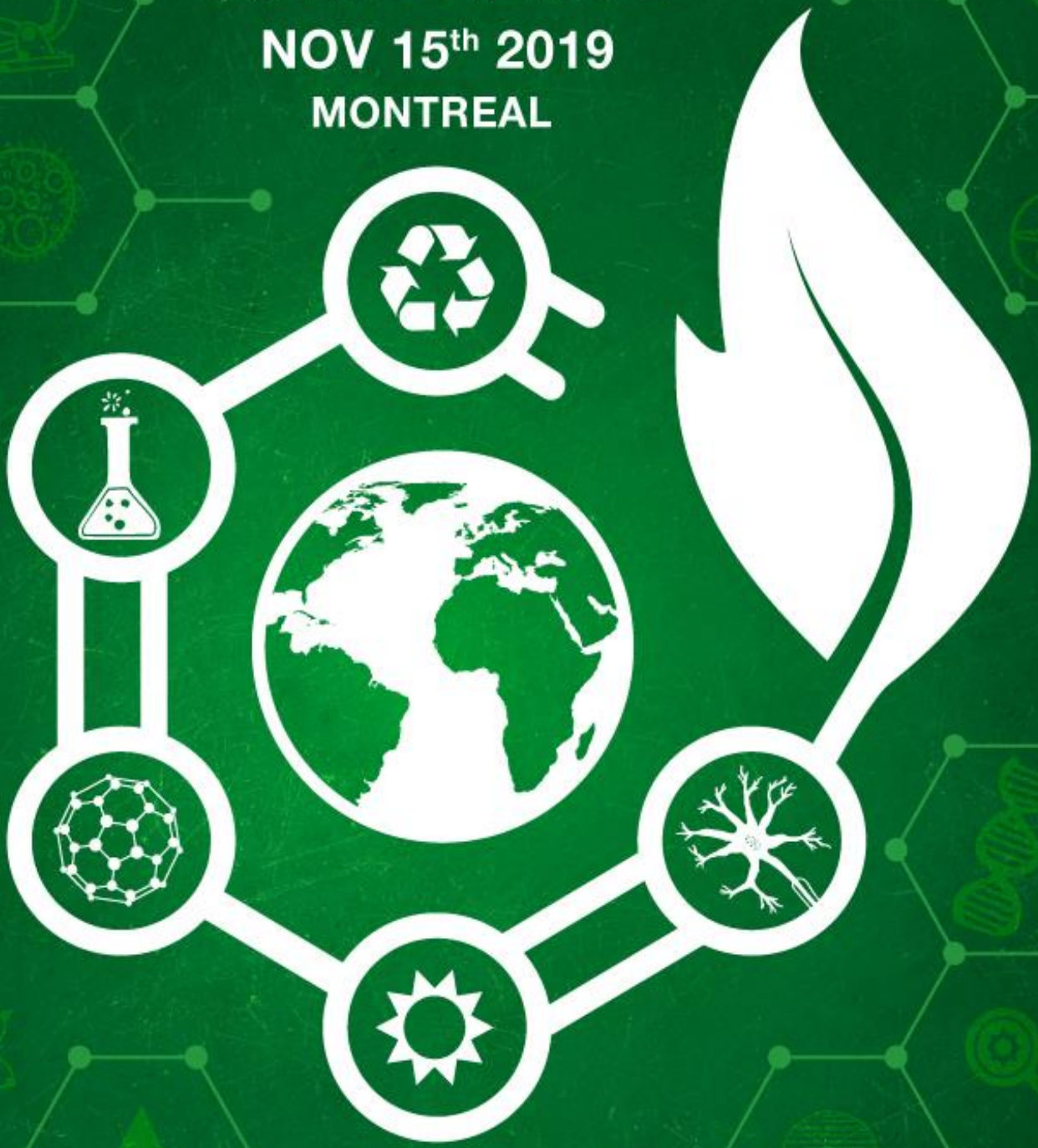
CONCORDIA
UNIVERSITY

22nd ANNUAL CONFERENCE

NOV 15th 2019

MONTREAL



CBGRC

Chemistry and Biochemistry
Graduate Research Conference

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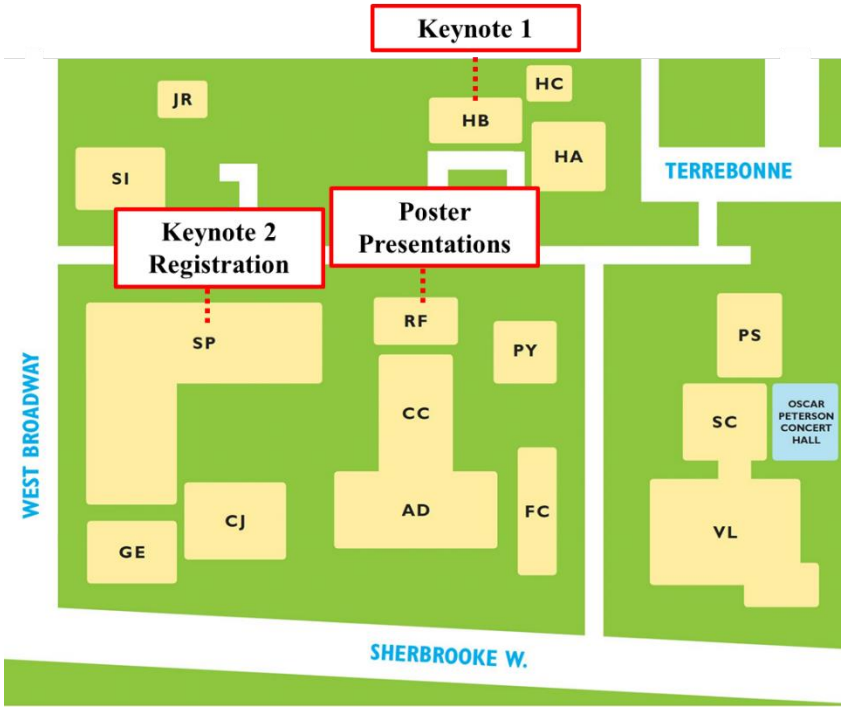
CAMPUS MAPS
PLAN DU CAMPUS

Buildings



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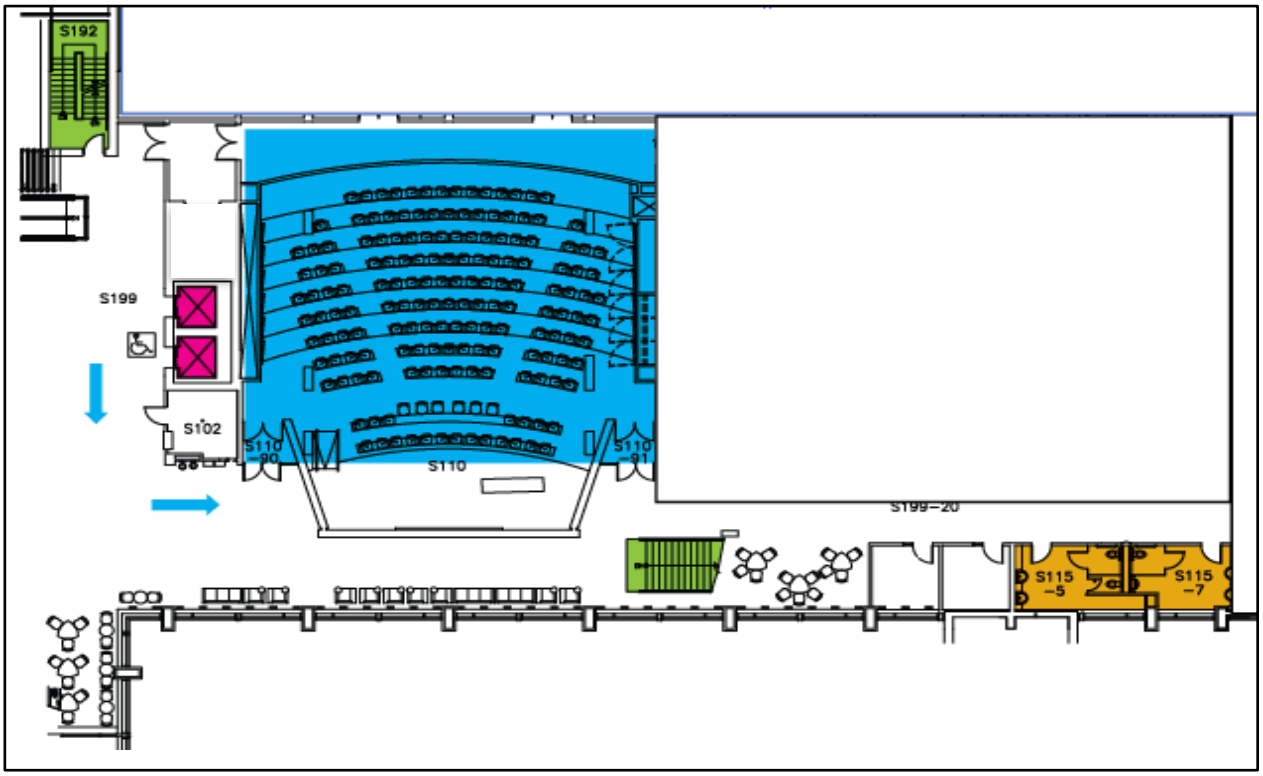
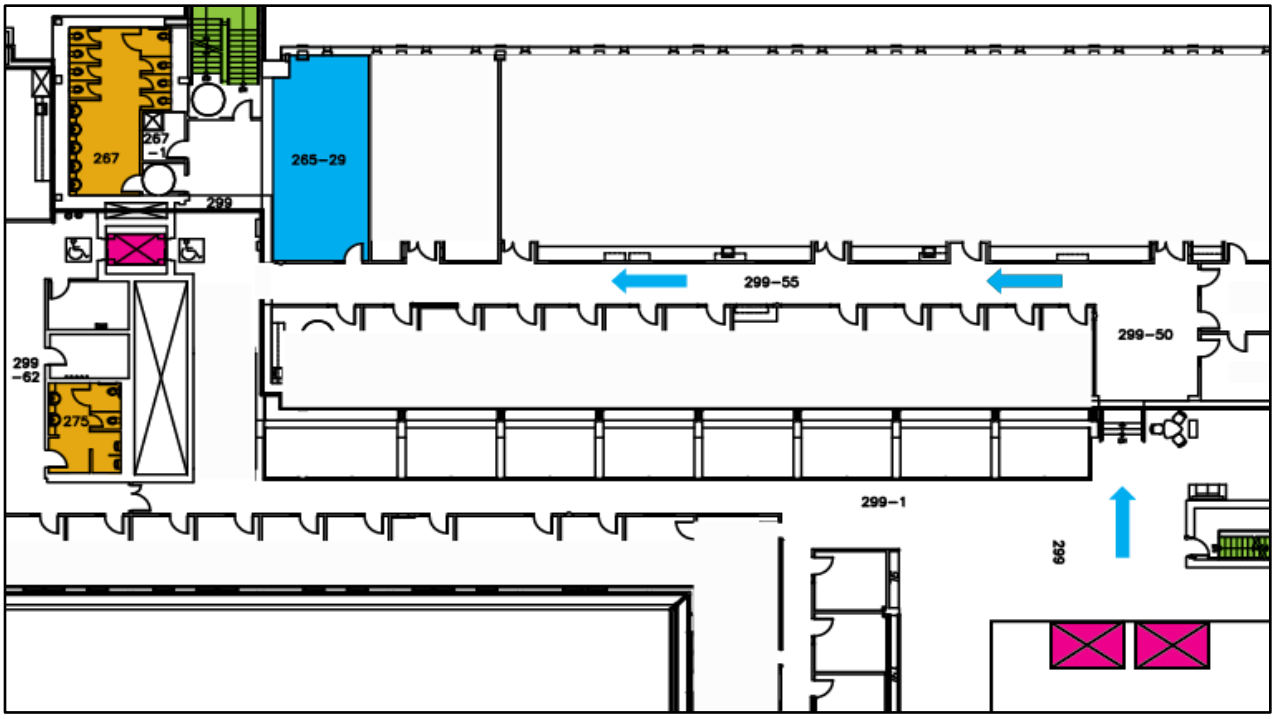


