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25. *A single-step preparation of carbohydrate functionalized mon (2020-8)*

### 1) Pre-exascale accelerated application development: The ORNL Summit experience

* Luo, L., Straatsma, T. P., Suarez, L. E., Broer, R., Bykov, D., D'Azevedo, E. F., Faraji, S. S., Gottiparthi, K. C., De Graaf, C., Harris, J. A., Havenith, R. W., Jensen, H. J., Joubert, W., Kathir, R. K., Larkin, J., Li, Y. W., Lyakh, D. I., Messer, O. E., Norman, M. R., Oefelein, J. C., Sankaran, R., Tillack, A. F., Barnes, A. L., Visscher, L., Wells, J. C., Wibowo, M.
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* IBM Journal of Research and Development
* https://doi.org/10.1147/JRD.2020.2965881
* Corresponding author: None
* Published 1 May 2020 (early online 15 Jan 2020)
* Processed: 2020-5

High-performance computing (HPC) increasingly relies on heterogeneous architectures to achieve higher performance. In the Oak Ridge Leadership Facility (OLCF), Oak Ridge, TN, USA, this trend continues as its latest supercomputer, Summit, entered production in early 2019. The combination of IBM POWER9 CPU and NVIDIA V100 GPU, along with a fast NVLink2 interconnect and other latest technologies, pushes system performance to a new height and breaks the exascale barrier by certain measures. Due to Summit's powerful GPUs and much higher GPU-CPU ratio, offloading to accelerators becomes a requirement for any application, which intends to effectively use the system. To facilitate navigating a complex landscape of competing heterogeneous architectures, a collection of applications from a wide spectrum of scientific domains is selected for early adoption on Summit. In this article, the experience and lessons learned are summarized, in the hope of providing useful guidance to address new programming challenges, such as scalability, performance portability, and software maintainability, for future application development efforts on heterogeneous HPC systems.

### 2) Differential Role of Serines and Threonines in Intracellular Loop 3 and C-Terminal Tail of the Histamine H4 Receptor in β-Arrestin and G Protein-Coupled Receptor Kinase Interaction, Internalization, and Signaling

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* ACS Pharmacology and Translational Science
* https://doi.org/10.1021/acsptsci.0c00008
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* Published 10 Apr 2020 (early online 16 Mar 2020)
* Processed: 2020-4

The histamine H4 receptor (H4R) activates Gαi-mediated signaling and recruits β-arrestin2 upon stimulation with histamine. β-Arrestins play a regulatory role in G protein-coupled receptor (GPCR) signaling by interacting with phosphorylated serine and threonine residues in the GPCR C-terminal tail and intracellular loop 3, resulting in receptor desensitization and internalization. Using bioluminescence resonance energy transfer (BRET)-based biosensors, we show that G protein-coupled receptor kinases (GRK) 2 and 3 are more quickly recruited to the H4R than β-arrestin1 and 2 upon agonist stimulation, whereas receptor internalization dynamics toward early endosomes was slower. Alanine-substitution revealed that a serine cluster at the distal end of the H4R C-terminal tail is essential for the recruitment of β-arrestin1/2, and consequently, receptor internalization and desensitization of G protein-driven extracellular-signal-regulated kinase (ERK)1/2 phosphorylation and label-free cellular impedance. In contrast, alanine substitution of serines and threonines in the intracellular loop 3 of the H4R did not affect β-arrestin2 recruitment and receptor desensitization, but reduced β-arrestin1 recruitment and internalization. Hence, β-arrestin recruitment to H4R requires the putative phosphorylated serine cluster in the H4R C-terminal tail, whereas putative phosphosites in the intracellular loop 3 have different effects on β-arrestin1 versus β-arrestin2. Mutation of these putative phosphosites in either intracellular loop 3 or the C-terminal tail did not affect the histamine-induced recruitment of GRK2 and GRK3 but does change the interaction of H4R with GRK5 and GRK6, respectively. Identification of H4R interactions with these proteins is a first step in the understanding how this receptor might be dysregulated in pathophysiological conditions.

