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### 1) Opportunities for Expanding Encoded Chemical Diversification and Improving Hit Enrichment in m

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RNA-Displayed Peptide LibrariesDNA-encoded small-molecule libraries and mRNA displayed peptide libraries both use numerically large pools of oligonucleotide-tagged molecules to identify potential hits for protein targets. They differ dramatically, however, in the ‘drug-likeness’ of the molecules that each can be used to discover. We give here an overview of the two techniques, comparing some advantages and disadvantages of each, and suggest areas where particularly mRNA display can benefit from adopting advances developed with DNA-encoded small molecule libraries. We outline cases where chemical modification of the peptide library has already been used in mRNA display, and survey opportunities to expand this using examples from DNA-encoded small molecule libraries. We also propose potential opportunities for encoding such reactions within the mRNA/cDNA tag of an mRNA-displayed peptide library to allow a more diversity-oriented approach to library modification. Finally, we outline alternate approaches for enriching target-binding hits from a pooled and tagged library, and close by detailing several examples of how an adjusted mRNA-display based approach could be used to discover new ‘drug-like’ modified small peptides.

### 2) Using zebrafish to assess developmental neurotoxicity

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It is widely accepted that the developing nervous system is especially vulnerable to a variety of chemicals, including drugs and environmental contaminants; however our understanding of the risks from chemical exposures during development is rudimentary. Zebrafish have become a popular test species in toxicology, pharmacology, and biomedical research. This chapter was written as an introduction to the use of zebrafish in developmental neurotoxicology, and to encourage the use of this model either for human or ecological risk characterizations. We have endeavored to make the reader aware of significant research findings, and to offer a balanced view of the advantages and limitations in using zebrafish as a model for investigating developmental neurotoxicity.

### 3) How the Chalcogen Atom Size Dictates the Hydrogen-Bond Donor Capability of Carboxamides, Thioamides, and Selenoamides

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The amino groups of thio- and selenoamides can act as stronger hydrogen-bond donors than of carboxamides, despite the lower electronegativity of S and Se. This phenomenon has been experimentally explored, particularly in organocatalysis, but a sound electronic explanation is lacking. Our quantum chemical investigations show that the NH2 groups in thio- and selenoamides are more positively charged than in carboxamides. This originates from the larger electronic density flow from the nitrogen lone pair of the NH2 group towards the lower-lying π\*C=S and π\*C=Se orbitals than to the high-lying π\*C=O orbital. The relative energies of the π\* orbitals result from the overlap between the chalcogen np and carbon 2p atomic orbitals, which is set by the carbon-chalcogen equilibrium distance, a consequence of the Pauli repulsion between the two bonded atoms. Thus, neither the electronegativity nor the often-suggested polarizability but the steric size of the chalcogen atom determines the amide's hydrogen-bond donor capability.

### 4) Enhanced underground metabolism challenges life at high temperature–metabolic thermoadaptation in hyperthermophilic Archaea

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The text-book picture of a perfect, well organised metabolism with highly specific enzymes, is challenged by non-enzymatic reactions and promiscuous enzymes. This, so-called ‘underground metabolism’, is a special challenge for hyperthermophilic Archaea that thrive at temperatures above 80 °C and possess modified central metabolic pathways often with promiscuous enzymes. Hence, the question arises how extremely thermophilic Archaea can operate their unusual metabolism at temperatures where many pathway intermediates are unstable? We herein discuss current insights in the underground metabolism and metabolic thermoadaptation of (hyper)thermophilic Archaea. So far, only a few repair enzymes and salvaging pathways have been investigated in Archaea. Studies of the central carbohydrate metabolism indicate that a number of different strategies have evolved: 1) reduction of the concentration of unstable metabolites, 2) different pathway topologies are used with newly induced enzymes, and 3) damaged metabolites are removed via new metabolic pathways.

### 5) The development of a generic analysis method for natural and synthetic dyes by ultra-high-pressure liquid chromatography with photo-diode-array detection and triethylamine as an ion-pairing agent

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In cultural heritage the characterization of organic colorants is a challenging task. Currently, different chromatographic techniques are used to analyze natural and synthetic dyes separately, since the classes differ significantly in chemical properties and, therefore, chromatographic behavior. To save time, costs and sample material, we developed a method suitable for a wide variety of organic colorants using ultra-high-performance liquid chromatography coupled to a photo-diode-array detector. Gradient elution was performed with a mobile phase consisting of water and methanol with 5 mM triethylamine added as an ion-pairing agent at a pH of 3. Both linear and step gradients were optimized using the ‘Program for Interpretive Optimization of Two-dimensional Resolution’ (PIOTR) Pirok et al. [22]. Two optimized linear gradients and two step gradients were evaluated experimentally. The method was applied on a complex dye mixture containing nearly 130 natural- and synthetic-dye reference compounds. More than 100 of these compounds could be identified in a single experiment. The feasibility of the method was demonstrated by analyzing samples of several precious objects that were found in the Texel shipwreck Vos et al. [2] and of two embroideries of Emile Bernard, the results of which are described in this paper.

### 6) Internal shortest absent word queries in constant time and linear space

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Given a string T of length n over an alphabet Σ⊂{1,2,…,nO(1)} of size σ, we are to preprocess T so that given a range [i,j], we can return a representation of a shortest string over Σ that is absent in the fragment T[i]⋯T[j] of T. We present an O(n)-space data structure that answers such queries in constant time and can be constructed in O(nlogσ⁡n) time.