CAMPUS MAPS
PLAN DU CAMPUS

SP- 265.29



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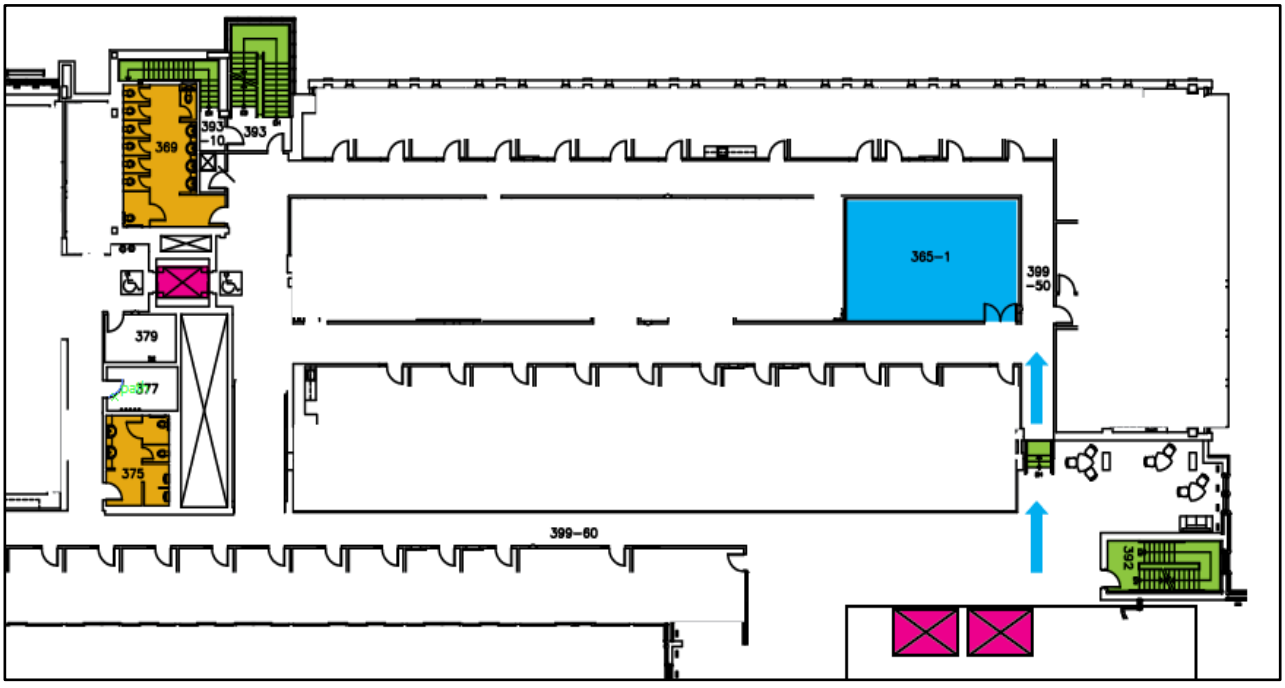

CAMPUS MAPS
PLAN DU CAMPUS

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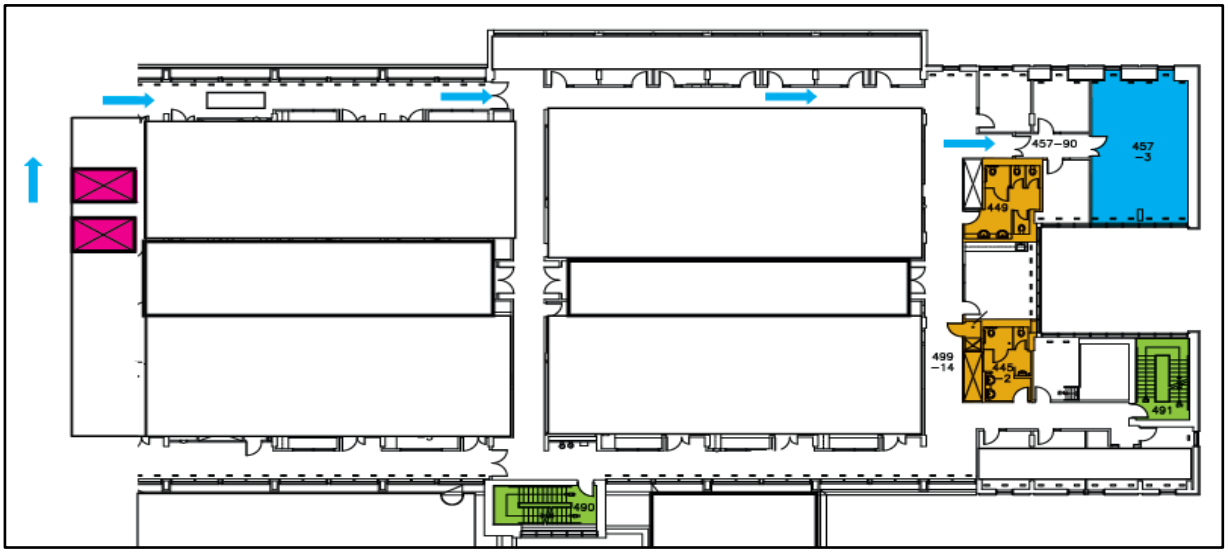
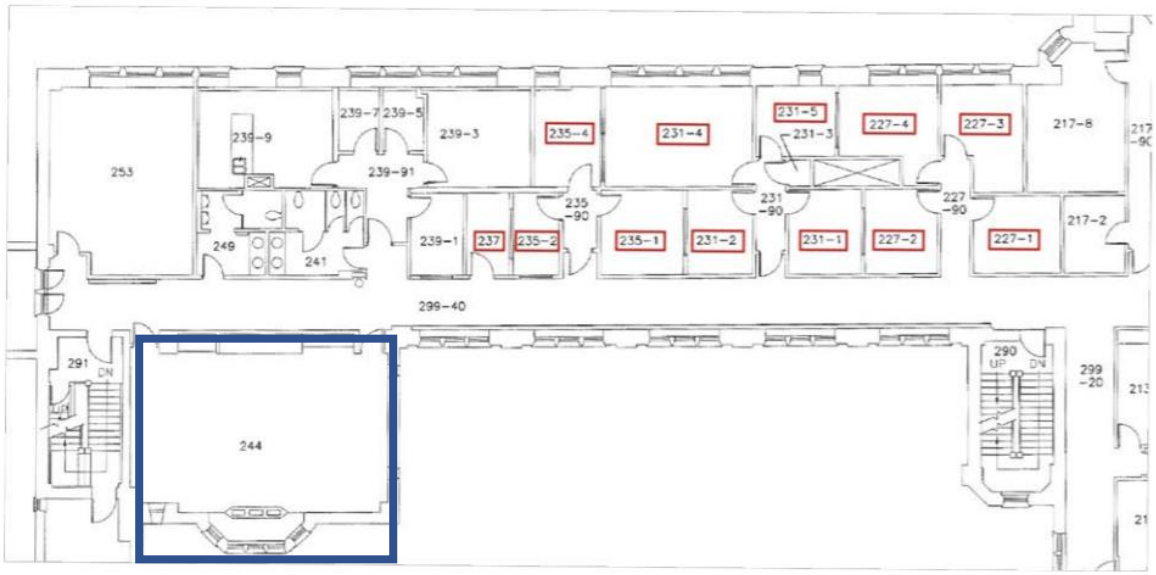


SP- PY-244



WELCOME NOTE
LETTRE DE BIENVENUE

Dear friends and colleagues,

It is with great pleasure that we welcome you all to the 22nd annual Chemistry and Biochemistry Graduate Research Conference. This year, we are especially proud of the continuous growth of our conference with over 250 participants, judges, sponsors and volunteers. Bringing together the research from 20 different institutions, we hope to encourage scientific discourse in a comfortable environment. At the CBGRC, graduate students, professors and industry representatives gather to share and discuss their research creating an extended network in the scientific community. We hope this conference will be a great experience to learn, be inspired and show pride in your research. As always, we would like to extend our gratitude to you for your help in making this year's CBGRC a success.

The CBGRC Organizing Committee

Chers amis et collègues,

C'est avec un grand plaisir que nous vous souhaitons à tous la bienvenue à la 22e Conférence annuelle sur la recherche aux cycle supérieurs en chimie et biochimie. Cette année, nous sommes particulièrement fiers de la croissance continue de notre conférence comptant plus de 250 participants, juges, commanditaires et bénévoles. En réunissant la recherche poursuivis à 20 institutions différentes, nous espérons encourager un discours scientifique dans un environnement confortable. Au CRCSCB, des étudiants aux cycles supérieurs, des professeurs et des représentants de l'industrie se réunissent pour partager et discuter de leurs recherches, créant ainsi un réseau étendu dans la communauté scientifique. Nous espérons que cette conférence sera une excellente expérience pour apprendre, être inspiré et faire preuve de fierté par rapport à votre recherche. Comme toujours, nous voudrions vous exprimer notre gratitude pour votre participation et contribution au succès de la CRCSCB.

Le Comité Organisateur de la CRCSCB

KEYNOTE SPEAKER
INTERVENANTS PRINCIPAUX

Dr. Alfonso Mucci

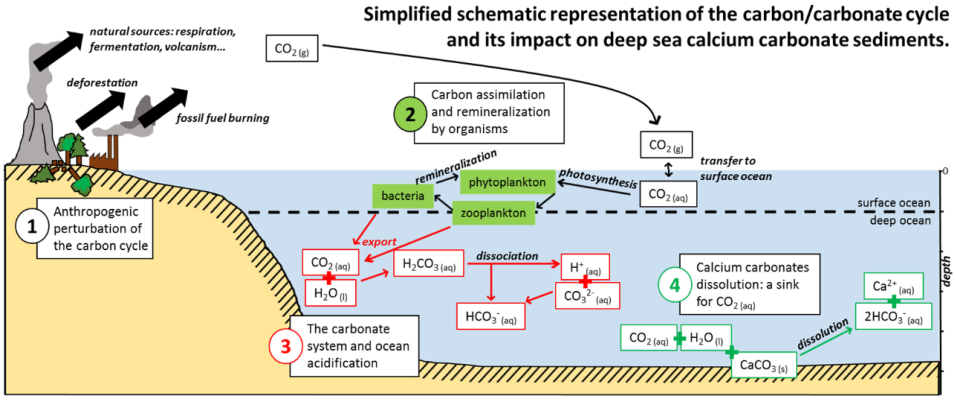
Professor, Department of Earth and Planetary Sciences
McGill University

Ocean acidification: The indisputable problem and the dissolution of deep-sea carbonates

In the context of climate change, ocean acidification (OA) is seen as the other carbon dioxide (CO_2) problem. Oceanic uptake of anthropogenic CO_2 decreases the pH, carbonate ion concentration and saturation state of surface ocean waters with respect to calcium carbonate ($CaCO_3$) minerals. OA is a potential threat to the health of marine ecosystems, notably to calcifying organisms whose ability to secrete their $CaCO_3$ skeletons might be hindered. OA also triggers the dissolution of carbonate minerals on the seafloor, neutralizing man-made CO_2, but estimates are yet available of the extent and foci of this dissolution.

We combined recent databases of bottom-water chemistry, benthic currents, and $CaCO_3$ content of deep-sea sediments with a new rate model to derive the global distribution of benthic calcite dissolution rates and obtained primary confirmation of an anthropogenic component. By comparing pre-industrial with present-day rates, we determined that significant anthropogenic dissolution now occurs in the western North Atlantic, accounting for 40-100% of the total seafloor dissolution at its most intense locations. At these locations, the calcite compensation depth has risen ~300 m. Increased benthic dissolution was also revealed at various hot spots in the southern extent of the Atlantic, Indian and Pacific Oceans.

According to the IPCC RCP8.5 or “business as usual” emission model, the oceans will acidify further by the end of this century. Nevertheless, results of a range of Earth System and climate models challenge the paradigm that seafloor $CaCO_3$ dissolution will grow in extent and intensify as ocean acidification persists. We find that while $CaCO_3$ dissolution will increase over the 21st century in some areas of the deep ocean, such as the eastern central Pacific Ocean, it is projected to decrease in the Northern Pacific and abyssal Atlantic Ocean.