### 3) Comparison of molecular recognition of trimethyllysine and trimethylthialysine by epigenetic reader proteins

* Hintzen, J. C., Poater, J., Kumar, K., Al Temimi, A. H., Pieters, B. J., Paton, R. S., Bickelhaupt, F. M., Mecinović, J.
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* Molecules
* https://doi.org/10.3390/molecules25081918
* Corresponding author: Paton, R. S.
* Published Apr 2020 (early online 21 Apr 2020)
* Processed: 2020-4

Gaining a fundamental insight into the biomolecular recognition of posttranslationally modified histones by epigenetic reader proteins is of crucial importance to understanding the regulation of the activity of human genes. Here, we seek to establish whether trimethylthialysine, a simple trimethyllysine analogue generated through cysteine alkylation, is a good trimethyllysine mimic for studies on molecular recognition by reader proteins. Histone peptides bearing trimethylthialysine and trimethyllysine were examined for binding with five human reader proteins employing a combination of thermodynamic analyses, molecular dynamics simulations and quantum chemical analyses. Collectively, our experimental and computational findings reveal that trimethylthialysine and trimethyllysine exhibit very similar binding characteristics for the association with human reader proteins, thereby justifying the use of trimethylthialysine for studies aimed at dissecting the origin of biomolecular recognition in epigenetic processes that play important roles in human health and disease.

### 4) Picofractionation & MS imaging: Analytics for pathology profiling of venoms

* Kool, J.
* BioAnalytical Chemistry, AIMMS
* Toxicon : official journal of the International Society on Toxinology
* https://doi.org/10.1016/j.toxicon.2019.10.024
* Corresponding author: None
* Published 20 Apr 2020 (early online None)
* Processed: 2020-4

### 5) Human exposure to synthetic endocrine disrupting chemicals (S-EDCs) is generally negligible as compared to natural compounds with higher or comparable endocrine activity. How to evaluate the risk of the S-EDCs?

* Autrup, H., Barile, F. A., Berry, S. C., Blaauboer, B. J., Boobis, A., Bolt, H., Borgert, C. J., Dekant, W., Dietrich, D., Domingo, J. L., Gori, G. B., Greim, H., Hengstler, J., Kacew, S., Marquardt, H., Pelkonen, O., Savolainen, K., Heslop-Harrison, P., Vermeulen, N. P.
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* Toxicology Letters
* https://doi.org/10.1016/j.toxlet.2020.04.008
* Corresponding author: Greim, H.
* Published 1 Oct 2020 (early online 30 Apr 2020)
* Processed: 2020-4

### 6) Human exposure to synthetic endocrine disrupting chemicals (S-EDCs) is generally negligible as compared to natural compounds with higher or comparable endocrine activity. How to evaluate the risk of the S-EDCs?

* Autrup, H., Barile, F. A., Berry, S. C., Blaauboer, B. J., Boobis, A., Bolt, H., Borgert, C. J., Dekant, W., Dietrich, D., Domingo, J. L., Gori, G. B., Greim, H., Hengstler, J., Kacew, S., Marquardt, H., Pelkonen, O., Savolainen, K., Heslop-Harrison, P., Vermeulen, N. P.
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* Toxicology in Vitro
* https://doi.org/10.1016/j.tiv.2020.104861
* Corresponding author: Blaauboer, B. J.
* Published Sep 2020 (early online 30 Apr 2020)
* Processed: 2020-4

Theoretically, both synthetic endocrine disrupting chemicals (S-EDCs) and natural (exogenous and endogenous) endocrine disrupting chemicals (N-EDCs) can interact with endocrine receptors and disturb hormonal balance. However, compared to endogenous hormones, S-EDCs are only weak partial agonists with receptor affinities several orders of magnitude lower. Thus, to elicit observable effects, S-EDCs require considerably higher concentrations to attain sufficient receptor occupancy or to displace natural hormones and other endogenous ligands. Significant exposures to exogenous N-EDCs may result from ingestion of foods such as soy-based diets, green tea and sweet mustard. While their potencies are lower as compared to natural endogenous hormones, they usually are considerably more potent than S-EDCs. Effects of exogenous N-EDCs on the endocrine system were observed at high dietary intakes. A causal relation between their mechanism of action and these effects is established and biologically plausible. In contrast, the assumption that the much lower human exposures to S-EDCs may induce observable endocrine effects is not plausible. Hence, it is not surprising that epidemiological studies searching for an association between S-EDC exposure and health effects have failed. Regarding testing for potential endocrine effects, a scientifically justified screen should use in vitro tests to compare potencies of S-EDCs with those of reference N-EDCs. When the potency of the S-EDC is similar or smaller than that of the N-EDC, further testing in laboratory animals and regulatory consequences are not warranted.