### 7) Degradation of 2,4-dichlorophenoxyacetic acid (2,4-D) and 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) by fungi originating from Vietnam

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* Processed: 2022-6

Three different fungi were tested for their ability to degrade 2,4-dichlorophenoxyacetic acid and 2,4,5-trichlorophenoxyacetic acid and for the role of laccases and cytochromes P450-type in this process. We studied a white-rot fungus Rigidoporus sp. FMD21, which has a high laccase activity, for its efficiency to degrade these herbicides. A positive correlation was found between its laccase activity and the corresponding herbicide degradation rate. Even more, the doubling of the enzyme activity in this phase corresponded with a doubling of the herbicide degradation rate. It is, therefore, tempting to speculate that laccase is the most dominant enzyme in the degradation of 2,4-D and 2,4,5-T under these conditions. In addition, it was shown that Rigidoporus sp. FMD21 partly relies on cytochromes P450-type for the breakdown of the herbicides as well. Two filamentous fungi were isolated from soil contaminated with herbicides and dioxins located at Bien Hoa airbase. They belong to genera Fusarium and Verticillium of the phylum Ascomycota as judged by their 18S rRNA gene sequences. Both isolated fungi were able to degrade the herbicides but with different rates. Their laccase activity, however, was very low and did not correlate with the rate of breakdown of the herbicides. These data indicate that the white-rot fungus most likely synthesizes laccase and cytochromes P450-type for the breakdown of the herbicides, while the types of enzyme used for the breakdown of the herbicides by the two Ascomycota remain unclear. Graphical abstract: [Figure not available: see fulltext.]

### 8) ELASTIC-DEGENERATE STRING MATCHING VIA FAST MATRIX MULTIPLICATION

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An elastic-degenerate (ED) string is a sequence of n sets of strings of total length N which was recently proposed to model a set of similar sequences. The ED string matching (EDSM) problem is to find all occurrences of a pattern of length m in an ED text. The EDSM problem has recently received some attention in the combinatorial pattern matching community, and an O (nm15 √log m+N)-time algorithm is known [Aoyama et al., CPM 2018]. The standard assumption in the prior work on this question is that N is substantially larger than both n and m, and thus we would like to have a linear dependency on the former. Under this assumption, the natural open problem is whether we can decrease the 1.5 exponent in the time complexity, similarly as in the related (but, to the best of our knowledge, not equivalent) word break problem [Backurs and Indyk, FOCS 2016]. Our starting point is a conditional lower bound for the EDSM problem. We use the popular combinatorial Boolean matrix multiplication (BMM) conjecture stating that there is no truly subcubic combinatorial algorithm for BMM [Abboud and Williams, FOCS 2014]. By designing an appropriate reduction, we show that a combinatorial algorithm solving the EDSM problem in \scrO (nm1.5 - \epsilon + N) time, for any \epsilon > 0, refutes this conjecture. Our reduction should be understood as an indication that decreasing the exponent requires fast matrix multiplication. String periodicity and fast Fourier transform are two standard tools in string algorithms. Our main technical contribution is that we successfully combine these tools with fast matrix multiplication to design a noncombinatorial \scrO \~(nm\omega -1 + N)-time algorithm for EDSM, where \omega denotes the matrix multiplication exponent and the \scrO \~(\cdot ) notation suppresses polylog factors. To the best of our knowledge, we are the first to combine these tools. In particular, using the fact that \omega < 2.373 [Alman and Williams, SODA 2021; Le Gall, ISSAC 2014; Williams, STOC 2012], we obtain an \scrO (nm1.373 + N)-time algorithm for EDSM. An important building block in our solution that might find applications in other problems is a method of selecting a small set of length-\ell substrings of the pattern, called anchors, so that any occurrence of a string from an ED text set contains at least one but not too many (on average) such anchors inside.

### 9) Manganese Modulates Metabolic Activity and Redox Homeostasis in Translationally Blocked Lactococcus cremoris, Impacting Metabolic Persistence, Cell Culturability, and Flavor Formation

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Manganese (Mn) is an essential trace element that is supplemented in microbial media with varying benefits across species and growth conditions. We found that growth of Lactococcus cremoris was unaffected by manganese omission from the growth medium. The main proteome adaptation to manganese omission involved increased manganese transporter production (up to 2,000-fold), while the remaining 10 significant proteome changes were between 1.4- and 4-fold. Further investigation in translationally blocked (TB), nongrowing cells showed that Mn supplementation (20 mM) led to approximately 1.5 X faster acidification compared with Mn-free conditions. However, this faster acidification stagnated within 24 h, likely due to draining of intracellular NADH that coincides with substantial loss of culturability. Conversely, without manganese, nongrowing cells persisted to acidify for weeks, albeit at a reduced rate, but maintaining redox balance and culturability. Strikingly, despite being unculturable, a-keto acid-derived aldehydes continued to accumulate in cells incubated in the presence of manganese, whereas without manganese cells predominantly formed the corresponding alcohols. This is most likely reflecting NADH availability for the alcohol dehydrogenase-catalyzed conversion. Overall, manganese influences the lactococcal acidification rate, and flavor formation capacity in a redox dependent manner. These are important industrial traits especially during cheese ripening, where cells are in a non-growing, often unculturable state. IMPORTANCE In nature as well as in various biotechnology applications, microorganisms are often in a nongrowing state and their metabolic persistence determines cell survival and functionality. Industrial examples are dairy fermentations where bacteria remain active during the ripening phases that can take up to months and even years. Here we investigated environmental factors that can influence lactococcal metabolic persistence throughout such prolonged periods. We found that in the absence of manganese, acidification of nongrowing cells remained active for weeks while in the presence of manganese it stopped within 1 day. The latter coincided with the accumulation of amino acid derived volatile metabolites. Based on metabolic conversions, proteome analysis, and a reporter assay, we demonstrated that the manganese elicited effects were NADH dependent. Overall the results show the effect of environmental modulation on prolonged cell-based catalysis, which is highly relevant to nongrowing cells in nature and biotechnological applications.

### 10) Quantification of endocannabinoids in human cerebrospinal fluid using a novel micro-flow liquid chromatography-mass spectrometry method

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The endocannabinoid system (ECS) is implicated in various brain disorders. Changes in the composition of the cerebrospinal fluid (CSF) may be associated with ECS-related pathologies. Endocannabinoids (eCBs) and their analogues are present at low concentrations in human CSF, which hampered the investigation of the ECS in this body fluid. In this study, we developed a highly sensitive and selective micro-flow liquid chromatography-tandem mass spectrometry (micro-LC-MS/MS) method for the analysis of eCBs and eCB analogues in human CSF. The developed method allowed for the quantitative analysis of 16 eCBs and their analogues in human CSF. Micro-LC-MS/MS analyses were performed at a flow-rate of 4 μL min−1 with a 0.3-mm inner diameter column. A minor modification of a novel spray needle was carried out to improve the robustness of our method. By using an injection volume of 3 μL, our method reached limits of detection in the range from 0.6 to 1293.4 pM and limits of quantification in range from 2.0 to 4311.3 pM while intra- and interday precisions were below 13.7%. The developed workflow was successfully used for the determination of eCBs in 288 human CSF samples. It is anticipated that the proposed approach will contribute to a deeper understanding of the role of ECS in various brain disorders.