KEYNOTE SPEAKER
INTERVENANTS PRINCIPAUX

Dr. Kattesh V. Katti

Professor of Radiology and Physics Director, Institute of Green Nanotechnology
University of Missouri

"Nano-Ayurvedic Medicine"—An Immunomodulatory Holistic Medicine Approach for Cancer Therapy—Through Green Nanotechnology

Cancer continues to be a major public health problem worldwide and there were an estimated 18 million cancer cases around the world in 2018 of which 9.5 million patients died. By 2040, the global burden is expected to grow to 27.5 million new cancer cases and 16.3 million cancer deaths simply due to the growth and aging of the population. The future burden will probably be even larger due to increasing prevalence of factors that increase risk, such as smoking, unhealthy diet, physical inactivity, and fewer childbirths, especially in economically transitioning countries. A number of new therapeutic interventions to combat various forms of human cancer have been developed over the last several decades. However, cures and lifesaving arrestation of this disease have been rare because tumors bear innate characteristics to become resistant to various forms of treatment. It is becoming increasingly clear that various chemotherapeutic, immunotherapeutic and radiation-based treatment modalities activate NF-κB transcription factors, which are responsible for triggering various pro-tumorigenic cascade of processes within the tumor microenvironment. Tumor progression and the evasion of systemic immune surveillance are all dictated by significantly high levels of various immunosuppressive factors, such as IL-10, IL-6, and TGF-β. Tumor progression is further catalyzed by the immune cells, including regulatory T cells, dendritic cells, MDSCs and TAMs, which are known to express a low level of MHC class I molecules within the tumor microenvironment. Most cancer drugs, in current use which belong to specific targeted or cytotoxic agents, rely on "one gene, one target, one disease" approach despite the fact that cancer is a very complicated multi-target and multi-gene defective disease. However, several examples of phytochemical-based therapeutic approaches have shown the power of cocktail of phytochemicals in traditional Indian Ayurvedic (Chinese and African) medicines to be multi targeted by enhancing the $CD4^+/CD8^+$ T cell ratio in the tumor microenvironment. Herbal-based Ayurvedic medicine are also known to reeducate the macrophage by promoting the M1 differentiation of TAM, suggesting the poly-pharmacological and poly-targeted nature of phyto agents.

This lecture will discuss application of innovative Green Nanotechnology discoveries, made in Dr. Katti's laboratory, to develop novel nanomedicine agents derived from combination of tumor specific phytochemicals encapsulated onto biocompatible gold nanoparticles. The longstanding objective of this approach focuses on providing credible scientific rationale to phytochemical-based herbal (Ayurvedic) medicine—all aimed at developing new Precision Medicine modality referred to as 'Nano-Ayurvedic Medicine. Green Nanotechnology also allows the development of reproducible formulations of herbal and classical Ayurvedic medicines thus providing a pathway for clinical trials for internal/external validity, to allow the safety and efficacy of specific herbal medicines in a more accurate and scientifically verifiable

way. This lecture will discuss details on how green nanotechnology can be used to develop small-molecule phytochemical(s)-functionalized gold nanoparticles to simultaneously achieve: (i) Inhibition of NfkB activation; (ii) Targeting TAM; and (iii) Inhibition of TNF-α induced p65 phosphorylation; and concomitant immunomodulatory therapeutic action. Details on the new invention of a medical modality, referred to as 'Nano-Ayurvedic Medicine', recently approved by the US Patents and Trade Marks Office will be presented. The lecture will also highlight the importance of clinical translation in medical research through recent results from human clinical trials on cancer patients of Nano-Ayurvedic Nanomedicine drugs derived through green nanotechnology. The overall importance of green nanotechnology in graduate education and toward developing nanomedicine agents for use in oncology and antibiotics with specific examples of recently commercialized pharmaceuticals would be presented.

SCHEDULE
HORAIRE

Time	Event	Location
07:30 - 17:00	Registration	SP Building Security Station
08:00 - 08:30	Breakfast	SP Atrium
08:30 - 10:00	**Student Presentation A**	**Biochemistry (SP-265.29)** **Organic Chemistry (SP-365.01)** **Analytical Chemistry (PY-244)** **Inorganic Chemistry and Computational Chemistry (SP 457.03)** **Molecular Biology (RF-110)**
10:00 - 10:30	Coffee Break and Sponsors Exhibition	SP Atrium
10:30 - 11:30	**Keynote Speaker - Dr. Alfonso Mucci**	**HB-130** **Overflow - (RF-110)**
11:30 - 13:00	Lunch and Sponsors Exhibition	SP Atrium
13:00 - 14:15	**Student Presentation B**	**Environmental Chemistry (SP-265.29)** **Organic Chemistry (SP-365.01)** **Nanochemistry (SP 457.03)** **Molecular Biology (RF-110)**
14:15 - 14:45	Coffee Break and Sponsors Exhibition	SP Atrium
14:45 - 15:45	**Keynote Speaker - Dr. Kattesh V. Katti**	**SP-S110**
16:00 - 17:30	**Student Presentation C**	**Biochemistry (SP-265.29)** **Organic Chemistry (SP-365.01)** **Physical Chemistry (SP 457.03)**
17:30 - 19:30	**Poster Presentations**	**Jesuit Hall RF-100**
17:30 - 22:00	Wine & Cheese	Jesuit Hall RF-100

STUDENT PRESENTATION A
9:15 - 10:15

Biochemistry - Room SP-265.29

08:30 - Y. Habibi (McGill University) - Characterizing Conformational Changes in the Haloduracin b Lanthipeptide Synthase (HalM2) by Utilizing Hydrogen-Deuterium Exchange Mass Spectrometry

08:45 - C. Leal Alves (Concordia University) - Agro Industrial By-Products Used for Production of Valuable Biomolecules

09:00 - A. de Aguiar Lopes (Concordia University)- LC-MS/MS Analysis of the Proteome Response to Miconazole Challenge in Saccharomyces cerevisiae

09:15 - A. Poulhazan (Université du Québec à Montréal (UQAM) - First Atomic Resolution Assignments of Chlamydomonas reinhardtii's Cell Wall and Starch Using 2D 13C Solid-State NMR

09:30 - S. Rajkumar (McGill University) - Delineating the Cooperativity of NF1 Loss-of-Function and Non-p.V600 BRAF Mutations in Cutaneous Melanoma

09:45 - K. Uggowitzer (McGill University)- Connecting Conformational Dynamics to Function of Class II Lanthipeptide Synthetases

Organic Chemistry - Room SP-365.01

08:45 - D. Bendahan (INRS) - Synthesis and Screening of a Fluorinated Library Applied to Fragment-Based Drug Discovery via 19F NMR

09:00 - C. Buonomano (Concordia University) - Use of Flow Chemistry for Decarboxylative Palladium-Catalyzed Cross-Coupling Reactions in the Synthesis of Heteroaromatics

09:15 - M. Cloutier (INRS)- Total Synthesis of Ananatosides as a Novel Class of Biosurfactant

09:30 - C. Cruché (Université de Montréal) - Visible-light-mediated Decarboxylative Alkynylation using Heteroleptic Copper Complexes

09:45 - J. Guerrero (Université de Montréal) - Alkynyl Sulfides Macrocyclic Peptidic Alkynyl Sulfides: Synthesis and Diversification

Analytical Chemistry - Room PY-244.00

08:30 - L. Cougnaud (Concordia University) - Evaluating the Effect of Temperature on Lipid Extraction using LC-MS-based Lipidomics

08:45 - M. Sansoucy (UQAM) - Reaction Between DOPA and Cysteine Thiol Studied by LC-MS/MS

09:00 - A. Malkawi (Concordia University) - Extraction of Peptide Hormones using Solid-Phase Microextraction (SPME)

09:15 - B. Garneau (Université du Québec à Trois-Rivières) - Chemistry against the New Psychoactive Substances (NPS) hydra : a flexible analytical framework to win the battle

09:30 - S. Dastpeyman (Concordia University) - Characterizing the H_2O_2 Stimulon in Saccharomyces cerevisiae Cells with Normal and Amplified H2O2 Sensing

09:45 - T. Geib (UQAM) - Investigating Drug-Related Protein Binding in Vitro by LC-MS/MS

STUDENT PRESENTATION B

13:00 - 14:15

Inorganic Chemistry and Computational Chemistry - Room SP-457.03

08:30 - W. Leal (Concordia University) - Conversion of Electrochemically Deposited Carbonates to Perovskites with Retention of Crystal Morphology

08:45 - M. Rupp (Université de Montréal) - Long-lived Photocatalytic Hydrogen Evolution using Ru(II) bis-terpyridine Complexes as Photosensitizers

09:00 - B. Thakuri (University of Vermont) - Time-resolved MS Studies Identify the Heme Degradation Products of Mycobacterium Tuberculosis MhuD

09:15 - Z. Singh (Concordia University) - Cuprophilia: Cu(I)/Cu(II) Photosensitizer/Catalyst Photosystem for Efficient Water Oxidation

09:30 - E. Azek (Université de Montréal) - Computational Mechanistic Study of Catalytic C-H Amination Reactions using Rhodium Dimers and N-Mesyloxycarbamates: Reaction Pathway and Byproducts Formation

09:45 - C. Pham (McGill University) - Computational Studies of Light-driven Pinacol Coupling by Hydrazine

Molecular Biology - Room RF-110

08:30 - N. Al-Deri (Concordia University) - Modelling Neurodevelopmental Disorders Linked to Single Point Mutations in TRAPPC2L

08:45 - M. Mahdavi (Concordia University) - Genomics-Based Analysis of Bacterio-Modulation as a Potential New Approach for Treating Bacterial Infections and Overcoming Antimicrobial Resistance

09:00 - L. Rili (Concordia University) - Regulation of Natural Product Biosynthesis

09:15 - D. Duncan (McGill University) - Synergistic Effects of pH on the Activity of the Antibacterial Metabolite Itaconate

09:30 - S. Grondin (Université de Montréal) - Systematic Whole-Exome Sequencing in Unexplained Cardiac Arrest: Results from the Canadian CASPER Registry and Biobank

09:45 - A. Gupta (Carelton University) - NRF2 transcriptional network in anoxia-tolerant vertebrates

Environmental Chemistry - Room SP-265.29

13:00 - M. Essifi (Concordia University) - Early Diagenesis and Preservation of Organic Matter in Anoxic Aquatic Environments: The Lagoon of Bizerte, Tunisia

13:15 - J. Fernandez Reynes (INRS-ETE) - CO_2 Sequestration by Mineral Carbonation with Iron Complexing using 2,2'-Bipyridine as Ligand

13:30 - B. Keenan (McGill University) - Stanol Concentrations and Ratios in Sediments as Indicators of Human and Animal Populations from Lakes Across Climatic and Land-Use Gradients in Mexico, Guatemala and Belize

STUDENT PRESENTATION B
13:00 - 14:15

Organic Chemistry - Room SP-365.01

13:00 - J.-P. Fontaine (Université de Sherbrooke) - Cyclization Cascade Followed by Non-Usual Indoline Formation Towards the Synthesis of Enantioenriched Aspidospermatan Alkaloids

13:15 - R. Hernandez (Concordia University) - Synthesis of GPCR68 Agonists to Promote Heart Muscle Cell Regeneration after Myocardial Infraction

13:30 - A. Labarre (McGill University) - Integrating Computational Methods and Organic Synthesis: Application to the Design and Discovery of Highly Selective Enzyme Inhibitors

13:45 - J. T. Liu (Concordia University) - Preliminary Structure-Activity Relationship Study and Biological Evaluation of Thienoisoquinoline Derivatives as Anticancer Agent

Nanochemistry - Room SP-457.03

13:00 - F. Victoria (Concordia University) - Inducing Chirality in Carbon Dots

13:15 - F. Noun (Concordia University) - Towards Uniform Optical Properties of Carbon Dots

13:30 - J. Ricardo-Noordberg (Concordia University) - Morphological Control of Cuprous Oxide Semiconductors Electrochemically Deposited onto a Zinc Oxide Nanowire Array and Their Use in Photocatalysis

13:45 - F. Yarur (Concordia University) - Metal Oxide-Carbon Dot Nanohybrids for Photocatalysis of Organic Reactions

14:00 - J.-R. Macairan (Concordia University) - Developing Multi-Sensing Imaging Probes Using Carbon Dots

Molecular Biology - Room RF-110

13:00 - S. Logan (Carleton University) - Brown and White Adipose from Hibernators Sense and Respond to Inflammatory Triggers Differently

13:15 - C. Brand (Université de Sherbrooke) - Characterization of the Protein-Protein Interaction Between NS3 and NS5 Within the Replication Complex of West Nile Virus

13:30 - **C.-A. Martineau (Université de Sherbrooke) -** The Role of Alternative Splicing Modifications in Virally Induced Cancer

13:45 - **A. Muguet (Université de Sherbrooke) -** Excised and Isolated Chromatin Rings, Containing the Entire rRNA Gene, Retain the Native Chromatin Structure: a Mass Spectrometry Analysis

14:00 - **A. Paillé (Université de Sherbrooke) -** Falloff of RNA Polymerases I at DNA Damage, and their Replacements by Nucleosomes, is Mirrored by the Inverse Activities of Transcription Coupled (TC-) and Global Genome (GG-) Nucleotide Excision Repair

STUDENT PRESENTATION C
16:00 - 17:30

Biochemistry - Room SP-265.29

16:00 - R. Mohamed (Carleton University) - Responses of Porcupine and Wntless proteins to oxidative, hypoxic and endoplasmic reticulum stresses in HEK293T and HCT116 cell lines

16:15 - P. Navals (Université de Sherbrooke) - Enhancing the Overall Profile of a Potent PACE4 Peptidic Inhibitor by the Formation of a Host-Guest Inclusion Complex with beta-Cyclodextrin.