### 7) Synthesis, Structures, and Electronic Properties of O- And S-Heterocyclic Carbene Complexes of Iridium, Copper, Silver, and Gold

* Joost, M., Nieger, M., Lutz, M., Ehlers, A. W., Slootweg, J. C., Lammertsma, K.
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* https://doi.org/10.1021/acs.organomet.0c00066
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* Published 26 May 2020 (early online 8 May 2020)
* Processed: 2020-5

O- and S-heterocyclic carbenes (OHCs, SHCs) are shown experimentally and computationally to be stronger πacceptors than NHCs and lack, of course, substituents at the heteroatoms. These different electronic and steric characteristics make OHCs and SHCs interesting ligands for coordination chemistry. Convenient synthetic routes are presented to access their iridium(I), iridium(III), and coinage-metal(I) (Cu, Ag, Au) complexes in good yields by means of dissociation of olefins, deprotonation of precursor salts, and transmetalation from a silver carbene complex. Molecular structures and detailed bonding analyses of these complexes are presented.

### 8) Human multidrug resistance protein 4 (MRP4) is a cellular efflux transporter for paracetamol glutathione and cysteine conjugates

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* Archives of Toxicology
* https://doi.org/10.1007/s00204-020-02793-4
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* Published 1 Sep 2020 (early online 29 May 2020)
* Processed: 2020-5

Paracetamol (acetaminophen, APAP) overdose is a leading cause of acute drug-induced liver failure. APAP hepatotoxicity is mediated by the reactive metabolite N-acetyl-p-benzoquinone imine (NAPQI). NAPQI is inactivated by conjugation with glutathione (GSH) to APAP-GSH, which is further converted into its cysteine derivative APAP-CYS. Before necrosis of hepatocytes occurs, APAP-CYS is measurable in plasma of the affected patient and it has been proposed as an early biomarker of acetaminophen toxicity. APAP-GSH and APAP-CYS can be extruded by hepatocytes, but the transporters involved are unknown. In this study we examined whether ATP-binding cassette (ABC) transporters play a role in the cellular efflux of APAP, APAP-GSH, and APAP-CYS. The ABC transport proteins P-gp/ABCB1, BSEP/ABCB11, BCRP/ABCG2, and MRP/ABCC1-5 were overexpressed in HEK293 cells and membrane vesicles were produced. Whereas P-gp, BSEP, MRP3, MRP5, and BCRP did not transport any of the compounds, uptake of APAP-GSH was found for MRP1, MRP2 and MRP4. APAP-CYS appeared to be a substrate of MRP4 and none of the ABC proteins transported APAP. The results suggest that the NAPQI metabolite APAP-CYS can be excreted into plasma by MRP4, where it could be a useful biomarker for APAP exposure and toxicity. Characterization of the cellular efflux of APAP-CYS is important for its development as a biomarker, because plasma concentrations might be influenced by drug-transporter interactions and upregulation of MRP4.

### 9) Compositional Tuning of Carrier Dynamics in Cs2Na1- x

* Zhu, D., Zito, J., Pinchetti, V., Dang, Z., Olivati, A., Pasquale, L., Tang, A., Zaffalon, M. L., Meinardi, F., Infante, I., De Trizio, L., Manna, L., Brovelli, S.
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* ACS Energy Letters
* https://doi.org/10.1021/acsenergylett.0c00914
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* Published 12 Jun 2020 (early online 8 May 2020)
* Processed: 2020-6