### 11) Chemical potential, derivative discontinuity, fractional electrons, jump of the Kohn-Sham potential, atoms as thermodynamic open systems, and other (mis)conceptions of the density functional theory of electrons in molecules

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Many references exist in the density functional theory (DFT) literature to the chemical potential of the electrons in an atom or a molecule. The origin of this notion has been the identification of the Lagrange multiplier μ = ∂E/∂N in the Euler-Lagrange variational equation for the ground state density as the chemical potential of the electrons. We first discuss why the Lagrange multiplier in this case is an arbitrary constant and therefore cannot be a physical characteristic of an atom or molecule. The switching of the energy derivative (“chemical potential”) from −I to −A when the electron number crosses the integer, called integer discontinuity or derivative discontinuity, is not physical but only occurs when the nonphysical noninteger electron systems and the corresponding energy and derivative ∂E/∂N are chosen in a specific discontinuous way. The question is discussed whether in fact the thermodynamical concept of a chemical potential can be defined for the electrons in such few-electron systems as atoms and molecules. The conclusion is that such systems lack important characteristics of thermodynamic systems and do not afford the definition of a chemical potential. They also cannot be considered as analogues of the open systems of thermodynamics that can exchange particles with an environment (a particle bath or other members of a Gibbsian ensemble). Thermodynamical (statistical mechanical) concepts like chemical potential, open systems, grand canonical ensemble etc. are not applicable to a few electron system like an atom or molecule. A number of topics in DFT are critically reviewed in light of these findings: jumps in the Kohn-Sham potential when crossing an integer number of electrons, the band gap problem, the deviation-from-straight-lines error, and the role of ensembles in DFT.

### 12) Developing a classification scheme of service innovation: Synthesizing degree and type of change in service innovation

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Innovation research has resulted in various methods to classify service innovations, which primarily feature either the degree of change or type of change. This paper develops a novel classification scheme, based on a four-dimensional view of innovativeness. The classification scheme simultaneously concerns both the degree and type of change in service innovations. A multiple-case study is conducted in the empirical settings of theme parks and airlines, with 11 service innovation projects situated in Walt Disney World, Singapore Airlines, or China Eastern Airlines. Following the proposed scheme, the 11 cases are analyzed and classified into four dimensions: environment-, technology-, market-, and organization-dominant service innovations. The scheme offers academics and practitioners an integral understanding through four dimensions that build on each other.

### 13) Clarifying notes on the bonding analysis adopted by the energy decomposition analysis

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* Processed: 2022-6

We discuss the fundamental aspects of the EDA-NOCV method and address some critical comments that have been made recently. The EDA-NOCV method unlike most other methods focuses on the process of bond formation between the interacting species and not just only on the analysis of the finally formed bond. This is demonstrated using LiF as an example. There is a difference between the interactions between the initial species which form the bond and are also the final product of bond cleavage, and the interactions between the fragments in the eventually formed molecule. The flexibility of the method allows the choice of the interacting fragments which helps to identify the charge and electron configuration of the fragments which describe the bond. This is very helpful in cases where the bond may be described with several Lewis structures. We reject the idea that it would be a disadvantage to have “bond path functions” as the energy components in the EDA, which actually indicate the variability of the method. The bonding analysis in a different sequence of the bond formation gives important results for the various questions that can be asked. This is demonstrated by using CH2, CO2 and the formation of a guanine quartet as examples. The fact that a bond is always defined by the bound molecule, the fragments, and their states is universal and deeply physical, as we show here again for various examples. The results of the EDA-NOCV method are in full accordance with the physical mechanism of the chemical bond as revealed by Ruedenberg.

### 14) Excess ribosomal protein production unbalances translation in a model of Fragile X Syndrome

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Dysregulated protein synthesis is a core pathogenic mechanism in Fragile X Syndrome (FX). The mGluR Theory of FX predicts that pathological synaptic changes arise from the excessive translation of mRNAs downstream of mGlu1/5 activation. Here, we use a combination of CA1 pyramidal neuron-specific TRAP-seq and proteomics to identify the overtranslating mRNAs supporting exaggerated mGlu1/5 -induced long-term synaptic depression (mGluR-LTD) in the FX mouse model (Fmr1−/y). Our results identify a significant increase in the translation of ribosomal proteins (RPs) upon mGlu1/5 stimulation that coincides with a reduced translation of long mRNAs encoding synaptic proteins. These changes are mimicked and occluded in Fmr1−/y neurons. Inhibiting RP translation significantly impairs mGluR-LTD and prevents the length-dependent shift in the translating population. Together, these results suggest that pathological changes in FX result from a length-dependent alteration in the translating population that is supported by excessive RP translation.

### 15) Quality criteria for in vitro human pluripotent stem cell-derived models of tissue-based cells

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The advent of the technology to isolate or generate human pluripotent stem cells provided the potential to develop a wide range of human models that could enhance understanding of mechanisms underlying human development and disease. These systems are now beginning to mature and provide the basis for the development of in vitro assays suitable to understand the biological processes involved in the multi-organ systems of the human body, and will improve strategies for diagnosis, prevention, therapies and precision medicine. Induced pluripotent stem cell lines are prone to phenotypic and genotypic changes and donor/clone dependent variability, which means that it is important to identify the most appropriate characterization markers and quality control measures when sourcing new cell lines and assessing differentiated cell and tissue culture preparations for experimental work. This paper considers those core quality control measures for human pluripotent stem cell lines and evaluates the state of play in the development of key functional markers for their differentiated cell derivatives to promote assurance of reproducibility of scientific data derived from pluripotent stem cell-based systems.