16:30 - D. Therien (McGill University) - Mechanoenzymatic Breakdown of Chitin into N-acetylglucosamine: Higher Activity and Reduced Waste in the Absence of Bulk Water

16:45 - J. Porro-Suardiaz (Concordia University) - Anticancer Potential of GL13K Peptidomimetics: A Biophysical Assessment of their Activity Based on the Interaction with Model Membranes

17:00 - A. Van Kessel (McGill University) - Development of Fluorescent tools to Study Cellular Lipid-Derived Electrophile Chemistry

17:15 - S. Ouellette (Concordia University) - Biosynthesis of Enterobactin in Escherichia coli – Adventures in Metabolon Mapping

Organic Chemistry - Room SP-365.01

16:00 - A. Gilbert (Université Laval) - Silver-promoted Synthesis of SF5-Containing Oxazolines and Lactones

16:15 - J. Majhi (Queen's University) - Stereoselective Synthesis of E-Tetrasubstituted Olefins via Dynamic Kinetic Resolution of Olefin Mixtures

16:30 - L. Mélin (UQAM) - Development of Small-Molecule YAP–TEAD Inhibitors Derived from Flufenamic Acid

16:45 - A. Shafeii (Concordia University) - Accessing Novel Thienoisoquinoline Analogues Through New Synthetic Modularity

STUDENT PRESENTATION C

16:00 - 17:30

Physical Chemistry - Room SP-457.03

16:00 - A. Bain (McGill University) - The Wavelength-Dependent Optical Properties of Weakly Absorbing Aqueous Aerosol: Model and Measurements

16:15 - J. Gaba (Concordia University) - π-π Stacking in Models of Phenolic Surfactant Monolayers

16:30 - C. Dab (Université de Montréal) - Novel Pressure-Sensors Based on Luminescent Chromium(III) Complexes

16:45 - J. Maurais (Université de Sherbrooke) - A Methodology to Enhance Absorption of Thin Films on Ice Using Reflection-Absorption Infrared Spectroscopy (RAIRS)

17:00 - J. Ramos-Sanchez (McGill University) - A Theoretical-empirical Strategy for the Rational Design of Efficient Triplet Quenchers via Photoinduced Electron Transfer

17:15 - E. Hamzehpoor (McGill University) - Crystal Engineering of Room Temperature Phosphorescence in Organic Solids: The Story of Carbonyl-bridged Triphenyl Amines (TANGOs)

POSTER SESSION
17:30 - 19:30 - RF-100

Analytical Chemistry

A01 - A. Dochenko - Development of a Method for Quantification of Toluene Diisocyanate and Methylenediphenyl Diisocyanate Migration from Polyurethane foam Sample Surface by HPLC-UV-M

A02 - B. Garneau - Analytical Workflow in the Era of the Opioids Crisis: Screening for Novel Synthetic Opioids

A03 - A. Joly - Développement de méthodes de conservation, d'extraction et de quantification du 4,4'-MDA dans les sols

A04 - M. Lépine - Characterization of the Human Tear Proteome by LC-MS/MS

A05 - M. Mireault - Untargeted LC-MS/MS Based Metabolomics to Decipher Metabolic Changes upon Acetaminophen Treatment in Rats

A06 - O. Ousji - In vitro Metabolism of Butylated Hydroxytoluene (BHT) by LC-HRMS/MS

Inorganic Chemistry

I01 - T. Auvray - In Depth Study of the Electronic Properties of NIR Emissive κ3N Terpyridine Rhenium(I) Dicarbonyl Complexes

I02 - P. Blanc - Spectroscopie Raman d'un complexe du nickel(II) commutable à ligand azoture

I03 - P. Donnarumma - Rare-earth Based fcu Metal-organic Framework for Aqueous Contaminants Degradation

I04 - H. Elasmy - One-pot Synthesis of Orgaoruthenium(II) Complexes bearing N,O-donor Ligands Under Microwave Irradiation: Isolation of a Rare Aldehyde Intermediate Complex

I05 - G. Golbaghi - Synthesis and Characterization of Ru(II) Complexes Bearing Triazole Containing Ligands for Potential Antifungal Applications

I06 - V. Picard - A New Cyclohexyl-Based Catalyst for Hydrogen Generation

I07 - V. Quezada - A New Family of Isostructural Rare Earth Metal-Organic Frameworks synthesized from a Tetratopic Linker

I08 - F. Saraci - Rare-Earth Metal-Organic Frameworks (RE-MOFs) as Potential Fluorescent-Based Chemical Sensors for Applications in Detecting Contaminants in Water

I09 - O. Schott - Photon to Chemical Bonds: TON and TOF for Supramolecular Ir-Co and Ru-Co Systems

I10 - N. Shevchenko - Coordination Polymers Based on Linear Terpyridine Ditopic Ligands

I11 - H. Singh - Partial Hydrogenation of Nitro to Hydroxylamine Group Tethered to Asymmetric Salen-type Ligands and Their Complexation with Metal Ions.

POSTER SESSION
17:30 - 19:30 - RF-100

Physical Chemistry

P01 - A. Ahmad - Component Exchange for Multiple Property Tailoring

P02 - Z. Alinia - Dynamic NMR Study of Thiobencarb (S-4-chlorobenzyl N,N-diethylcarbamothioate)

P03 - S. Bhagat - Synthesis and Characterization of Polyaniline Capped Silver Nanoparticles to be Used in Dye Sensitized Silver Nanoparticles

P04 - H. Hase - Formation of Ion Pairs and Charge-Transfer Complexes in the Doping of Organic Semiconductors

P05 - C. Hennecker - Reconstructing the Parallel Folding Pathways of Guanine Quadruplexes by Thermal Hysteresis

P06 - H. H. Hu - Quantum Chemical Simulation of Thermal-Mechanical Coupling in High Pressure and Temperature Materials Synthesis

P07 - A. Laramee - Quantification of Molecular Orientation in Polymeric Nanomaterials Using Raman Spectroscopy

P08 - K. Kumar - Intramolecular Hydrogen Bond Directed Conformation Stability in N,N'-(pyridine-2,6-diyl)dibenzamide derivatives. Extensive NMR Investigations Supported by X-ray Studies and DFT Computations

P09 - V. Roux - Protocol for Probing the Free-state Behaviour of Drugs and Their Tendency to Self-associate into Nano-entities

P10 - P. Roy - Second-Order Many-Body Perturbation Theory Exchange-Correlation Hole

P11 - C. Yao - Dual Electrochromic and Electrofluorochromic Role of a Red Emissive Fluorophore

Organic Chemistry

O01 - Y. Jimenez - Synthesis of NSC14778 and evaluation of its DNMT inhibitory activity

O02 - C Batisse - Toward a Greener Approach to the Deoxofluorination Reaction Using XtalFluor-E®

O03 - B. Bueno - Synthesis of Aryl Cyclopropyl Sulfides via Copper-Catalyzed S-Cyclopropylation of Thiophenols using Tricyclopropylbismuth

O04 - S. Charoughchi - Bulk Heterojunction Photovoltaics with Improved Efficiencies Using Stem Leaf, Shish-Kebab and Double-Fibrillar Nano-Hybrids Based on Modified Carbon Nanotubes and Poly(3-hexylthiophene)

O05 - M. Cloutier - Total Synthesis of Ananatosides as a Novel Class of Biosurfactants

O06 - E. Delar - Synthèse totale d'anthocyanes et anthocyanidines naturelles à visée thérapeutique pour la prévention du déclin cognitive

O07 - D. Farajat - Exploring the Scope of the Mechanochemical Friedländer Synthesis

O08 - A. Fnaiche - Copper Acetate-Promoted S-Cyclopropylation using Cyclopropylboronic Acid

O09 - J. Fontaine - Cyclization Cascade Followed by Non-usual Indoline Formation Towards the Synthesis of Enantioenriched Aspidospermatan Alkaloids

O10 - O. Gamboa - Synthesis of Imino Sugar Analogues of Kdo as Potential LPS and EPS Biosynthesis Inhibitors in Gram-Negative Bacteria

O11 - R. Gauthier - Gold-Catalyzed Hydrofluorination of Internal Alkynes Using Aqueous HF

O12 - C. Houle - Organocatalyzed Amination of Benzylic Fluorides

O13 - M. Lerond - Towards Organic Stretchable Conductive Films

O14 - Y. Liu - Biacenaphthylene-based Molecules: A Novel Building Block for n-type Organic Field-Effect Transistor (OFET)

O15 - T. Lussier - Iodine(III)-mediated Method to Access Polysubstituted γ-Butyrolactone Derivatives

O16 - R. Vidal - Development of Antibiotics with a High Selectivity for N. gonorrhoeae and N. meningitidis.

O17 - X. Bertrand - Direct Hydrofluorination of Methallyl Alkenes Using a Methanesulfonic acid/triethylamine Trihydrofluoride Combination

Molecular Biology

M01 - A. Gupta - Holding back Jumonji: OCT-1 induced epigenetic changes combat oxidative stress

M02 - S. Hirka - Towards Increasing the Chemical Diversity of Aptamers

M03 - S. Logan - Fat but Fit: How Hibernating Ground Squirrel Adipose Tissue Regulates pro-inflammatory Signaling Pathways

M04 - A. Muguet - Excised and Isolated Chromatin Rings, Containing the Entire rRNA Gene, Retain the Native Chromatin Structure: a Mass Spectrometry Analysis

M05 - I. Iasenza - Investigating Novel Targeted Therapeutics Against Acute Myeloid Leukemia Stem Cells

M06 - M. Hassan - Selective Targeting of HDAC8 Using Novel Small Molecule Scaffolds for Cancer Treatment

Biochemistry

B01 - Z. Aryanpour (Concordia University) - Characterization of the Role of Position 64 in Saccharomyces cerevisiae tRNA Nucleotidyltransferase

B02 - R. Baradan (McGill University) - Preparation and characterization of recombinant Plasmodium falciparum glyceraldehyde-3-phosphate dehydrogenase

B03 - J. Ducharme (McGill University) - Probing P450 3A4 Allosteric site via the Bioconjugation of Ligand Analogues

B04 - M. Ferdebouh (Université de Montréal) - Lymphocytes Implications in Osteoclastogenesis Modulation

B05 - J. McCain (McGill University) - Development of ROS-Activated Dormant Photosensitizers with Theranostic Capabilities

B06 - P. Navals (University of Sherbrooke) - Formulation of a Peptidomimetic PACE4 Inhibitor for the Administration of a Potential Prostate Cancer Treatment

B07 - J. Pierscianowski (McGill University) - In Vitro Reconstitution of the Salmonella Itaconate Degradation Pathway: an Immune System Evasion Mechanism and Antibacterial Target

B08 - S. Jmii (UQAM) - Détermination de la sensibilité de biomarqueur, suite à une contamination au Palladium chez Lemna minor

B09 - G. Singh (Carleton University) - MondoA is a Master Regulator of Sugar-Induced Gene Expression and Link to Circadian Rhythms in Frozen Wood Frog

Environmental Chemistry

E01 - S. Fok (Carleton University) - Biotransformation of 8:2 Monosubstituted Polyfluoroalkyl Phosphate in Rat Liver, Intestinal, and Fecal Suspensions

E02 - C. Fortin-Lecomte (INRS) - Indium Recovery in a Leachate Produced from Spent Liquid Crystal Displays (LCD) of Computers and Laptops

E03 - A. Tétrault (Concordia University) - Mechanisms of Chemical Bonding Between Organic Matter and Sulfidic Sediments in the Saint Lawrence Estuary - A Protecting Role

POSTER SESSION
17:30 - 19:30 - RF-100

Computational Chemistry

C01 - P. Archambault (Concordia University) - Electronic Structure Analysis on the Effects of Purine Hoogsteen Edge Hydration on Sugar Edge H-bonding

C02 - É. Cuierrier (Université de Montréal) - The Exchange-Correlation Factor Model in Density Functional Theory

C03 - A. Fleury (Université de Sherbrooke) - Linear Polymers Heterogeneity and Dynamic seen by Simulation

C04 - H. Ji (York University) - Estimating Reaction Energy Barriers with Machine Learning

C05 - Z. Luo (McGill University) - Balancing act Between the Orthogonality and Locality of One-electron Orbitals

C06 - R. Wang (Université de Montréal)- Construction of Self-Interaction-Corrected Exchange-Correlation Functionals Within the Correlation Factor Approach

Nanochemistry

N01 - K. Duke (Concordia University) - Synthesis and Characterization of a Chemically Modified Parallel-Stranded poly(A) RNA Duplex for Applications as a Stimuli Responsive Nanomaterial

N02 - H. Y. Huang (Concordia University) - Photoactive Nanofiber with Upconverting Nanoparticles for Wound Healing

N03 - N. Jodaeeasl - Molecular dynamics simulation of noble gases adsorption on homogeneous and heterogeneous Carbon nanotube bundles

N04 - A. Macina (Concordia University) - Carbon Dot-Catalyzed Biodiesel Production

N05 - S. Osman (Ryerson University) - First Steps to Nanomedicine: Assessing Interactions Between Polystyrene Nanoparticles and Albumin Proteins

N06 - M. G. Rafique (McGill University) - Sequence-defined (DNA-oligomer)-based 2-D Nanostructures

N07 - F. Shahout (INRS) - Immune Response of Small Drug-like Molecules: Influence of Self-aggregation.