AgxBiCl6Double-Perovskite NanocrystalsWe devised a hot-injection synthesis to prepare colloidal double-perovskite Cs2NaBiCl6 nanocrystals (NCs). We also examined the effects of replacing Na+ with Ag+ cations by preparing and characterizing Cs2Na1-xAgxBiCl6 alloy NCs with x ranging from 0 to 1. Whereas Cs2NaBiCl6 NCs were not emissive, Cs2Na1-xAgxBiCl6 NCs featured a broad photoluminescence band at ∼690 nm, Stokes-shifted from the respective absorption by ≥1.5 eV. The emission efficiency was maximized for low Ag+ amounts, reaching ∼3% for the Cs2Na0.95Ag0.05BiCl6 composition. Density functional theory calculations coupled with spectroscopic investigations revealed that Cs2Na1-xAgxBiCl6 NCs are characterized by a complex photophysics stemming from the interplay of (i) radiative recombination via trapped excitons localized in spatially connected AgCl6-BiCl6 octahedra; (ii) surface traps, located on undercoordinated surface Bi centers, behaving as phonon-assisted nonradiative decay channels; and (iii) a thermal equilibrium between trapping and detrapping processes. These results offer insights into developing double-perovskite NCs with enhanced optoelectronic efficiency.

### 10) Biphasic Cell-Size and Growth-Rate Homeostasis by Single Bacillus subtilis Cells

* Nordholt, N., van Heerden, J. H., Bruggeman, F. J.
* Systems Bioinformatics, AIMMS
* Current Biology
* https://doi.org/10.1016/j.cub.2020.04.030
* Corresponding author: Bruggeman, F. J.
* Published 22 Jun 2020 (early online 14 May 2020)
* Processed: 2020-6

Nordholt et al. show how growth-rate and protein-concentration homeostasis is achieved in Bacillus subtilis, through systematic rate adjustments during cell-cycle progression. They identify two distinct growth regimes in this bacterium's cell cycle, suggesting a link between growth-rate dynamics and size homeostasis.

### 11) Biosignature Analysis of Mars Soil Analogs from the Atacama Desert: Challenges and Implications for Future Missions to Mars

* Aerts, J. W., Riedo, A., Melton, D. J., Martini, S., Flahaut, J., Meierhenrich, U. J., Meinert, C., Myrgorodska, I., Lindner, R., Ehrenfreund, P.
* Molecular Cell Physiology, AIMMS, Leiden University, Centre de recherches pétrographiques et géochimiques, Université Côte d’Azur, University of Bristol, ESTEC
* Astrobiology
* https://doi.org/10.1089/ast.2019.2063
* Corresponding author: None
* Published Jun 2020 (early online 10 Jun 2020)
* Processed: 2020-6

The detection of biosignatures on Mars is of outstanding interest in the current field of astrobiology and drives various fields of research, ranging from new sample collection strategies to the development of more sensitive detection techniques. Detailed analysis of the organic content in Mars analog materials collected from extreme environments on Earth improves the current understanding of biosignature preservation and detection under conditions similar to those of Mars. In this article, we examined the biological fingerprint of several locations in the Atacama Desert (Chile), which include different wet and dry, and intermediate to high elevation salt flats (also named salars). Liquid chromatography and multidimensional gas chromatography mass spectrometry measurement techniques were used for the detection and analysis of amino acids extracted from the salt crusts and sediments by using sophisticated extraction procedures. Illumina 16S amplicon sequencing was used for the identification of microbial communities associated with the different sample locations. Although amino acid load and organic carbon and nitrogen quantities were generally low, it was found that most of the samples harbored complex and versatile microbial communities, which were dominated by (extremely) halophilic microorganisms (most notably by species of the Archaeal family Halobacteriaceae). The dominance of salts (i.e., halites and sulfates) in the investigated samples leaves its mark on the composition of the microbial communities but does not appear to hinder the potential of life to flourish since it can clearly adapt to the higher concentrations. Although the Atacama Desert is one of the driest and harshest environments on Earth, it is shown that there are still sub-locations where life is able to maintain a foothold, and, as such, salt flats could be considered as interesting targets for future life exploration missions on Mars.