### 16) Assessing MP2 frozen natural orbitals in relativistic correlated electronic structure calculations

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* Published 14 Jun 2022 (early online 9 Jun 2022)
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The high computational scaling with the basis set size and the number of correlated electrons is a bottleneck limiting applications of coupled cluster algorithms, in particular for calculations based on two- or four-component relativistic Hamiltonians, which often employ uncontracted basis sets. This problem may be alleviated by replacing canonical Hartree-Fock virtual orbitals by natural orbitals (NOs). In this paper, we describe the implementation of a module for generating NOs for correlated wavefunctions and, in particular, second order Møller-Plesset perturbation frozen natural orbitals (MP2FNOs) as a component of our novel implementation of relativistic coupled cluster theory for massively parallel architectures [Pototschnig et al. J. Chem. Theory Comput. 17, 5509, (2021)]. Our implementation can manipulate complex or quaternion density matrices, thus allowing for the generation of both Kramers-restricted and Kramers-unrestricted MP2FNOs. Furthermore, NOs are re-expressed in the parent atomic orbital (AO) basis, allowing for generating coupled cluster singles and doubles NOs in the AO basis for further analysis. By investigating the truncation errors of MP2FNOs for both the correlation energy and molecular properties - electric field gradients at the nuclei, electric dipole and quadrupole moments for hydrogen halides HX (X = F-Ts), and parity-violating energy differences for H2Z2 (Z = O-Se) - we find MP2FNOs accelerate the convergence of the correlation energy in a roughly uniform manner across the Periodic Table. It is possible to obtain reliable estimates for both energies and the molecular properties considered with virtual molecular orbital spaces truncated to about half the size of the full spaces.

### 17) Optimization of Peptide Linker-Based Fluorescent Ligands for the Histamine H1Receptor

* Kok, Z. Y., Stoddart, L. A., Mistry, S. J., Mocking, T. A., Vischer, H. F., Leurs, R., Hill, S. J., Mistry, S. N., Kellam, B.
* Medicinal chemistry, AIMMS, University of Nottingham, University of Birmingham
* Journal of medicinal chemistry
* https://doi.org/10.1021/acs.jmedchem.2c00125
* Corresponding author: Kellam, B.
* Published 23 Jun 2022 (early online 3 Jun 2022)
* Processed: 2022-6

The histamine H1 receptor (H1R) has recently been implicated in mediating cell proliferation and cancer progression; therefore, high-affinity H1R-selective fluorescent ligands are desirable tools for further investigation of this behavior in vitro and in vivo. We previously reported a H1R fluorescent ligand, bearing a peptide-linker, based on antagonist VUF13816 and sought to further explore structure-activity relationships (SARs) around the linker, orthostere, and fluorescent moieties. Here, we report a series of high-affinity H1R fluorescent ligands varying in peptide linker composition, orthosteric targeting moiety, and fluorophore. Incorporation of a boron-dipyrromethene (BODIPY) 630/650-based fluorophore conferred high binding affinity to our H1R fluorescent ligands, remarkably overriding the linker SAR observed in corresponding unlabeled congeners. Compound 31a, both potent and subtype-selective, enabled H1R visualization using confocal microscopy at a concentration of 10 nM. Molecular docking of 31a with the human H1R predicts that the optimized peptide linker makes interactions with key residues in the receptor.

### 18) Transition metal-catalysed carbene- and nitrene transfer to carbon monoxide and isocyanides

* Roose, T. R., Verdoorn, D. S., Mampuys, P., Ruijter, E., Maes, B. U., Orru, R. V.
* Organic Chemistry, AIMMS, Chemistry and Pharmaceutical Sciences, Maastricht University, University of Antwerp
* Chemical Society Reviews
* https://doi.org/10.1039/d1cs00305d
* Corresponding author: Ruijter, E.
* Published 24 Jun 2022 (early online None)
* Processed: 2022-6

Transition metal-catalysed carbene- and nitrene transfer to the C1-building blocks carbon monoxide and isocyanides provides heteroallenes (i.e. ketenes, isocyanates, ketenimines and carbodiimides). These are versatile and reactive compounds allowing in situ transformation towards numerous functional groups and organic compounds, including heterocycles. Both one-pot and tandem processes have been developed providing valuable synthetic methods for the organic chemistry toolbox. This review discusses all known transition metal-catalysed carbene- and nitrene transfer reactions towards carbon monoxide and isocyanides and in situ transformation of the heteroallenes hereby obtained, with a special focus on the general mechanistic considerations.

### 19) Full humanization of the glycolytic pathway in Saccharomyces cerevisiae

* Boonekamp, F. J., Knibbe, E., Vieira-Lara, M. A., Wijsman, M., Luttik, M. A., van Eunen, K., Ridder, M. D., Bron, R., Almonacid Suarez, A. M., van Rijn, P., Wolters, J. C., Pabst, M., Daran, J. M., Bakker, B. M., Daran-Lapujade, P.
* Molecular Cell Physiology, AIMMS, Delft University of Technology, University of Groningen
* Cell Reports
* https://doi.org/10.1016/j.celrep.2022.111010
* Corresponding author: None
* Published 28 Jun 2022 (early online None)
* Processed: 2022-6

Although transplantation of single genes in yeast plays a key role in elucidating gene functionality in metazoans, technical challenges hamper humanization of full pathways and processes. Empowered by advances in synthetic biology, this study demonstrates the feasibility and implementation of full humanization of glycolysis in yeast. Single gene and full pathway transplantation revealed the remarkable conservation of glycolytic and moonlighting functions and, combined with evolutionary strategies, brought to light context-dependent responses. Human hexokinase 1 and 2, but not 4, required mutations in their catalytic or allosteric sites for functionality in yeast, whereas hexokinase 3 was unable to complement its yeast ortholog. Comparison with human tissues cultures showed preservation of turnover numbers of human glycolytic enzymes in yeast and human cell cultures. This demonstration of transplantation of an entire essential pathway paves the way for establishment of species-, tissue-, and disease-specific metazoan models.