Biochemistry

Characterizing Conformational Changes in the Haloduracin b Lanthipeptide Synthase (HalM2) by Utilizing Hydrogen-Deuterium Exchange Mass Spectrometry

Y. Habibi*, K. Uggowitzer, H. Issak, C. Thibodeaux

McGill University

Lanthipeptides belong to the family of ribosomally synthesized and post translationally modified peptide (RiPP) natural products. Lanthipeptides are genetically encoded precursor peptides that undergo multistep modification catalyzed by lanthipeptide synthetases. These enzymes function iteratively during the stepwise modification of the precursor peptide into a structurally complex peptide macrocycle, which often exhibits antibiotic activity. The relaxed substrate specificity of lanthipeptide (and other RiPP) synthetases likely results, in part, from conformational changes of lanthipeptide synthases in presence of their substrate(s). In this study, we have utilized hydrogen-deuterium exchange mass spectrometry (HDX-MS) to investigate the involvement of conformational changes in the model class II lanthipeptide synthetase, HalM2. Consistent with our hypothesis, we find HalM2 to be a highly dynamic enzyme, and we have uncovered changes in the dynamic properties of the enzyme that have enabled us to locate structural elements involved in precursor peptide binding as well as allosteric communication between the two active sites of the enzyme. The functional assignments for these structural elements is supported by biochemical and kinetic studies of a panel of mutant enzymes. This work has revealed mechanistic paradigms that will likely be shared with other RiPP biosynthetic enzymes.

Agro Industrial By-Products Used for Production of Valuable Biomolecules

C. Leal Alves[1]*, T. Denardi de Souza[2], K. Cristina Massarollo[2], E. Badiale-Furlong[2]

[1]Concordia University, [2]Universidade Federal do Rio Grande

The necessity of environmentally sustainable alternatives to produce chemicals motivates this work, which evaluates the use of different agro industrial by-products as a carbon source in solid state fermentation for production of lipase, glucosamine and omega 3. The microorganism used was Rhizopus oryzae CCT 7560 isolated from rice in tray bioreactor along 120 h using wheat bran (WB), soybean meal (SM) and rice bran (RB), initial moisture of 50% and initial spore concentration of 2x108 spore/g. The largest lipase activities were of 138.58 U/min for 72 h using WB, 266.22 U/min for 72 h using SM and 355.55 U/min for 120 h using RB. The glucosamine content achieved was 2.55 mg/g in 24 h for using SM, 3.21 mg/g in 48 h for using WB and 5.65 mg/g in 48 h for using RB. For omega 3 production, we achieved the maximum production of 6.38 mg/g using RB in 120h, and for WB and SB, 1.5 mg/g in 24 h and 1.31 mg/g in 96 h, respectively. Thus, rice bran in solid-state fermentation of Rhizopus oryzae has become a promising alternative for lipase, glucosamine and omega 3 productions, although those processes have to be optimized for maximum production.

LC-MS/MS Analysis of the Proteome Response to Miconazole Challenge in Saccharomyces cerevisiae

A. de Aguiar Lopes*, A. English

Concordia University

Miconazole is an azole antifungal used in the treatment of yeast infections. Its fungicidal activity includes increased production of reactive oxygen species (ROS) in cells as well as DNA damage and apoptosis. To establish the main metabolic pathways affected by miconazole, we are characterizing the proteome of Saccharomyces cerevisiae after miconazole treatment. Cells were grown in SCD medium to OD600 ~0.8 and treated with 0.4 µg/µL miconazole or ethanol (control) for 10 and 60 min. Cell lysates were analyzed using nanoLC-MS/MS and proteins were identified using Proteome Discover 2.4 software and the Uniprot Saccharomyces cerevisiae proteome database. A total of 1,398 proteins were identified and samples treated with miconazole for 10 and 60 min showed upregulation of 104 and 84 proteins and downregulation of 93 and 67 proteins, respectively. Our ongoing analysis will provide insights into what are the main metabolic pathways and proteins impacted by the antifungal activity of miconazole.

First Atomic Resolution Assignments of Chlamydomonas reinhardtii's Cell Wall and Starch Using 2D ^{13}C Solid-State NMR

A. Poulhazan[1]*, A. A. Arnold[1], D. E. Warschawski[2], I. Marcotte[1]

[1]Université du Québec à Montréal (UQAM), [2]Laboratoire de Biologie Physico-Chimique des Protéines Membranaires, UMR 7099, CNRS, Université Paris Diderot and IBPC, Paris, France

Sugar is an important building block for life. In microalgae such as Chlamydomonas reinhardtii, saccharides play an important energetic and structural role within starch and hydroxyproline-rich cell-wall, for example. First, we characterize starch in C. reinhardtii. This glucose polymer is made of amorphous and crystalline domains, the latter being mainly found into two different crystalline structures, i.e., A and B-types, with different physicochemical properties and processing. Using solid-state NMR on ^{13}C-labelled starch, we were able to identify starch constituents and type, even in vivo. The 2D-INADEQUATE experiments enabled the first assignment of non-reducing end groups, as well as the assessment of starch chain length and conformational disorder. After starch, we investigate the structure of C. reinhardtii's cell wall, with a special focus on glycans. Using ss-NMR on ^{13}C labelled cell-wall extracts, we identified several amino acids, saccharides, as well as links between them. Moreover, highly crystalline and hydrated regions could be differentiated, showing that glycans are essential for the cell wall structure and rigidity. Altogether, these results show how these NMR methods provide atomic resolution details of cell key components, even in living microorganisms, making in situ solid-state NMR a powerful tool to study molecules directly in their native environment.

Delineating the Cooperativity of NF1 Loss-of-Function and Non-p.V600 BRAF Mutations in Cutaneous Melanoma

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[1]McGill University, [2]University of Massachusetts

The Mitogen Activated Protein Kinase (MAPK) RAS-RAF-MEK-ERK pathway regulates cellular growth and survival. Tumour suppressors like NF1 negatively regulate this cascade by hydrolyzing active, RAS-GTP to its inactive, RAS-GDP form. Genetic studies have uncovered activating, mutations in BRAF (p.V600), N-RAS (p.G12, G13, Q61) and loss-of-function mutations of NF1 in approximately 50%, 20% and 15% of cutaneous melanoma patients respectively. Past studies have characterized a subset of BRAF non-p.V600 mutants that co-operate with oncogenic RAS, driving MAPK activation through BRAF mutant-CRAF heterodimers. We observed that NF1 loss-of-function mutations are anti-correlated with BRAF p.V600 mutations but co-occur with non-p.V600 BRAF mutations in melanoma. Expression of BRAF p.D594N mutant, found to co-occur with NF1 loss-of-function mutation, in NF1 knockdown/knockout model systems resulted in MAPK activation. Interestingly, MAPK activation of the BRAF p.D594N mutant within an NF1 null context was not due to increased RAF-RAF dimers nor the binding to MAPK scaffold proteins. We uncovered that the BRAF p.D594N mutant signals monomerically within an NF1 loss context in contrast to dimerizing within an oncogenic RAS context. We tested BRAF inhibitor combination therapies targeting monomeric and dimeric RAF proteins. Our preliminary results reveal synergy between RAF inhibitors in treating melanoma lines harbouring BRAF non-p.V600 mutations.

Connecting Conformational Dynamics to Function of Class II Lanthipeptide Synthetases

K. Uggowitzer*, Y. Habibi, H. Issak, C. J. Thibodeaux

McGill University

Lanthipeptides are a family of ribosomally synthesized and post-translationally modified peptide natural products that contain characteristic thioether rings. These rings are installed into the C-terminal core region of the precursor lanthipeptide (LanA). In class II lanthipeptides, these modifications are tailored into the LanA through a multistep mechanistic pathway catalyzed by a single lanthipeptide synthetase (LanM). These synthetases modify their substrates in an iterative process achieving an extraordinary degree of biosynthetic fidelity. For instance, the HalM2 synthetase catalyzes the formation of four thioether rings and seven net dehydrations in its precursor peptide (HalA2). Out of many possible isomers, fully modified HalA2 will consist of only one constitutional isomer. The conformational dynamics of these synthetases most likely play a pivotal role in orchestrating this remarkable biosynthetic fidelity. Using hydrogen-deuterium exchange mass spectrometry (HDX-MS), we were able to directly observe the conformational dynamics of lanthipeptide synthetases (HalM2) for the first time. By observing changes in deuterium uptake under different conditions, once overlooked regions appeared to be potentially vital to HalM2 function. By mutating these interesting regions, we were able to link changes in conformational dynamics to specific functions like substrate binding, catalytic efficiency and allosteric communication.

Organic Chemistry

Synthesis and Screening of a Fluorinated Library Applied to Fragment-Based Drug Discovery via ^{19}F NMR

D. Bendahan[1]*, P. Forgione[2], S. LaPlante[1]
[1]INRS, [2]Concordia University

The discovery of biologically active drugs has played a crucial role in modern medicine and has resulted in an increase to the human lifespan and quality of life. Nonetheless, there is an urgent need for the discovery of new small molecule drugs. Classical methods for identifying the seeds for new drugs have notoriously low success rates, are expensive, time consuming, and require large teams of talented scientists. Fortunately, fragment-based drug discovery (FBDD) holds promise for overcoming many of the traditional hurdles. In short, rather than the high-throughput strategy of screening millions of compounds to find a unique lead, FBDD screens a smaller library of molecular fragments from which a potent lead is built up by growing and/or merging different binding fragments. This bottom-up approach has its advantages, but many methods need to be developed to maximize its successes. Nuclear magnetic resonance (NMR) spectroscopy has proven to be a valuable biophysical technique for binding detection in FBDD and ^{19}F NMR provides added advantages over 1H NMR for drug discovery. The present research revolves around the use of ^{19}F NMR spectroscopy and the synthesis of a fluorinated, thiophene based, fragment library to be screened against several drug targets.

Use of Flow Chemistry for Decarboxylative Palladium-Catalyzed Cross-Coupling Reactions in the Synthesis of Heteroaromatics

C. Buonomano[1]*, P. Forgione

[1]Concordia University, [2]Concordia University and Centre in Green Chemistry and Catalysis

The chemical industry plays a major role in the production of chemicals; however, it often results in pollution and the release of toxic contaminants. Green chemistry is the design of more environmentally friendly protocols that could reduce the generation of toxic substances. We decided to implement some aspects of this approach in our research for the synthesis of heteroaromatics using catalysis and flow chemistry. Heteroaromatics are key motifs present in many biologically active compounds. Their synthesis can be achieved via palladium-catalyzed cross-coupling reactions. Recently, decarboxylative cross-couplings have emerged as advantageous and greener alternatives to the classical methods reducing the production of harmful by-products. We have been investigating these cross-coupling methodologies for the past decades proving their usefulness. In order to increase the attractiveness of our methodologies for industrial applications, it is crucial to adapt them to new synthetic technologies. Continuous flow is a powerful technique using micro-tubes and small benchtop reactors. It offers advantages versus the batch processes commonly used in organic synthesis. The purpose of this research project is to apply the decarboxylative cross-coupling methodology developed by our group, and make it more efficient, versatile and cleaner using the flow chemistry techniques.