### 12) Empowering women through probiotic fermented food in East Africa

* Reid, G., Sybesma, W., Matovu, W., Onyango, A., Westerik, N., Kort, R.
* Molecular Cell Physiology, AIMMS, Western University, Yoba for Life Foundation, Heifer International, Jomo Kenyatta University of Agriculture and Technology
* Journal of global health
* https://doi.org/10.7189/jogh.10.010330
* Corresponding author: Reid, G.
* Published Jun 2020 (early online None)
* Processed: 2020-6

### 13) Unary Words Have the Smallest Levenshtein k-Neighbourhoods

* Charalampopoulos, P., Pissis, S. P., Radoszewski, J., Walen, T., Zuba, W.
* Bioinformatics, AIMMS, Bio Informatics (IBIVU), University of Warsaw
* None
* https://doi.org/10.4230/LIPIcs.CPM.2020.10
* Corresponding author: None
* Published 9 Jun 2020 (early online None)
* Processed: 2020-6

The edit distance (a.k.a. the Levenshtein distance) between two words is defined as the minimum number of insertions, deletions or substitutions of letters needed to transform one word into another. The Levenshtein k-neighbourhood of a word w is the set of words that are at edit distance at most k from w. This is perhaps the most important concept underlying BLAST, a widely-used tool for comparing biological sequences. A natural combinatorial question is to ask for upper and lower bounds on the size of this set. The answer to this question has important algorithmic implications as well. Myers notes that "such bounds would give a tighter characterisation of the running time of the algorithm" behind BLAST. We show that the size of the Levenshtein k-neighbourhood of any word of length n over an arbitrary alphabet is not smaller than the size of the Levenshtein k-neighbourhood of a unary word of length n, thus providing a tight lower bound on the size of the Levenshtein k-neighbourhood. We remark that this result was posed as a conjecture by Dufresne at WCTA 2019. 2012 ACM Subject Classification Theory of computation ! Pattern matching.

### 14) Dual catalytic enantioselective desymmetrization of allene-tethered cyclohexanones

* Zhang, L., Yamazaki, K., Leitch, J. A., Manzano, R., Atkinson, V. A., Hamlin, T. A., Dixon, D. J.
* Theoretical Chemistry, AIMMS, University of Oxford
* Chemical Science
* https://doi.org/10.1039/d0sc02878a
* Corresponding author: Dixon, D. J.
* Published 28 Jun 2020 (early online 24 Jun 2020)
* Processed: 2020-6

The construction of enantioenriched azabicyclo[3.3.1]nonan-6-one heterocycles via an enantioselective desymmetrization of allene-linked cyclohexanones, enabled through a dual catalytic system, that provides synchronous activation of the cyclohexanone with a chiral prolinamide and the allene with a copper(i) co-catalyst to deliver the stereodefined bicyclic core, is described. Successful application to oxygen analogues was also achieved, thereby providing a new enantioselective synthetic entry to architecturally complex bicyclic ethereal frameworks. The mechanistic pathway and the origin of enantio- and diastereoselectivities has been uncovered using density functional theory (DFT) calculations. This journal is

### 15) Monitoring Allosteric Interactions with CXCR4 Using Nano

* Soave, M., Heukers, R., Kellam, B., Woolard, J., Smit, M. J., Briddon, S. J., Hill, S. J.
* Medicinal chemistry, AIMMS, University of Nottingham
* None
* https://doi.org/10.1016/j.chembiol.2020.06.006
* Corresponding author: Hill, S. J.
* Published 30 Jun 2020 (early online 30 Jun 2020)
* Processed: 2020-6

BiT Conjugated NanobodiesCamelid single-domain antibody fragments (nanobodies) offer the specificity of an antibody in a single 15-kDa immunoglobulin domain. Their small size allows for easy genetic manipulation of the nanobody sequence to incorporate protein tags, facilitating their use as biochemical probes. The nanobody VUN400, which recognizes the second extracellular loop of the human CXCR4 chemokine receptor, was used as a probe to monitor specific CXCR4 conformations. VUN400 was fused via its C terminus to the 11-amino-acid HiBiT tag (VUN400-HiBiT) which complements LgBiT protein, forming a full-length functional NanoLuc luciferase. Here, complemented luminescence was used to detect VUN400-HiBiT binding to CXCR4 receptors expressed in living HEK293 cells. VUN400-HiBiT binding to CXCR4 could be prevented by orthosteric and allosteric ligands, allowing VUN400-HiBiT to be used as a probe to detect allosteric interactions with CXCR4. These data demonstrate that the high specificity offered by extracellular targeted nanobodies can be utilized to probe receptor pharmacology.