### 20) Polycyclic aromatic hydrocarbon growth in a benzene discharge explored by IR-UV action spectroscopy

* Lemmens, A. K., Rap, D. B., Brünken, S., Buma, W. J., Rijs, A. M.
* BioAnalytical Chemistry, AIMMS, University of Amsterdam, Radboud University Nijmegen
* Physical Chemistry Chemical Physics
* https://doi.org/10.1039/d2cp01631a
* Corresponding author: Lemmens, A. K.
* Published 28 Jun 2022 (early online 13 Jun 2022)
* Processed: 2022-6

Infrared signatures of polycyclic aromatic hydrocarbons (PAHs) are detected towards many phases of stellar evolution. PAHs are major players in the carbon chemistry of the interstellar medium, forming the connection between small hydrocarbons and large fullerenes. However, as details on the formation of PAHs in these environments are still unclear, modeling their abundance and chemistry has remained far from trivial. By combining molecular beam mass-selective IR spectroscopy and calculated IR spectra, we analyze the discharge of benzene and identify resulting products including larger PAHs, radicals and intermediates that serve as promising candidates for radio astronomical searches. The identification of various reaction products indicates that different gas-phase reaction mechanisms leading to PAH growth must occur under the same conditions to account for all observed PAH-related species, thereby revealing the complex and interconnected network of PAH formation pathways. The results of this study highlight key (exothermic) reactions that need to be included in astrochemical models describing the carbon chemistry in our universe.

### 21) Nicotinamide Riboside and Dihydronicotinic Acid Riboside Synergistically Increase Intracellular NAD+ by Generating Dihydronicotinamide Riboside

* Ciarlo, E., Joffraud, M., Hayat, F., Giner, M. P., Giroud‐gerbetant, J., Sanchez‐garcia, J. L., Rumpler, M., Moco, S., Migaud, M. E., Cantó, C.
* Molecular and Computational Toxicology, AIMMS, Nestle, University of South Alabama, Swiss Federal Institute of Technology Lausanne
* Nutrients
* https://doi.org/10.3390/nu14132752
* Corresponding author: Migaud, M. E.
* Published 1 Jul 2022 (early online None)
* Processed: 2022-7

Through evolution, eukaryote organisms have developed the ability to use different molecules as independent precursors to generate nicotinamide adenine dinucleotide (NAD+), an essential molecule for life. However, whether these different precursors act in an additive or complementary manner is not truly well understood. Here, we have evaluated how combinations of different NAD+ precursors influence intracellular NAD+ levels. We identified dihydronicotinic acid riboside (NARH) as a new NAD+ precursor in hepatic cells. Second, we demonstrate how NARH, but not any other NAD+ precursor, can act synergistically with nicotinamide riboside (NR) to increase NAD+ levels in cultured cells and in mice. Finally, we demonstrate that the large increase in NAD+ prompted by the combination of these two precursors is due to their chemical interaction and conversion to dihydronicotinamide riboside (NRH). Altogether, this work demonstrates for the first time that NARH can act as a NAD+ precursor in mammalian cells and how different NAD+ precursors can interact and influence each other when co‐administered.

### 22) Overexpression of the Bam Complex Improves the Production of Chlamydia trachomatis MOMP in the E. coli Outer Membrane

* Huynh, D. T., Jong, W. S., Koningstein, G. M., van Ulsen, P., Luirink, J.
* Molecular Microbiology, AIMMS, LaserLaB - Analytical Chemistry and Spectroscopy, LaserLaB - Molecular Biophysics
* International Journal of Molecular Sciences
* https://doi.org/10.3390/ijms23137393
* Corresponding author: van Ulsen, P.
* Published 1 Jul 2022 (early online None)
* Processed: 2022-7

A licensed Chlamydia trachomatis (Ct) vaccine is not yet available. Recombinant Chlamydia trachomatis major outer membrane protein (Ct-MOMP), the most abundant constituent of the chlamydial outer membrane complex, is considered the most attractive candidate for subunit-based vaccine formulations. Unfortunately, Ct-MOMP is difficult to express in its native structure in the E. coli outer membrane (OM). Here, by co-expression of the Bam complex, we improved the expression and localization of recombinant Ct-MOMP in the E. coli OM. Under these conditions, recombinant Ct-MOMP appeared to assemble into a β-barrel conformation and express domains at the cell surface indicative of correct folding. The data indicate that limited availability of the Bam complex can be a bottleneck for the production of heterologous OM vaccine antigens, information that is also relevant for strategies aimed at producing recombinant OMV-based vaccines.

### *23) IGF-1R is a molecular determinant for response to p53 reactivation therapy in conjunctival melanoma*

* Song, D., Cismas, S., Crudden, C., Trocme, E., Worrall, C., Suleymanova, N., Lin, T., Zheng, H., Seregard, S., Girnita, A., Girnita, L.Pages:600-611
* Medicinal chemistry, AIMMS
* Oncogene
* https://doi.org/10.1038/s41388-021-02111-x
* Corresponding author: None
* Published 21 Jan 2022 (early online None)
* Processed: 2022-1

...

### *24) ENT-A010, a Novel Steroid Derivative, Displays Neuroprotective Functions and Modulates Microglial Responses*

* Yilmaz, C., Rogdakis, T., Latorrata, A., Thanou, E., Karadima, E., Papadimitriou, E., Siapi, E., Li, K. W., Katsila, T., Calogeropoulou, T., Charalampopoulos, I., Alexaki, V. I.
* Amsterdam Neuroscience - Neurodegeneration, Molecular and Cellular Neurobiology, AIMMS, Amsterdam Neuroscience - Cellular & Molecular Mechanisms, University Hospital Carl Gustav Carus, University of Crete, Foundation for Research and Technology-Hellas, National Hellenic Research Foundation
* Biomolecules
* https://doi.org/10.3390/biom12030424
* Corresponding author: Alexaki, V. I.
* Published Mar 2022 (early online 12 Mar 2022)
* Processed: 2022-3

Tackling neurodegeneration and neuroinflammation is particularly challenging due to the complexity of central nervous system (CNS) disorders, as well as the limited drug accessibility to the brain. Th ...