Total Synthesis of Ananatosides as a Novel Class of Biosurfactants

M. Cloutier*, M.-J. Prévost, C. Gauthier

INRS - Centre Armand-Frappier Santé Biotechnologie

Microbial glycolipids possess a variety of therapeutic activities owing to their ability to form pores and destabilize biological membranes. Our group has recently reported that the proteobacterium Panteoa ananatis produces novel biosurfactants, named ananatosides A and B. These atypical biosurfactants are composed of a β-D-glucose moiety to which is attached a dilipidic side chain. Ananatoside A additionally features an unprecedented scaffold consisting of a 13-membered macrodilactone ring formed through the intramolecular lactonization of ananatoside B, its opened form congener. Noteworthy, various glycolipids featuring di- and trilactones of different macrocycle sizes produced by plants and microorganisms are known to exhibit potent antiviral activities. We have therefore hypothesized that ananatosides A and B, as well as their non-natural derivatives, represent potential therapeutic agents. Thus, we have designed a high-yielding multi-step synthetic route involving a late-stage intramolecular glycosylation step which allowed us to prepare ananatoside A. We also showed that the latter could be prepared through enzyme-catalyzed macrolactonization of ananatoside B. (1-->2)-, (1-->3)- and (1-->4)-Macrodilactone-containing rhamnolipids were prepared via our optimized late-stage intramolecular glycosylation approach. With the new interest of macrocyclic compounds in a therapeutic context, this project could lead to the identification of new biologically active glycosidic macrolactones.

Visible-light-mediated Decarboxylative Alkynylation using Heteroleptic Copper Complexes

C. Cruché

Université de Montréal

Photocatalysis employing visible-light promotes chemical transformations under mild conditions with complementary reactivity patterns to thermally-promoted reactions. While previous photocatalysis was dominated by ruthenium and iridium complexes, the use of more earth-abundant metals like copper has emerged. The Collins group has been studying libraries of heteroleptic copper complexes in different photocatalytic processes. One of these is the decarboxylative Csp3-Csp bond coupling to construct substituted alkynes. Optimization and mechanism hypothesis will be presented. L'utilisation de lumière visible en photocatalyse permet des transformations chimiques sous conditions douces avec une réactivité complémentaire aux réactions thermiques. Si la photocatalyse est dominée par des complexes de ruthénium et d'iridium, l'utilisation de métaux plus abondants tel que le cuivre commence à émerger. Le groupe Collins étudie une bibliothèque de complexes de cuivre hétéroleptiques dans différentes réactions photochimiques. L'une d'entre elle est le couplage décarboxylant de liens Csp3-Csp pour la formation d'alcynes substitués. L'optimisation de la réaction ainsi que les hypothèses mécanistiques seront présentées.

Alkynyl Sulfides Macrocyclic Peptidic Alkynyl Sulfides: Synthesis and Diversification.

J. Guerrero*, E. Godin

Université de Montréal

Our group has developed a novel Cu-catalyzed Csp-S cross-coupling of thiols and bromoalkynes and applied it to the synthesis of macrocyclic peptides. Alkynyl sulfides are particularly attractive as macrocyclic "linkers" as the functional groups as easily functionalized at the sulfur center or - and -position of the alkyne. Macrocyclic peptides were synthesized and further diversified via S-oxidation, halide addition and Ir-catalyzed azide-alkyne cycloadditions to incorporate valuable fluorophores, biotinylated sidechains, PEG motifs or farnesylated units.

Analytical Chemistry

Evaluating the Effect of Temperature on Lipid Extraction using LC-MS-based Lipidomics

L. Cougnaud, S. Nishu, D. Vuckovic

Concordia University

The vital role of lipids has been demonstrated in many human diseases, including cardiovascular diseases and cancers. Along with lipid identification, proper extraction is vital to interpret any findings obtained from a lipidomics analysis. The handling parameters, specifically temperature used during extraction, may affect the measured lipid profiles due to possible oxidation, loss of fatty acyl chain and lipase enzymatic activity. The effects of lipid storage temperature have been investigated in several studies. However, the effect of the extraction temperature has not been evaluated until now. The aim of this study is to evaluate whether the extraction temperature impacts the observed lipid profile in human plasma using LC-MS-based untargeted lipidomics. Three different extraction temperatures were tested (i) room temperature, (ii) 4°C and (iii) -80°C. Along with temperatures, lipase activity was also evaluated using orlistat (an anti-lipase agent) at a concentration of 5 µM and 25 µM. Among the 17 identified lipid classes, the sub-class of diacylglycerols was affected by the extraction temperature. For all the temperatures tested, there was no evidence of lipase activity. In summary, the current study revealed that subtle effects of extraction temperature on certain lipid species do exist and may impact their measurement during lipidomics workflows.

Reaction Between DOPA and Cysteine Thiol Studied by LC-MS/MS

M. Sansoucy*, L. Sleno

UQAM

The usage of 3,4-dihydroxyphenyl-L-alanine (L-DOPA) represents the first therapy for cognitive disorders. In addition, DOPA is observed as a post-translational modification in some proteins and serves as an oxidative stress biomarker. When metabolized, DOPA is rapidly oxidized to electrophilic dopaquinone and reacts with cysteine to yield 5S (or 2S)-cysteinyldopa (Cys-DOPA). Currently few studies have addressed the consequences of DOPA-related protein covalent binding with nucleophile cysteines. High-resolution hybrid quadrupole time-of-flight tandem mass spectrometry identified Cys-DOPA with very high mass accuracy, following its formation in vitro with tyrosinase. Complementary incubations with deuterated tyrosine have confirmed the 5S isomer as the predominant species. Covalent modification on free cysteine was also observed with 3,4-dihydroxyphenyl-acetic acid (DOPAC) and dopamine. Further incubations with model peptides to examine the stability of Cys-DOPA under conditions used in bottom-up proteomics workflows are currently ongoing for future studies on protein crosslinking.

Extraction of Peptide Hormones using Solid-Phase Microextraction (SPME)

A. Malkawi

Concordia university

Peptide hormones play major physiological roles in the body, such as muscle contraction. Conventionally, these hormones are analyzed by immunoassays, which have some drawbacks such as poor specificity and/or inter-batch repeatability. Herein, the ability to extract a panel of hormones with a wide chemical and physiological properties using solid-phase microextraction (SPME) was examined for the first time.HLB-type of fibers were used for SPME extraction. The Design of Experiment (DOE) approach, specifically the full factorial design, was used to optimize the desorption conditions for HLB fibers. The factors tested were desorption solvent composition, desorption solvent volume, time of desorption, and agitation speed. Peptide measurement was performed using reversed-phase chromatography coupled to electrospray ionization LC-MS (LTQ-Orbitrap). Baseline separation was achieved for the hormones of interest. The method linearity was established for each hormone, for example from 1 ng/ml-1 µg/ml for oxytocin. Endomorphin, oxytocin, and neurotensin maximum extraction recovery were found to be 90%, 64%, and 60%, respectively, while the recoveries of glucagon and insulin were< 20% for both. Leptin was not recovered at all. Desorption solvent type and agitation speed were found to be the major two factors that have a significant effect on desorption.

Chemistry against the New Psychoactive Substances (NPS) hydra : a flexible analytical framework to win the battle

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[1]*Université du Québec à Trois-Rivières,* [2]*Laboratoire de sciences judiciaires et de médecine légale*

New psychoactive substances (NPS) have a short life cycle, with new analogues of high structural similarity constantly appearing on the black market. Combined with their low biological concentrations, the resulting challenge to forensic toxicology laboratories is unprecedented. This calls for a novel analytical framework, at the center of which resides an LC-MS/MS method for NPS and metabolites.
Knowledge of the enemy's weaknesses resulted in a method able to differentiate pairs of isomers via careful chromatography development and mass transition selection. Furthermore, opening up the method to metabolites in addition to parent drugs widens the detection time window. Above all, swiftness is essential to follow NPS emerging trends. This method allows dynamic compound addition and removal, with validation being completed in a single experiment. A few days only are now necessary from the identification of a new threat to its inclusion in the standard screening method.
Since the implementation of this comprehensive, flexible and responsive LC-MS/MS method, NPS detection has increased near 10-fold in the laboratory, demonstrating its usefulness and importance in the current setting. Where regular, fixed methods targeting only a handful of compounds have failed, this analytical framework has a chance of winning the battle against the NPS hydra.

Characterizing the H_2O_2 Stimulon in Saccharomyces cerevisiae Cells with Normal and Amplified H_2O_2 Sensing

S. Dastpeyman, H. Jiang, A. M. English

Concordia University

We aim to quantify all proteins that respond to H_2O_2 challenge in yeast to elucidate at the proteome level various survival strategies in a eukaryotic cell. Specifically, we are comparing wild-type (WT) yeast expressing the native form of the H_2O_2 sensor protein, cytochrome c peroxidase (Ccp1), and a strain producing its W191F variant, which is a hyper H_2O_2 sensor. The reproducibility of our LC-MS/MS-based label-free quantitative proteomics method was confirmed by examining three biological replicates. We then challenged cells with 0.4 mM H_2O_2 and identified ~1700 proteins, including 201 and 141 responsive targets in WT cells at 10 and 60 min after treatment, respectively, compared to 220 and 468 responsive targets in cells producing Ccp1W191F. The global response to exogenous H_2O_2 challenge clearly exposes a switch of cellular activity from biosynthesis to defense and redirecting of carbohydrate metabolism to NADPH production in both strains. However, hyper sensing by Ccp1W191F produces a dramatically more sustained response. Our observations underline the complexity of yeast systems biology and highlight the power of LC-MS/MS as a reliable and rapid technology in unravelling such complexity.

Investigating Drug-Related Protein Binding in Vitro by LC-MS/MS

T. Geib *, L. Sleno

UQAM

Drug-induced liver injury is often related to the metabolism of xenobiotics. Examples include the commonly used painkiller, acetaminophen (APAP), and related antipsychotics clozapine (CLZ) and olanzapine (OLZ), which are all known to form reactive metabolites, and covalently bind to proteins. We have investigated these compounds and their reactive metabolite binding to glutathione and specific proteins in vitro. Covalent binding of APAP, CLZ and OLZ was studied using rat liver microsomes or purified human CYPs (Supersomes). Several liquid chromatography-tandem mass spectrometry (LC-MS/MS) strategies have been developed and compared for identification of covalent drug-protein adducts. For protein binding, traditional shotgun proteomics (using data-depended acquisition) was employed on a quadrupole–time-of-flight system with database searching. A targeted multiple reaction monitoring method was also optimized for APAP-modified peptides on a quadrupole-linear ion trap, to increase sensitivity and reproducibility of site identification with higher throughput of analysis. By using highly sensitive LC-MS/MS techniques we successfully identified multiple hepatic protein targets modified by APAP, CLZ and OLZ, and their primary metabolites. These proteins included several human glutathione S-transferase and human serum albumin, the latter being a vital biomarker of exposure to reactive metabolites.

Inorganic Chemistry and Computational Chemistry

Conversion of Electrochemically Deposited Carbonates to Perovskites with Retention of Crystal Morphology

W. Leal*, M. Majewski

Concordia University

Perovskite materials have been identified as strong candidates for use in many light-driven processes and devices including; water splitting, solar cells, light-emitting diodes, and radiation detectors. This stems from their intrinsic photophysical properties such as low exciton binding energy, long carrier diffusion length, and a tunable band gap. However, direct synthesis limits the morphologies that can be made, and control over the shape of perovskite crystallites may allow us to further tap into their potential. It has been reported that conversion of carbonate to perovskite microstructures can be achieved through ion-exchange reactions, with structure retention. The present work aims to deposit different morphologies of calcium carbonate on transparent conducting oxide substrates and convert the resulting microstructures to perovskites while retaining the crystal structure. Targeted morphologies of calcium carbonate include calcite, aragonite, and vaterite, which have trigonal, orthorhombic, and hexagonal crystal systems, respectively. After electrochemical deposition, the microstructures are exposed to a concentrated solution of lead nitrate to enable cation exchange. Subsequent exposure to either an organic ammonium or Group 1 halide leads to the conversion of the expected perovskite. These structures are characterized through scanning electron microscopy (SEM), energy dispersive X-ray spectroscopy (EDS), and (photo)electrochemistry.

