure with O(logw n) query time, where w = Ω(log n) is the word size. Our construction is based on a non-trivial reduction allowing for us to apply a recently introduced optimal geometric data structure [Chan et al., ICALP 2018]. Additionally, we present an O(n)-word data structure with O(√ n logɛ n) query time, where ɛ > 0 is an arbitrarily small constant. The latter data structure relies heavily on another geometric data structure [Nekrich and Navarro, SWAT 2012].

### 10) Bromo-cyclobutenaminones as new covalent udp-n-acetylglucosamine enolpyruvyl transferase (Mura) inhibitors

* Hamilton, D. J., Ábrányi-Balogh, P., Keeley, A., Petri, L., Hrast, M., Imre, T., Wijtmans, M., Gobec, S., de Esch, I. J., Keserű, G. M.
* Medicinal chemistry, AIMMS, Chemistry and Pharmaceutical Sciences, Vrije Universiteit Amsterdam, Research Centre for Natural Sciences, University of Ljubljana
* Pharmaceuticals
* https://doi.org/10.3390/ph13110362
* Corresponding author: Keserű, G. M.
* Published Nov 2020 (early online 3 Nov 2020)
* Processed: 2020-11

Drug discovery programs against the antibacterial target UDP-N-acetylglucosamine enolpyruvyl transferase (MurA) have already resulted in covalent inhibitors having small threeand five-membered heterocyclic rings. In the current study, the reactivity of four-membered rings was carefully modulated to obtain a novel family of covalent MurA inhibitors. Screening a small library of cyclobutenone derivatives led to the identification of bromo-cyclobutenaminones as new electrophilic warheads. The electrophilic reactivity and cysteine specificity have been determined in a glutathione (GSH) and an oligopeptide assay, respectively. Investigating the structure-activity relationship for MurA suggests a crucial role for the bromine atom in the ligand. In addition, MS/MS experiments have proven the covalent labelling of MurA at Cys115 and the observed loss of the bromine atom suggests a net nucleophilic substitution as the covalent reaction. This new set of compounds might be considered as a viable chemical starting point for the discovery of new MurA inhibitors.

### 11) Stress-based high-throughput screening assays to identify inhibitors of cell envelope biogenesis

* Steenhuis, M., Ten Hagen-Jongman, C. M., van Ulsen, P., Luirink, J.
* Molecular Microbiology, AIMMS, LaserLaB - Analytical Chemistry and Spectroscopy, LaserLaB - Molecular Biophysics
* Antibiotics
* https://doi.org/10.3390/antibiotics9110808
* Corresponding author: Luirink, J.
* Published Nov 2020 (early online None)
* Processed: 2020-11

The structural integrity of the Gram-negative cell envelope is guarded by several stress responses, such as the σE, Cpx and Rcs systems. Here, we report on assays that monitor these responses in E. coli upon addition of antibacterial compounds. Interestingly, compromised peptidoglycan synthesis, outer membrane biogenesis and LPS integrity predominantly activated the Rcs response, which we developed into a robust HTS (high-throughput screening) assay that is suited for phenotypic compound screening. Furthermore, by interrogating all three cell envelope stress reporters, and a reporter for the cytosolic heat-shock response as control, we found that inhibitors of specific envelope targets induce stress reporter profiles that are distinct in quality, amplitude and kinetics. Finally, we show that by using a host strain with a more permeable outer membrane, large-scaffold antibiotics can also be identified by the reporter assays. Together, the data suggest that stress profiling is a useful first filter for HTS aimed at inhibitors of cell envelope processes.

### 12) Assessing the Legitimacy of Technological Innovation in the Public Sphere: Recovering Raw Materials from Waste Water This paper researches legitimacy creation in a publicly-funded trajectory of innovative technological development. It develops a framework of input, throughput and output legitimacy. The framework is developed based on a review of the literature on the creation of legitimacy in innovative technological development. The framework assists in further exploring the potential of the integrated assessment of the legitimacy of technological innovation trajectories in the public sphere, in terms of (1) public accountability (ensuring input legitimacy); (2) science, technology and innovation policy (ensuring throughput legitimacy); and (3) the potential for the implementation of the technology itself in practical contexts (ensuring output legitimacy). The framework is used to analyze a case study about the publicly-funded development of innovative technology for the retrieval of raw materials from waste water. Theoretically, the value of a more processual approach to the conceptualization of legitimacy becomes apparent. Furthermore, the framework assists in the development of practical recommendations on the ways in which to optimize the legitimacy in an earlier stage in the innovation’s trajectory. However, due attention should also be paid to the role of regulatory arrangements in the optimization of the legitimacy of publicly-funded technological innovation. This is an avenue for further research.General information