### *25) Phosphine addition to dehydroalanine for peptide modification*

* Liu, M., Sovrovic, M., Suga, H., Jongkees, S. A.
* AIMMS, Chemistry and Pharmaceutical Sciences, Utrecht University, University of Tokyo
* Organic and Biomolecular Chemistry
* https://doi.org/10.1039/d2ob00410k
* Corresponding author: Jongkees, S. A.
* Published 24 Mar 2022 (early online None)
* Processed: 2022-3

Thiols are a functional group commonly used for selective reactions in a biochemical setting because of their high nucleophilicity. Phosphorus nucleophiles can undergo some similar reactions to thiols ...

### *26) Metabolic Modeling of Wine Fermentation at Genome Scale*

* Mendoza, S. N., Saa, P. A., Teusink, B., Agosin, E.
* Systems Bioinformatics, AIMMS, Systems Bioinformatics, Pontificia Universidad Católica de Chile
* None
* https://doi.org/10.1007/978-1-0716-1831-8\_16
* Corresponding author: Agosin, E.
* Published 2022 (early online None)
* Processed: 2022-4

Wine fermentation is an ancient biotechnological process mediated by different microorganisms such as yeast and bacteria. Understanding of the metabolic and physiological phenomena taking place during ...

### *27) C−X Bond Activation by Palladium: Steric Shielding versus Steric Attraction*

* Hansen, T., Sun, X., Dalla Tiezza, M., van Zeist, W. J., van Stralen, J. N., Geerke, D. P., Wolters, L. P., Poater, J., Hamlin, T. A., Bickelhaupt, F. M.
* Chemistry and Pharmaceutical Sciences, Theoretical Chemistry, Molecular and Computational Toxicology, AIMMS, Vrije Universiteit Amsterdam
* Chemistry - A European Journal
* https://doi.org/10.1002/chem.202201093
* Corresponding author: Hamlin, T. A.
* Published 11 Apr 2022 (early online None)
* Processed: 2022-4

The C−X bond activation (X = H, C) of a series of substituted C(n°)−H and C(n°)−C(m°) bonds with C(n°) and C(m°) = H3C− (methyl, 0°), CH3H2C− (primary, 1°), (CH3)2HC− (secondary, 2°), (CH3)3C− (tertia ...

### *28) How Ionization Catalyzes Diels-Alder Reactions*

* Vermeeren, P., Hamlin, T. A., Bickelhaupt, F. M.
* Theoretical Chemistry, AIMMS, Chemistry and Pharmaceutical Sciences
* Chemistry - A European Journal
* https://doi.org/10.1002/chem.202200987
* Corresponding author: Hamlin, T. A.
* Published 20 Apr 2022 (early online None)
* Processed: 2022-4

The catalytic effect of ionization on the Diels-Alder reaction between 1,3-butadiene and acrylaldehyde has been studied using relativistic density functional theory (DFT). Removal of an electron from ...

### *29) Studying Metabolism by NMR-Based Metabolomics*

* Moco, S.
* Molecular and Computational Toxicology, AIMMS
* Frontiers in Molecular Biosciences
* https://doi.org/10.3389/fmolb.2022.882487
* Corresponding author: Moco, S.
* Published 27 Apr 2022 (early online None)
* Processed: 2022-4

During the past few decades, the direct analysis of metabolic intermediates in biological samples has greatly improved the understanding of metabolic processes. The most used technologies for these ad ...

### *30) Probing Noncovalent Interactions in [3,3]Metaparacyclophanes*

* Jian, J., Hammink, R., Tinnemans, P., Bickelhaupt, F. M., McKenzie, C. J., Poater, J., Mecinović, J.
* Chemistry and Pharmaceutical Sciences, AIMMS, University of Southern Denmark, Radboud University Nijmegen
* Journal of Organic Chemistry
* https://doi.org/10.1021/acs.joc.2c00350
* Corresponding author: Mecinović, J.
* Published 6 May 2022 (early online 26 Apr 2022)
* Processed: 2022-5

Arene-arene interactions are fundamentally important in molecular recognition. To precisely probe arene-arene interactions in cyclophanes, we designed and synthesized (2,6-phenol)paracyclophanes and ( ...

### *31) Probing the redox-conversion of Co(II)-disulfide to Co(III)-thiolate complexes: the effect of ligand-field strength*

* Marvelous, C., de Azevedo Santos, L., Siegler, M. A., Fonseca Guerra, C., Bouwman, E.
* Theoretical Chemistry, AIMMS, Leiden University, Johns Hopkins University
* Dalton transactions (Cambridge, England : 2003)
* https://doi.org/10.1039/d2dt00356b
* Corresponding author: None
* Published 24 May 2022 (early online 11 Apr 2022)
* Processed: 2022-5

The redox-conversion reaction of cobalt(II)-disulfide to cobalt(III)-thiolate complexes triggered by addition of the bidentate ligand 2,2'-bipyridine has been investigated. Reaction of the cobalt(II)- ...

### *32) Modern venomics-Current insights, novel methods, and future perspectives in biological and applied animal venom research*

* von Reumont, B. M., Anderluh, G., Antunes, A., Ayvazyan, N., Beis, D., Caliskan, F., Crnković, A., Damm, M., Dutertre, S., Ellgaard, L., Gajski, G., German, H., Halassy, B., Hempel, B. F., Hucho, T., Igci, N., Ikonomopoulou, M. P., Karbat, I., Klapa, M. I., Koludarov, I., Kool, J., Lüddecke, T., Ben Mansour, R., Vittoria Modica, M., Moran, Y., Nalbantsoy, A., Ibáñez, M. E. P., Panagiotopoulos, A., Reuveny, E., Céspedes, J. S., Sombke, A., Surm, J. M., Undheim, E. A., Verdes, A., Zancolli, G.
* BioAnalytical Chemistry, AIMMS, Goethe University Frankfurt, LOEWE Centre for Translational Biodiversity Genomics, Justus Liebig University Giessen, National Institute of Chemistry Ljubljana, University of Porto, National Academy of Sciences of the Republic of Armenia, Academy of Athens, Osmangazi University, Technical University of Berlin, Université de Montpellier, University of Copenhagen, Institute for Medical Research and Occupational Health, Vrije Universiteit Amsterdam, University of Zagreb, Charité – Universitätsmedizin Berlin, University of Cologne, Nevsehir Haci Bektas Veli Universitesi, IMDEA Food Institute, University of Queensland, Weizmann Institute of Science, Foundation for Research and Technology-Hellas, Fraunhofer Institute for Molecular Biology and Applied Ecology, Gafsa University, Stazione Zoologica Anton Dohrn Napoli, Hebrew University of Jerusalem, Ege University, Hospital Universitario Virgen del Rocio, Instituto de Salud Carlos III, University of Patras, University of Vienna, University of Oslo, CSIC, University of Lausanne, Swiss Institute of Bioinformatics
* GigaScience
* https://doi.org/10.1093/gigascience/giac048
* Corresponding author: None
* Published 2022 (early online 18 May 2022)
* Processed: 2022-5