Long-lived Photocatalytic Hydrogen Evolution using Ru(II) bis-terpyridine Complexes as Photosensitizers

M. Rupp[1]*, T. Auvray[2], G. Hanan[2], D. Kurth[3]

[1]Université de Montréal, Julius-Maximilians-Universitaet Wuerzburg, [2]Université de Montréal, [3]Julius-Maximilians-Universitaet Wuerzburg

The photocatalytic reduction of water to form hydrogen gas is one of the approaches to collect and store solar energy. Ruthenium tris-bipyridine [Ru(bpy)3]2+ and its numerous derivatives have been applied as photosensitizers (PSs) in a variety of photocatalytic conditions. The bis-terpyridine analogs, however, have been disregarded for this application due to their poor photophysical properties. Yet, by introducing electron donating or withdrawing groups on the terpyridine ligands, the photophysical and electrochemical properties can be tuned. Furthermore, additional coordination sites, e.g. peripheral pyridine rings, offer the possibility of the PS to coordinate to the catalyst and transfer electrons efficiently. In this study, a new terpyridine ligand Bipytpy (4‘-(4-bromophenyl)-4,4’’’:4‘‘,4’’’’-di-pyridinyl-2,2‘:6‘,2‘‘-terpyridine) was prepared and used in the complexes 1 [Ru(Tolyltpy)(Bipytpy)](PF6)2 (Tolyltpy : 4’-tolyl-2,2’:6’,2’’-terpyridine) and 2 [Ru(Bipytpy)2](PF6)2. Both complexes exhibit enhanced photophysical properties compared to bis-terpyridine complexes without pyridine substituents. Additionally, the less negative reduction potentials facilitate the reductive quenching by a sacrificial electron donor which appears to be the rate limiting step in hydrogen evolution in this system. The use of complexes 1 and 2 as PS and a cobaloxime catalyst in visible light driven hydrogen evolution, with triethanolamine as sacrificial electron donor, led to a sustained activity under blue light irradiation.

Time-resolved MS Studies Identify the Heme Degradation Products of Mycobacterium Tuberculosis MhuD

B. Thakuri

University of Vermont

In the heme uptake machinery of Mycobacterium Tuberculosis, MhuD is involved in catalyzing the degradation of heme. Canonical heme oxygenase (HO) such as human HO have been shown to degrade heme to iron, CO and biliverdin. However, MhuD has demonstrated to degrade heme to iron and mycobilin. The formation of a distinct organic byproduct by MhuD means that it follows a unique heme degradation mechanism. The results of the time-resolved mass spectrometry (MS) study on heme degradation by Wild Type (WT) MhuD will be presented. This study identified the formation of both mycobilin and biliverdin. This is an interesting discovery that warrants further investigation. Due to the dynamic nature of heme in the active site of MhuD, the conformation of heme may be responsible for the different products. To test this hypothesis, two different variants housing different conformations of heme in their active sites were studied. F23W and W66F MhuD has been shown to stabilize more and less ruffled heme respectively in their active sites. Time-resolved MS study identified mycobilin as major product F23W MhuD and biliverdin for W66F MhuD. Therefore, ruffling may play a major role in the formation of mycobilin and biliverdin during heme degradation by MhuD.

Cuprophilia: Cu(I)/Cu(II) Photosensitizer/Catalyst Photosystem for Efficient Water Oxidation

Z. Singh*, M. Majewski

Concordia University

With a surging demand for non-renewable energy, the storage of solar energy in chemical bonds holds promise as alternative energy source for the future. Photochemical splitting of H2O to H2 and O2 is one approach to generate "solar fuel." Cu(II) based electrochemical water oxidation systems in aqueous solution have been studied previously, but driving these systems photochemically still remains a challenge. Light harvesting units can be employed for this purpose, that upon photoexcitation generate a high energy excited state and give rise to a long living charge separated state (CSS). In this work, a new bis-diimime copper(I) based donor-chromophore-acceptor (D-C-A) system is synthesized, characterized, and studied. This molecular system was integrated onto a zinc oxide (ZnO) nanowire surface on a fluorine-doped tin oxide (FTO) glass slide. Upon photoexcitation, chronoamperometric studies reveal that the integrated triad can inject electrons directly into the conduction band of ZnO generating oxidizing equivalents that are then transferred to a Cu(II) water oxidation catalyst in aqueous solution. This Cu(I)/Cu(II) PS/Cat photosystem is proposed to function via reductive quenching of our oxidized electron donor moiety by electron transfer from water oxidation catalyst.

Computational Mechanistic Study of Catalytic C-H Amination Reactions using Rhodium Dimers and N-Mesyloxycarbamates: Reaction Pathway and Byproducts Formation

E. Azek

Université de Montréal

Catalytic amination reactions with transition metals via nitrenes species[1] is an interesting alternative synthetic approach to classic procedures for the preparation of amines. Although, many synthetic applications of these reactions have been developped, their mechanistic investigation remains limited. A computational mechanistic study of catalytic amination reactions using Rh2(OAc)4, with N-sulfonyloxycarbamates as nitrenes species precursors,[2] was thus investigated by the Density Functional Theory (DFT). The surfaces of potential energy of insertion reactions of rhodium-nitrenes species into C-H bonds[3] were examined. In this study, some mechanistic hypotheses have been elucidated, while other reactions key parameters were highlighted. In this oral presentation, experimental and kinetic studies will be reported, as well as different possible reactions pathways. In addition, an exhustive study of the origin of byproducts observed during these reactions will be presented.

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Computational Studies of Light-driven Pinacol Coupling by Hydrazine

C. Pham*, R. Khaliullin, C.-J. Li, Z. Qiu

McGill University

Efficient carbon–carbon bond formation is of great importance in modern organic synthetic chemistry. The pinacol coupling discovered over a century ago is still one of the most efficient coupling reactions to build the C–C bond in one step. However, traditional pinacol coupling often requires over-stoichiometric amounts of active metals as reductants, causing long-lasting metal waste issues and sustainability concerns. An experimental investigation proposes a light-driven pinacol coupling protocol without use of any metals, but with NH_4, used as a clean non-metallic hydrogen-atom-transfer (HAT) reductant. Computational investigation, hence, is needed to gain detailed insights into elementary steps and structural transformations along the pathway. Herein, we present our collaborative work on elucidating the proposed mechanism regarding processes of ketyl radical formation, the HAT behavior of $N_2H_4$and the C–C bond formation of the product. Our results are consistent with experimental data which suggests that the proposed mechanism proceeds via a HAT process between photo-excited ketone and N_2H instead of the common single-electron-transfer (SET) process for metal reductants.

Molecular Biology

Modelling Neurodevelopmental Disorders Linked to Single Point Mutations in TRAPPC2L

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Concordia University

The TRAPP family of protein complexes have been implicated in membrane traffic in the secretory pathway as well as playing a role in autophagy. Within the TRAPP complexes is a TRAPPC2-related protein called TRAPPC2L. Here we characterize the first identified mutations in TRAPPC2L. One mutation, found in two unrelated individuals, is a missense mutation of the conserved Asp37 (p.Asp37Tyr). These mutations manifested as a combination of neurodevelopmental delay, febrile illness-induced encephalopathy and episodes of rhabdomyolysis, followed by developmental arrest, epilepsy and tetraplegia. Studies in patient fibroblasts as well as in a yeast system showed that the mutated proteins were present but not functional and resulted in specific membrane trafficking delays. The human missense mutations ablated the interactions between TRAPPC2L and the TRAPP subunits. Since TRAPP II activates the GTPase RAB11, we examined the activation state of this protein and found increased levels of the active RAB, correlating with changes in its cellular morphology. We propose to generate neuronal cell populations from direct conversion of human fibroblasts into mature and functional neurons, termed induced neurons (iNs) to better model these mutations in TRAPPC2L and their effect on the nervous system.

Genomics-Based Analysis of Bacterio-Modulation as a Potential New Approach for Treating Bacterial Infections and Overcoming Antimicrobial Resistance

M. Mahdavi*, B. Findlay

Concordia University

Antimicrobial resistance is becoming an increasingly large problem for human health. Novel antibiotic production is the current method for combatting antimicrobial resistance, however, this is only prolonging the effects because eventually the bacteria will become resistant. Bacterio-modulation can provide an effective alternative to this problem. This can be applied to Salmonella Typhimurium, a prominent gram-negative bacteria, and it's interactions with macrophages in the human body. Through genetic mutations, S. typhimuriumacquires resistance against itaconic acid (ITA), a virulence molecule produced by human macrophages. However, we have found that macrophage activity against S. Typhimurium is restored upon the addition of the compound 3-nitro-pantothenate (3-NP). To understand the bacterio-modulation interactions at the genomic level, a SAGE plate system was used to enable bacterial evolution to occur, so that resistant S. Typhimurium cells could be obtained. The collected clonal and population samples were sent for genomic sequencing (Illumina HiSeq), and it was found that that 3-NP alone does not confer genetic mutations in the S. Typhimurium cells. This further supports the hypothesis that 3-NP does not impose a selective pressure on S. Typhimurium, unless in the presence of ITA.

Regulation of Natural Product Biosynthesis

L. Rili

Concordia University

The majority of antibiotics are developed from secondary metabolites produced by microbes. However, most biosynthetic gene clusters (BGCs) are inactive in a laboratory setting. Photorhabdus luminescens is an insect pathogen which kills through a large array of natural products, which is why we chose it. Through antiSMASH analysis we have identified 22 potential BGCs in Photorhabdus luminescens TT01. 16 of these BGCs contained a binding site for the global regulator Sigma-54, suggesting that this regulator plays an active role in natural product biosynthesis. We have also found that P. luminescens genome contains 7 possible enhancer binding proteins (EBPs) that could serve as activators of sigma-54.Through transcriptomic and metabolomics analysis I will identify the function of these EBPs and linking them to the BGCs that they may regulate. Then I will move to identifying and characterising the secondary metabolites expressed by these BGCs. Ultimately, this work will allow us to identify and characterize a general EBP that can be used to activate silent BGCs in P. luminescens and other related bacteria, allowing the discovery of new, potent antibiotics.

Synergistic Effects of pH on the Activity of the Antibacterial Metabolite Itaconate

D. Duncan*, K. Auclair

McGill University

Globally, bacterial infections are becoming more dangerous and life-threatening due to rising antibiotic resistance. In order to overcome this global health crisis, we need to provide new ways to fight bacterial infections. Among these methods is to take advantage of the natural defences of the immune system to improve its capacity of fighting pathogens. Itaconate is a metabolite produced in macrophages that has an important role in the immune response and vital role in managing bacterial invasion. This metabolite is an effective inhibitor of isocitrate lyase, an essential enzyme for pathogenesis. The minimum inhibitory concentrations (MICs) for itaconate in vitro against a variety of pathogens (ca. 10 – 20 mM) tend to be a greater concentration than what is found within macrophages (ca. 60 µM). Considering the low pH of the phagolysosome within the macrophage, we decided to explore the effect pH has on the antimicrobial activity of itaconate. We use two bacterial models where one (Escherichia coli) is intrinsically sensitive to itaconate, whereas the other (Salmonella enterica spp. Typhimurium) has intrinsic resistance to itaconate. We convincingly show that there is a synergistic effect between pH and itaconate activity irrespective of level of itaconate resistance by the bacterium.

Systematic Whole-Exome Sequencing in Unexplained Cardiac Arrest: Results from the Canadian CASPER Registry and Biobank

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Ventricular fibrillation (VF) in the absence of coronary disease or left ventricular (LV) dysfunction often remains unexplained. Given its heritability, identifying the genetic culprit is important for family screening. Systematic whole-exome sequencing (WES) identifies a causal variant in a significant proportion of unexplained cardiac arrest (UCA) survivors. We performed WES in unrelated survivors of UCA, defined as VF in the absence of overt structural or electrical disease. Joint variant calling was performed as per the GATK best practice guidelines. We limited our analysis to rare protein-coding variants in 60 genes associated with cardiac conditions. WES was performed in 234 UCA probands (66% males; age at arrest 38±13). WES identified a total of 17.6M high quality variants, of which 172 were rare variants in the 60 genes. We observed a significant enrichment of rare missense RYR2 variants in UCA as well as an enrichment of rare truncating variants in cardiomyopathy genes. Of the 234 probands, 30 (12.8%) had ≥1 causal variants. Systematic comprehensive genetic testing of cardiac genes identifies a disease-causing variant in 13% of unexplained cardiac arrest survivors. Truncating variants in cardiomyopathy genes are enriched in UCA supporting an association of structural genes with ventricular arrhythmias.

NRF2 transcriptional network in anoxia-tolerant vertebrates

A. Gupta*, K. B. Storey

Carleton University

Wood frogs (Rana sylvatica) endure prolonged periods of freezing (as much as ~70% of total body water turned to ice) causing a halt in blood circulation and oxygen deliver to all organs. These frogs also tolerate anoxia independently of freezing with full survival after aerobic recovery. Episodes of anoxia/recovery can elevate the formation of reactive oxygen species and initiate destructive pathways that could result in cell death. Oxidative damage must be combated with strong antioxidant defences to allow survival. Nuclear Factor erythroid 2-related factor 2 (NRF2) is a stress-responsive transcription factor that regulates the expression of antioxidant and detoxifying enzymes and plays an important role in anoxia endurance. As such, we investigated wood frog responses to anoxia and recovery by a network of antioxidant genes including glutathione S-transferases (GSTs) and aldoketoreductases (AKRs) under the control of NRF2. Our results indicate that GSTs and AKRs are regulated in a tissue-specific manner in liver and muscle. GSTP1 and GSTT1 showed a conserved response in both tissues, whereas AKRs showed tissue-specific responses. All together, our results suggest that wood frogs have a strong antioxidant defence response to oxidative stress, and NRF2 plays a significant role in allowing survival under anoxic conditions.