### 16) Correction to: Signaling lipids as diagnostic biomarkers for ocular surface cicatrizing conjunctivitis

* Di Zazzo, A., Yang, W., Coassin, M., Micera, A., Antonini, M., Piccinni, F., De Piano, M., Kohler, I., Harms, A. C., Hankemeier, T., Bonini, S., Mashaghi, A.
* BioAnalytical Chemistry, AIMMS, Universita Campus Bio-Medico di Roma, Leiden University, IRCCS Fondazione G.B. Bietti per lo studio e la ricerca in oftalmologia- Roma
* Journal of Molecular Medicine
* https://doi.org/10.1007/s00109-020-01938-3
* Corresponding author: Mashaghi, A.
* Published Jul 2020 (early online 10 Jun 2020)
* Processed: 2020-7

The correct name of the 11th Author and the missing Acknowledgment is presented in this paper. Acknowledgements: The project was partially funded by the Italian Ministry of Health (AM and MDP). AM and MDP thank Fondazione Roma for continuous support.

### 17) Human exposure to synthetic endocrine disrupting chemicals (S-EDCs) is generally negligible as compared to natural compounds with higher or comparable endocrine activity: how to evaluate the risk of the S-EDCs?

* Autrup, H., Barile, F. A., Berry, S. C., Blaauboer, B. J., Boobis, A., Bolt, H., Borgert, C. J., Dekant, W., Dietrich, D., Domingo, J. L., Gori, G. B., Greim, H., Hengstler, J., Kacew, S., Marquardt, H., Pelkonen, O., Savolainen, K., Heslop-Harrison, P., Vermeulen, N. P.
* Chemistry and Pharmaceutical Sciences, AIMMS, Aarhus University, St. John's University, Queen Mary University of London, Utrecht University, Imperial College London, Dortmund University, Applied Pharmacology and Toxicology, Inc., University of Würzburg, University of Konstanz, Pere Virgili Health Research Institute, The Health Policy Center, Technical University of Munich, University of Ottawa, Toxicology, University of Oulu, Finnish Institute of Occupational Health, University of Leicester
* Archives of Toxicology
* https://doi.org/10.1007/s00204-020-02800-8
* Corresponding author: Greim, H.
* Published Jul 2020 (early online 8 Jun 2020)
* Processed: 2020-7

Theoretically, both synthetic endocrine disrupting chemicals (S-EDCs) and natural (exogenous and endogenous) endocrine disrupting chemicals (N-EDCs) can interact with endocrine receptors and disturb hormonal balance. However, compared to endogenous hormones, S-EDCs are only weak partial agonists with receptor affinities several orders of magnitude lower. Thus, to elicit observable effects, S-EDCs require considerably higher concentrations to attain sufficient receptor occupancy or to displace natural hormones and other endogenous ligands. Significant exposures to exogenous N-EDCs may result from ingestion of foods such as soy-based diets, green tea and sweet mustard. While their potencies are lower as compared to natural endogenous hormones, they usually are considerably more potent than S-EDCs. Effects of exogenous N-EDCs on the endocrine system were observed at high dietary intakes. A causal relation between their mechanism of action and these effects is established and biologically plausible. In contrast, the assumption that the much lower human exposures to S-EDCs may induce observable endocrine effects is not plausible. Hence, it is not surprising that epidemiological studies searching for an association between S-EDC exposure and health effects have failed. Regarding testing for potential endocrine effects, a scientifically justified screen should use in vitro tests to compare potencies of S-EDCs with those of reference N-EDCs. When the potency of the S-EDC is similar or smaller than that of the N-EDC, further testing in laboratory animals and regulatory consequences are not warranted.