Venoms have evolved >100 times in all major animal groups, and their components, known as toxins, have been fine-tuned over millions of years into highly effective biochemical weapons. There are many ...

### *33) Fragmentation Dynamics of Fluorene Explored Using Ultrafast XUV-Vis Pump-Probe Spectroscopy*

* Garg, D., Lee, J. W., Tikhonov, D. S., Chopra, P., Steber, A. L., Lemmens, A. K., Erk, B., Allum, F., Boll, R., Cheng, X., Düsterer, S., Gruet, S., He, L., Heathcote, D., Johny, M., Kazemi, M. M., Köckert, H., Lahl, J., Loru, D., Maclot, S., Mason, R., Müller, E., Mullins, T., Olshin, P., Passow, C., Peschel, J., Ramm, D., Rompotis, D., Trippel, S., Wiese, J., Ziaee, F., Bari, S., Burt, M., Küpper, J., Rijs, A. M., Rolles, D., Techert, S., Eng-Johnsson, P., Brouard, M., Vallance, C., Manschwetus, B., Schnell, M.
* BioAnalytical Chemistry, AIMMS, German Electron Synchrotron, University of Hamburg, University of Oxford, Kiel University, University of Amsterdam, Radboud University Nijmegen, European XFEL, Lund University, University of Gothenburg, Ulsan National Institute of Science and Technology, Kansas State University, University of Göttingen
* Frontiers in Physics
* https://doi.org/10.3389/fphy.2022.880793
* Corresponding author: Schnell, M.
* Published May 2022 (early online 12 May 2022)
* Processed: 2022-5

We report on the use of extreme ultraviolet (XUV, 30.3nm) radiation from the Free-electron LASer in Hamburg (FLASH) and visible (Vis, 405nm) photons from an optical laser to investigate the relaxation ...

### *34) Acute, Sublethal, and Developmental Toxicity of Kratom (Mitragyna speciosa Korth.) Leaf Preparations on Caenorhabditis elegans as an Invertebrate Model for Human Exposure*

* Hughes, S., van de Klashorst, D., Veltri, C. A., Grundmann, O.
* E&H: Environmental Health and Toxicology, AIMMS, AMS - Ageing & Vitality, AMS - Musculoskeletal Health, HAN University of Applied Sciences, Midwestern University Glendale, University of Florida
* International Journal of Environmental Research and Public Health
* https://doi.org/10.3390/ijerph19106294
* Corresponding author: Grundmann, O.
* Published 2 May 2022 (early online None)
* Processed: 2022-5

Kratom (Mitragyna speciosa Korth.) is a tree native to Southeast Asia with stimulant and opioid-like effects which has seen increased use in Europe and North America in recent years. Its safety and ph ...

### *35) Genetic Elements Orchestrating Lactobacillus crispatus Glycogen Metabolism in the Vagina*

* Hertzberger, R., May, A., Kramer, G., van Vondelen, I., Molenaar, D., Kort, R.
* Molecular Cell Physiology, AIMMS, Systems Bioinformatics, Micropia, Natura Artis Magistra, DSM Food Specialties, University of Amsterdam, Vrije Universiteit Amsterdam
* International Journal of Molecular Sciences
* https://doi.org/10.3390/ijms23105590
* Corresponding author: Kort, R.
* Published 2 May 2022 (early online None)
* Processed: 2022-5

Glycogen in the female lower reproductive tract is a major carbon source for colonization and acidification by common vaginal Lactobacillus species, such as Lactobacillus crispatus. Previously, we ide ...

### *36) Plasma Levels of Endocannabinoids and Their Analogues Are Related to Specific Fecal Bacterial Genera in Young Adults: Role in Gut Barrier Integrity*

* Ortiz-Alvarez, L., Xu, H., Di, X., Kohler, I., Osuna-Prieto, F. J., Acosta, F. M., Vilchez-Vargas, R., Link, A., Plaza-Díaz, J., van der Stelt, M., Hankemeier, T., Clemente-Postigo, M., Tinahones, F. J., Gil, A., Rensen, P. C., Ruiz, J. R., Martinez-Tellez, B.
* BioAnalytical Chemistry, AIMMS, University of Granada, Leiden University, Research and Development of Functional Food Center (CIDAF), University of Turku, Otto von Guericke University Magdeburg, University of Ottawa, Hospital Universitario Reina Sofía, Hospital Universitari Virgen de la Victoria, Instituto de Salud Carlos III, Instituto de Investigación Biosanitaria de Granada, University of Almeria
* Nutrients
* https://doi.org/10.3390/nu14102143
* Corresponding author: Ruiz, J. R.
* Published 2 May 2022 (early online None)
* Processed: 2022-5

Objective: To investigate the association of plasma levels of endocannabinoids with fecal microbiota. Methods: Plasma levels of endocannabinoids, anandamide (AEA) and 2-arachidonoylglycerol (2-AG), as ...