* Blankesteijn, M., Bossink, B.
* Biophysics Photosynthesis/Energy, Science & Business Innovation, AIMMS
* Sustainability
* https://doi.org/https://doi.org/10.3390/su1222940810.3390/su12229408
* Corresponding author: Bossink, B.
* Published 12 Nov 2020 (early online None)
* Processed: 2020-11

Assessing the Legitimacy of Technological Innovation in the Public Sphere: Recovering Raw Materials from Waste Water This paper researches legitimacy creation in a publicly-funded trajectory of innovative technological development. It develops a framework of input, throughput and output legitimacy. The framework is developed based on a review of the literature on the creation of legitimacy in innovative technological development. The framework assists in further exploring the potential of the integrated assessment of the legitimacy of technological innovation trajectories in the public sphere, in terms of (1) public accountability (ensuring input legitimacy); (2) science, technology and innovation policy (ensuring throughput legitimacy); and (3) the potential for the implementation of the technology itself in practical contexts (ensuring output legitimacy). The framework is used to analyze a case study about the publicly-funded development of innovative technology for the retrieval of raw materials from waste water. Theoretically, the value of a more processual approach to the conceptualization of legitimacy becomes apparent. Furthermore, the framework assists in the development of practical recommendations on the ways in which to optimize the legitimacy in an earlier stage in the innovation’s trajectory. However, due attention should also be paid to the role of regulatory arrangements in the optimization of the legitimacy of publicly-funded technological innovation. This is an avenue for further research.

### *13) 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 h ...

### *14) Innovation in pharmaceutical R&D: mapping the research landscape*

* Romasanta, A. K., van der Sijde, P., van Muijlwijk-Koezen, J. E.
* Innovations in Human Health & Life Sciences, AIMMS, Organization & Processes of Organizing in Society (OPOS), Network Institute, Organization Sciences
* None
* https://doi.org/https://doi.org/10.1007/s11192-020-03707-y
* Corresponding author: Romasanta, A. K.
* Published 10 Oct 2020 (early online None)
* Processed: 2020-10

In response to the increasing number and breadth of innovation studies on the pharmaceutical industry, we mapped the literature to show the trends in recent research and to indicate areas for further ...

### *15) Shifting Towards αVβ6 Integrin Ligands Using Novel Aminoproline-Based Cyclic Peptidomimetics*

* Bugatti, K., Bruno, A., Arosio, D., Sartori, A., Curti, C., Augustijn, L., Zanardi, F., Battistini, L.
* Medicinal chemistry, AIMMS, University of Parma, National Research Council of Italy
* Chemistry - A European Journal
* https://doi.org/10.1002/chem.202002554
* Corresponding author: Battistini, L.
* Published 21 Oct 2020 (early online 7 Jul 2020)
* Processed: 2020-10

In recognition of the key role played by integrins in several life-threatening dysfunctions, the search for novel small-molecule probes that selectively recognize these surface receptors is still open ...

### *16) Improving the Environmental Risk Assessment of Substances of Unknown or Variable Composition, Complex Reaction Products, or Biological Materials*

* Salvito, D., Fernandez, M., Jenner, K., Lyon, D. Y., de Knecht, J., Mayer, P., MacLeod, M., Eisenreich, K., Leonards, P., Cesnaitis, R., León-Paumen, M., Embry, M., Déglin, S. E.
* E&H: Environmental Bioanalytical Chemistry, AIMMS, Research Institute for Fragrance Materials Inc., Environment and Climate Change Canada, Givaudan, Shell Oil, National Institute of Public Health and the Environment, Technical University of Denmark, Stockholm University, United States Environmental Protection Agency, European Chemicals Agency, ExxonMobil Biomedical Sciences Inc., Health and Environmental Sciences Institute
* Environmental toxicology and chemistry
* https://doi.org/10.1002/etc.4846
* Corresponding author: Déglin, S. E.
* Published 1 Nov 2020 (early online 11 Aug 2020)
* Processed: 2020-11

Substances of unknown or variable composition, complex reaction products, or biological materials (UVCBs) pose unique risk assessment challenges to regulators and to product registrants. These substan ...