### 18) Computationally Guided Molecular Design to Minimize the LE/CT Gap in D-π-A Fluorinated Triarylboranes for Efficient TADF via D and π-Bridge Tuning

* Narsaria, A. K., Rauch, F., Krebs, J., Endres, P., Friedrich, A., Krummenacher, I., Braunschweig, H., Finze, M., Nitsch, J., Bickelhaupt, F. M., Marder, T. B.
* Theoretical Chemistry, Chemistry and Pharmaceutical Sciences, AIMMS, University of Würzburg
* Advanced Functional Materials
* https://doi.org/10.1002/adfm.202002064
* Corresponding author: Bickelhaupt, F. M.
* Published 1 Aug 2020 (early online 2 Jun 2020)
* Processed: 2020-8

In this combined experimental and theoretical study, a computational protocol is reported to predict the excited states in D-π-A compounds containing the B(FXyl)2 (FXyl = 2,6-bis(trifluoromethyl)phenyl) acceptor group for the design of new thermally activated delayed fluorescence (TADF) emitters. To this end, the effect of different donor and π-bridge moieties on the energy gaps between local and charge-transfer singlet and triplet states is examined. To prove this computationally aided design concept, the D-π-B(FXyl)2 compounds 1–5 were synthesized and fully characterized. The photophysical properties of these compounds in various solvents, polymeric film, and in a frozen matrix were investigated in detail and show excellent agreement with the computationally obtained data. Furthermore, a simple structure–property relationship is presented on the basis of the molecular fragment orbitals of the donor and the π-bridge, which minimize the relevant singlet–triplet gaps to achieve efficient TADF emitters.

### 19) New Generations of MS2 Variants and MCP Fusions to Detect Single m

* Pichon, X., Robert, M. C., Bertrand, E., Singer, R. H., Tutucci, E.
* Systems Bioinformatics, AIMMS, Université de Montpellier, Equipe labélisée Ligue Nationale Contre le Cancer, Yeshiva University, Howard Hughes Medical Institute
* None
* https://doi.org/10.1007/978-1-0716-0712-1\_7
* Corresponding author: None
* Published 2020 (early online None)
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RNAs in Living Eukaryotic CellsLive imaging of single RNA from birth to death brought important advances in our understanding of the spatiotemporal regulation of gene expression. These studies have provided a comprehensive understanding of RNA metabolism by describing the process step by step. Most of these studies used for live imaging a genetically encoded RNA-tagging system fused to fluorescent proteins. One of the best characterized RNA-tagging systems is derived from the bacteriophage MS2 and it allows single RNA imaging in real-time and live cells. This system has been successfully used to track the different steps of mRNA processing in many living organisms. The recent development of optimized MS2 and MCP variants now allows the labeling of endogenous RNAs and their imaging without modifying their behavior. In this chapter, we discuss the improvements in detecting single mRNAs with different variants of MCP and fluorescent proteins that we tested in yeast and mammalian cells. Moreover, we describe protocols using MS2-MCP systems improved for real-time imaging of single mRNAs and transcription dynamics in S. cerevisiae and mammalian cells, respectively.

### 20) Simultaneous Detection of m

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RNA and Protein in S. cerevisiae by Single-Molecule FISH and ImmunofluorescenceSingle-molecule fluorescent in situ hybridization (smFISH) enables the detection and quantification of endogenous mRNAs within intact fixed cells. This method utilizes tens of singly labeled fluorescent DNA probes hybridized against the mRNA of interest, which can be detected by using standard wide-field fluorescence microscopy. This approach provides the means to generate absolute quantifications of gene expression within single cells, which can be used to link molecular fluctuations to phenotypes. To be able to correlate the expression of an mRNA and a protein of interest in individual cells, we combined smFISH with immunofluorescence (IF) in yeast cells. Here, we present our smFISH-IF protocol to visualize and quantify two cell cycle-controlled mRNAs (CLN2 and ASH1) and the cell cycle marker alpha-tubulin in S. cerevisiae. This protocol, which is performed over 2days, can be used to visualize up to three colors at the time (i.e., two mRNAs, one protein). Even if the described protocol is designed for S. cerevisiae, we think that the considerations discussed here can be useful to develop and troubleshoot smFISH-IF protocols for other model organisms.