### *37) Fate of Per- and Polyfluoroalkyl Substances from Durable Water-Repellent Clothing during Use*

* Van Der Veen, I., Schellenberger, S., Hanning, A. C., Stare, A., De Boer, J., Weiss, J. M., Leonards, P. E.
* E&H: Environmental Bioanalytical Chemistry, AIMMS, E&H: Environmental Health and Toxicology, Stockholm University, RISE Research Institutes of Sweden AB, Swerea AB
* Environmental Science and Technology
* https://doi.org/10.1021/acs.est.1c07876
* Corresponding author: Van Der Veen, I.
* Published 3 May 2022 (early online None)
* Processed: 2022-5

To make outdoor clothing water- or dirt-repellent, durable water-repellent (DWR) coatings based on side-chain fluorinated polymers (SFPs) are used. During use of outdoor clothing, per- and polyfluoroa ...

### *38) Natural range separation of the Coulomb hole*

* Via-Nadal, M., Rodríguez-Mayorga, M., Ramos-Cordoba, E., Matito, E.
* Theoretical Chemistry, AIMMS, Donostia International Physics Center
* The Journal of chemical physics
* https://doi.org/10.1063/5.0085284
* Corresponding author: None
* Published 14 May 2022 (early online 10 May 2022)
* Processed: 2022-5

A natural range separation of the Coulomb hole into two components, one of them being predominant at long interelectronic separations (hcI ) and the other at short distances (hcII ), is exhaustively a ...

### *39) Convergent evolution of toxin resistance in animals*

* van Thiel, J., Khan, M. A., Wouters, R. M., Harris, R. J., Casewell, N. R., Fry, B. G., Kini, R. M., Mackessy, S. P., Vonk, F. J., Wüster, W., Richardson, M. K.
* Chemistry and Pharmaceutical Sciences, AIMMS, Leiden University, University of Queensland, Liverpool School of Tropical Medicine, National University of Singapore, Virginia Commonwealth University, University Northern Colorado, Bangor University
* Biological Reviews
* https://doi.org/10.1111/brv.12865
* Corresponding author: van Thiel, J.
* Published 17 May 2022 (early online None)
* Processed: 2022-5

Convergence is the phenomenon whereby similar phenotypes evolve independently in different lineages. One example is resistance to toxins in animals. Toxins have evolved many times throughout the tree ...

### *40) Frankenstein's followers. Maintenance of human cells outside the body.*

* Pfaller, W., Jennings, P.
* Molecular and Computational Toxicology, AIMMS, Innsbruck Medical University
* Toxicology in Vitro
* https://doi.org/10.1016/j.tiv.2022.105387
* Corresponding author: Jennings, P.
* Published Aug 2022 (early online 17 May 2022)
* Processed: 2022-5

Issue 1Although science can endeavour to do a great many things, unachievable thus far, these activities should be, but seldom are, tempered with the question, should we really do it? This is not nece ...

### *41) Methods Included: Standardizing Computational Reuse and Portability with the Common Workflow Language*

* Crusoe, M. R., Abeln, S., Iosup, A., Amstutz, P., Chilton, J., Tijanić, N., Ménager, H., Soiland-Reyes, S., Goble, C.
* Computer Systems, Network Institute, Computer Systems, Bioinformatics, AIMMS, Integrative Bioinformatics, Massivizing Computer Systems
* Communications of the ACM
* https://doi.org/10.1145/3486897
* Corresponding author: None
* Published 20 May 2022 (early online None)
* Processed: 2022-5

A widely used standard for portable multilingual data analysis pipelines would enable considerable benefits to scholarly publication reuse, research/industry collaboration, regulatory cost control, an ...

### *42) 3-nitroimidazo[1,2-b]pyridazine as a novel scaffold for antiparasitics with sub-nanomolar anti-Giardia lamblia activity*

* Zheng, Y., Müller, J., Kunz, S., Siderius, M., Maes, L., Caljon, G., Müller, N., Hemphill, A., Sterk, G. J., Leurs, R.
* Medicinal chemistry, AIMMS, University of Bern, University of Antwerp
* International Journal for Parasitology: Drugs and Drug Resistance
* https://doi.org/10.1016/j.ijpddr.2022.05.004
* Corresponding author: Leurs, R.
* Published Aug 2022 (early online 26 May 2022)
* Processed: 2022-5

As there is a continuous need for novel anti-infectives, the present study aimed to fuse two modes of action into a novel 3-nitroimidazo[1,2-b]pyridazine scaffold to improve antiparasitic efficacy. Fo ...

### *43) Escape from planarity in fragment-based drug discovery: A synthetic strategy analysis of synthetic 3D fragment libraries*

* Klein, H. F., Hamilton, D. J., de Esch, I. J., Wijtmans, M., O'Brien, P.
* Medicinal chemistry, AIMMS, Chemistry and Pharmaceutical Sciences, University of York
* Drug Discovery Today
* https://doi.org/10.1016/j.drudis.2022.05.021
* Corresponding author: O'Brien, P.
* Published 27 May 2022 (early online None)
* Processed: 2022-5

In fragment-based drug discovery (FBDD), there is a developing appreciation that 3D fragments could offer opportunities that are not provided by 2D fragments. This review provides an overview of the s ...

### *44) Direct transcriptomic comparison of xenobiotic metabolism and toxicity pathway induction of airway epithelium models at an air–liquid interface generated from induced pluripotent stem cells and primary bronchial epithelial cells*

* Djidrovski, I., Georgiou, M., Tasinato, E., Leonard, M. O., Van den Bor, J., Lako, M., Armstrong, L.
* Medicinal chemistry, AIMMS, Newcells Biotech Ltd., Newcastle University, Public Health England
* Cell biology and toxicology
* https://doi.org/10.1007/s10565-022-09726-0
* Corresponding author: Armstrong, L.
* Published 31 May 2022 (early online None)
* Processed: 2022-5

Abstract: The airway epithelium represents the main barrier between inhaled air and the tissues of the respiratory tract and is therefore an important point of contact with xenobiotic substances into ...

### *45) Liquid Core Waveguide Cell with in Situ Absorbance Spectroscopy and Coupled to Liquid Chromatography for Studying Light-Induced Degradation*

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In many areas, studying photostability or the mechanism of photodegradation is of high importance. Conventional methods to do so can be rather time-consuming, laborious, and prone to experimental erro ...