### *17) Exploring metal availability in the natural niche of Streptococcus pneumoniae to discover potential vaccine antigens*

* van Beek, L. F., Surmann, K., van den Berg van Saparoea, H. B., Houben, D., Jong, W. S., Hentschker, C., Ederveen, T. H., Mitsi, E., Ferreira, D. M., van Opzeeland, F., van der Gaast–de Jongh, C. E., Joosten, I., Völker, U., Schmidt, F., Luirink, J., Diavatopoulos, D. A., de Jonge, M. I.
* Molecular Microbiology, AIMMS, LaserLaB - Molecular Biophysics, Radboud Institute for Molecular Life Sciences, Radboud Center for Infectious Diseases, University of Greifswald, Radboud University Nijmegen, Liverpool School of Tropical Medicine, Weill Cornell Medical College in Qatar
* Virulence
* https://doi.org/10.1080/21505594.2020.1825908
* Corresponding author: van Beek, L. F.
* Published 5 Oct 2020 (early online None)
* Processed: 2020-10

Nasopharyngeal colonization by Streptococcus pneumoniae is a prerequisite for pneumococcal transmission and disease. Current vaccines protect only against disease and colonization caused by a limited ...

### *18) An Optimal Transport Approach for the Schrödinger Bridge Problem and Convergence of Sinkhorn Algorithm*

* Marino, S. D., Gerolin, A.
* Theoretical Chemistry, AIMMS, Scuola Normale Superiore di Pisa, University of Genoa
* Journal of Scientific Computing
* https://doi.org/10.1007/s10915-020-01325-7
* Corresponding author: Gerolin, A.
* Published 1 Nov 2020 (early online 19 Oct 2020)
* Processed: 2020-11

This paper exploit the equivalence between the Schrödinger Bridge problem (Léonard in J Funct Anal 262:1879–1920, 2012; Nelson in Phys Rev 150:1079, 1966; Schrödinger in Über die umkehrung der naturge ...

### *19) A protein tertiary structure mimetic modulator of the Hippo signalling pathway*

* Adihou, H., Gopalakrishnan, R., Förster, T., Guéret, S. M., Gasper, R., Geschwindner, S., Carrillo García, C., Karatas, H., Pobbati, A. V., Vazquez‐Chantada, M., Davey, P., Wassvik, C. M., Pang, J. K. S., Soh, B. S., Hong, W., Chiarparin, E., Schade, D., Plowright, A. T., Valeur, E., Lemurell, M., Grossmann, T. N., Waldmann, H.
* Organic Chemistry, AIMMS, AstraZeneca Sweden, AstraZeneca, Max Planck Institute of Molecular Physiology, Kiel University, Agency for Science, Technology and Research, National University of Singapore, Guangzhou Medical College, Dortmund University
* Nature Communications
* https://doi.org/10.1038/s41467-020-19224-8
* Corresponding author: Waldmann, H.
* Published 1 Nov 2020 (early online None)
* Processed: 2020-11

Transcription factors are key protein effectors in the regulation of gene transcription, and in many cases their activity is regulated via a complex network of protein–protein interactions (PPI). The ...

### *20) Is it worthwhile to go beyond the local-density approximation in subsystem density functional theory?*

* Grimmel, S. A., Teodoro, T. Q., Visscher, L.
* Theoretical Chemistry, AIMMS, Vrije Universiteit Amsterdam, Vrije Universiteit Amsterdam
* International Journal of Quantum Chemistry
* https://doi.org/10.1002/qua.26111
* Corresponding author: Visscher, L.
* Published 1 Nov 2020 (early online 11 Dec 2019)
* Processed: 2020-11

Frozen density embedding (FDE) theory is one of the major techniques aiming to bring modeling of extended chemical systems into the realm of high accuracy calculations. To improve its accuracy it is o ...