### 21) The CTD Is Not Essential for the Post-Initiation Control of RNA Polymerase II Activity

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* Processed: 2020-7

Interest in the C-terminal domain (CTD) of the RPB1 subunit of the RNA polymerase II (Pol II) has been revived in recent years, owing to its numerous posttranslational modifications and its “phase-separation” properties. A large number of studies have shown that the status of CTD modifications is associated with the activity of Pol II during the transcription cycle. However, because this domain is essential in living cells, the functional requirement of the full CTD for the control of Pol II activity at endogenous mammalian genes has never been addressed directly in living cells. Using an inducible Pol II-degradation system that we previously established, we investigated here the roles of the CTD in the post-initiation control of Pol II. The selective ablation of the RPB1 CTD, post-initiation, at promoter-proximal pause-sites revealed that this domain, and by extension the CTD heptads and their modifications, is functionally neither absolutely required to maintain pausing in the absence of CDK9 activity nor essential for the release of Pol II into productive elongation.

### 22) High resolution effect-directed analysis of steroid hormone (ant)agonists in surface and wastewater quality monitoring

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Monitoring of chemical water quality is extremely challenging due to the large variety of compounds and the presence of biologically active compounds with unknown chemical identity. Previously, we developed a high resolution Effect-Directed Analysis (EDA) platform that combines liquid chromatography with high resolution mass spectrometry and parallel bioassay detection. In this study, the platform is combined with CALUX bioassays for (anti)androgenic, estrogenic and glucocorticoid activities, and the performance of the platform is evaluated. It appeared to render very repeatable results, with high recoveries of spiked compounds and high consistency between the mass spectrometric and bioassay results. Application of the platform to wastewater treatment plant effluent and surface water samples led to the identification of several compounds contributing to the measured activities. Eventually, a workflow is proposed for the application of the platform in a routine monitoring context. The workflow divides the platform into four phases, of which one to all can be performed depending on the research question and the results obtained. This allows one to make a balance between the effort put into the platform and the certainty and depth by which active compounds will be identified. The EDA platform is a valuable tool to identify unknown bioactive compounds, both in an academic setting as in the context of legislative, governmental or routine monitoring.

### 23) A single-step preparation of carbohydrate functionalized monoliths for separation and trapping of polar compounds

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* Published 27 Sep 2020 (early online 16 Aug 2020)
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A single-step copolymerization strategy was developed for the preparation of carbohydrate (glucose and maltose) functionalized monoliths using click reaction. Firstly, novel carbohydrate-functionalized methacrylate monomers were synthesized through Cu(I)-catalyzed 1,3-dipolar cycloaddition (alkyne-azide reaction) of terminal alkyne with azide of carbohydrate derivatives. The corresponding carbohydrate functionalized monolithic columns were then prepared through a single-step in-situ copolymerization. The physicochemical properties and performance of the fabricated monolithic columns were evaluated using scanning electron microscopy, Fourier-transform infrared spectroscopy, and nano-liquid chromatography. For the optimized monolithic column, satisfactory column permeability and good separation performance were demonstrated for polar compounds including nucleoside, phenolic compounds and benzoic acid derivatives. The monolithic column is also highly useful for selective and efficient enrichment of glycopeptides from human IgG tryptic digests. This study not only provided a novel hydrophilic column for separation and selective trapping of polar compounds, but also proposed a facile and efficient approach for preparing carbohydrate functionalized monoliths.

### *24) Computationally Guided Molecular Design to Minimize the LE/CT Gap in D-π-A Fluorinated Triarylboranes for Efficient TADF via D and π-Bridge Tuning*

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* Processed: 2020-8

In this combined experimental and theoretical study, a computational protocol is reported to predict the excited states in D-π-A compounds containing the B(FXyl)2 (FXyl = 2,6-bis(trifluoromethyl)pheny ...

### *25) A single-step preparation of carbohydrate functionalized monoliths for separation and trapping of polar compounds*

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A single-step copolymerization strategy was developed for the preparation of carbohydrate (glucose and maltose) functionalized monoliths using click reaction. Firstly, novel carbohydrate-functionalize ...