Environmental Chemistry

Early Diagenesis and Preservation of Organic Matter in Anoxic Aquatic Environments: The Lagoon of Bizerte, Tunisia

M. Essifi

Concordia University

The main objective of this work was studying the early diagenesis of organic matter (OM) in recent aquatic sediments (Lagoon of Bizerte) to characterize sediment origin and depositional conditions. Lithological and mineralogical analyses revealed that the core evolved from a heterogeneous sandy detrital layer to carbonate mud containing a small proportion of clay at depth. The geochemical analyses showed low values of total organic carbon (TOC; 1.38-2.22%) and nitrogen (N; 0.09-0.24%) in the sandy sediment layer. However, sediments rich in carbonate mud present high values of TOC (1.54-5.84%) and N (0.71-0.95%). The TOC/N molar ratios revealed that OM is clearly of marine origin with small continental contributions and an increased predominance of marine inputs towards the base of the core. The hydrodynamics in the Bizerte Lagoon can be divided into two periods. The first period is characterized by high concentrations of marine OM, with humic substances accounting for 65% of this TOC suggesting that this sediment layer was characterized by anaerobic conditions. The second period is characterized by a mixture of marine and continental material, with a relatively low humic substances content suggesting a sediment layer characterized by aerobic conditions that lead to an increased degradation rate of OM.

CO_2 Sequestration by Mineral Carbonation with Iron Complexing using 2,2'-Bipyridine as Ligand

J. Fernandez Reynes

INRS-ETE

A new Mineral Carbonation (MC) Design was demonstrated by iron complexation using 2,2'-bipyridine as a ligand to obtain the stable complex [Fe(bipy)3]2+ which avoids iron hydroxide precipitation and leaves, in reaction with CO_2(aq) in a basic medium, the formation of iron carbonate. First, a leaching step of the mining residue was necessary to extract the cations (Fe mainly) for the MC. The leaching acid used was ammonium bisulphate (NH4HSO4). Afterwards, 2,2'-bipyridine was added to form the complex ([Fe(bipy)3]2+) and stabilize the iron in solution. The complex stability for 7 days between pH 1-12 were studied using UV-Vis spectroscopy. Afterwards, the CO_2(aq) was reacted with [Fe(bipy)3]2+ at different temperature (25, 60 and 80 °C) and pH (9-12) conditions. NaOH was used as a base to increase the pH. The effectiveness of the reaction was followed by TIC and ICP-OES Analysis. The precipitate samples obtained were characterized by SEM-EDS, CHNS and ICP-OES to verify carbonate production. Finally, in order to know if it would also be economically viable for a future industrial establishment, a recirculation study of 2,2'-bipyridine and leaching acid (ammonium bisulfate) was carried out for reuse in the process, which would reduce costs and make it suitable for industry.

Stanol Concentrations and Ratios in Sediments as Indicators of Human and Animal Populations from Lakes Across Climatic and Land-Use Gradients in Mexico, Guatemala and Belize

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Faecal stanols offer an exciting opportunity to determine population change in the past but the controls of their concentrations and ratios within lake sediments are not well understood. We present the variability in stanol concentrations and ratios from lakes across environmental gradients, both between and in lakes across climatic and land-use gradients in Mexico, Guatemala, and Belize in order to determine the factors controlling preservation and degradation in lacustrine sediments. We explore the hypothesis that a dominant control on concentrations and ratios is proximity to a human settlement. We evaluate this hypothesis where we collected samples at varying distances from major population centres. In addition to this work we will share three intriguing preliminary palaeo-records of stanol concentrations from Guatemala (Laguna Itzan, Laguna Peten-Itza, and Lago Izabal). These records imply highly dynamic millennial scale changes in human populations, and we apply the modern sediment data to better constrain the interpretation of these data. Our work shows that faecal stanols have a strong potential as proxies for changes in human population and land-use change through time and can be used to complement archaeological datasets to link human populations with palaeoenvironmental change.

Organic Chemistry

Cyclization Cascade Followed by Non-Usual Indoline Formation Towards the Synthesis of Enantioenriched Aspidospermatan Alkaloids

J.-P. Fontaine*, C. Hauduc, G. Bélanger

Université de Sherbrooke

Indole and its bioisosteres are recognized as biologically active functional groups and are found in a wide variety of alkaloids and drugs. The strategy generally used for the synthesis of aspidospermatan indole alkaloids is to begin with the indole portion and then construct the rest of the molecule around it. Over the last years, our research group developed a one-pot sequence of Vilsmeier-Haack cyclization and non-stabilized azomethine ylide intramolecular (3+2) cycloaddition to rapidly increase the molecular complexity. We have already applied this strategy to effectively synthesize an advanced tricyclic intermediate for the synthesis of racemic tubotaiwine and congeners. A major advantage of cyclization cascades resides in the control of the absolute configuration of all stereogenic centers, induce by only one stereogenic center on the cascade precursor. Recently, different approaches have been successfully explored to allow a non-racemic synthesis of this key step precursor using Evans auxiliaries. Another objective of this project is the incorporation of indoline at the end of synthesis. Because of ring strain, known methods based on thermodynamic enolization (e.g. Fischer) are not suitable. To address this problem, we proposed an approach consisting of an oxidative radical decarboxylation and trapping with an adjacent aniline.

Synthesis of GPCR68 Agonists to Promote Heart Muscle Cell Regeneration after Myocardial Infraction

R. Hernandez*, P. Forgione

Concordia University

Myocardial infarction (MI) or a heart attack is among the most common cardiovascular disease worldwide. In Canada the Public Health Agency reported that 6% of Canadians above the age of 20 were living with a cardiovascular disease, where the most prominent is MI. There are a very limited number of drug candidates that allow the regeneration of muscle tissue after MI. Isoxazole compounds have shown to regenerate muscle tissue in a mouse model by agonising GPCR68. We have synthesized a library of isoxazole containing compounds using a conventional synthetic pathway. However, this pathway is limited by the five-member heteroaromatic ring adjacent to the central isoxazole. Herein, we discuss a versatile synthetic alternative pathway that incorporates a palladium catalyzed decarboxylative cross-coupling reaction, which allows access to broad library of five-member heteroaromatic rings adjacent to the central isoxazole ring.

Integrating Computational Methods and Organic Synthesis: Application to the Design and Discovery of Highly Selective Enzyme Inhibitors

A. Labarre

McGill University

The pair of proteins dipeptidyl peptidases 8 and 9 (DPP8/9) are two serine proteases involved in the immune function. In particular, their inhibition was found to lead to tumor regression via up-regulation of the immune system which makes these two proteases of therapeutic interest. Selectivity challenges amongst members of the DPP8/9 family are to be considered due to the similarities in the active sites. Selectivity is a very important concept in drug development as off-target interactions can lead to undesired biological side effects. The design of selective inhibitors is therefore an important focus in the conception of therapeutics. Despite the advances of docking platforms, in silico selectivity predictions are still lacking concise and accurate methodologies. We have developed the high rating docking platform FITTED and we are currently working on the implementation of methodologies in selectivity predictions. Furthermore, the strength of our approach relies on the integration of our computational and synthetic expertise. We have already started the synthesis of hits that were predicted to have high affinity for DPP8/9.

Preliminary Structure-Activity Relationship Study and Biological Evaluation of Thienoisoquinoline Derivatives as Anticancer Agent

J. T. Liu*, P. Forgione

Concordia University

A thienoisoquinoline derivative C75 (compound 1) was discovered with potent anti-cancer activity against cancer cell lines A549, HeLa, HCT-116 in the nanomolar concentration range. Structure-activity relationship (SAR) studies on 24 derivatives aided in identifying key pharmacophores in the lead compound. In conclusion, there are three promising derivatives that show low nanomolar IC50 values against lung cancer cell lines (A549). Immunomicroscopic images illustrate microtubules disruption in the cancer cells. Further biological evaluation via a tubulin polymerization assay and competition studies indicate the plausible biological mechanism of the lead compound possibly binds to the colchicine site.

Nanochemistry

Inducing Chirality in Carbon Dots

F. Victoria*, R. Naccache

Concordia University

Chirality has been an important factor in pharmaceutical research for drug development and design, as well as in applications of catalysis, enantioselective recognition and sensing. This is due to the fact that enantioselectivity is observed in many biochemical reactions and interactions in nature. As such, we are interested in exploring residual chirality in carbon dots, a fluorescent carbon nanoparticle composed primarily of sp2 carbons and oxygens. These nanoparticles have excellent tunable fluorescence, low toxicity, chemical inertness and biocompatibility and as such making them an ideal candidate for applications ranging from drug-delivery, bioimaging, chemical sensing to catalysis. These versatile properties of CDs are determined by the starting materials and they can be synthesized from various carbon sources and passivating agents. We report a facile, one-step microwave-assisted synthesis of chiral CDs from enantiomers of amino acids and investigate the effect of reaction parameters on the residual chirality observed in the nanoparticle.

Towards Uniform Optical Properties of Carbon Dots

F. Noun*, J. Manioudakis, R. Naccache

Concordia University

Carbon dots have versatile optical properties and have been investigated for integration in applications including photocatalysis, photovoltaics, imaging and drug delivery, among others. The preparation of these nanodots is accompanied by the formation of multiple fluorophore-like side-products, which can be difficult to separate. In the absence of thorough purification protocols, the reported optical properties are often heterogenous, which hinders our understanding of their fluorescence mechanisms and limits concrete application development. Here, we have prepared two hydrophilic carbon dot systems starting with citric acid and diethylenetriamine. We demonstrate the impact of purification, which includes dialysis, ultrafiltration and successive organic washes, on the steady-state and dynamic optical properties of the dots. We show that it is possible to monitor the purification endpoint using fluorescence and absorbance spectroscopies. Moreover, we demonstrate that fluorescence quantum yields can be used as a reliable tool to determine a purification endpoint. The proposed purification protocols can become an indispensable tool for the preparation of carbon dots with homogeneous optical properties, particularly when exploring new systems. Finally, our work can be easily extended towards the purification of other hydrophilic organic and inorganic nanomaterials.

Morphological Control of Cuprous Oxide Semiconductors Electrochemically Deposited onto a Zinc Oxide Nanowire Array and Their Use in Photocatalysis

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Concordia University

Zinc and copper oxides are well-studied materials in the context of solar energy conversion due to their low toxicity and high abundance. The combination of ZnO, an n-type semiconductor, and Cu2O, a p-type semiconductor, results in the formation of a p-n junction. The p-n junction allows for the effective separation of charge carriers upon photoexcitation, resulting in reduced charge carrier recombination and higher cell efficiency (in photovoltaic devices). In our work, this junction is formed through the hydrothermal deposition of a ZnO nanowire array onto a fluorine doped tin oxide (FTO) surface. The Cu2O is then electrodeposited onto the nanowire array creating a high surface area p-n junction. Furthermore, different morphologies of Cu2O (cubes, tetrahedra, spheres) are obtained through varying the deposition conditions. The intrinsic bandgap of Cu2O (ca. 2.17 eV) results in the absorption of visible light at wavelengths ≤ 570 nm and the different morphologies of Cu2O may show different efficiencies compared to one another when used in photocatalytic reactions, as well as affording varying selectivity. The high abundance, and low toxicities of the materials used, along with accessible synthetic methods, lead to the potential for a high degree of scalability.

Metal Oxide-Carbon Dot Nanohybrids for Photocatalysis of Organic Reactions

F. Yarur*, J. Manioudakis, R. Naccache, M. Majewski

Concordia University

The engineering of efficient solar energy conversion devices with Earth-abundant elements is of paramount importance to meet the energy demands of a carbon-neutral society and to decrease environmental pollution. Converting solar energy into chemical fuels (i.e. artificial photosynthesis) and industrially relevant chemicals is an attractive alternative to address the global energy problem. Typical methods to produce solar fuels make use of molecular complex catalysts/photosensitizers containing precious metals in order to harvest visible light. Carbon dots have recently been considered as suitable candidates to sensitize metal oxide structures due to their low cost and ability to absorb visible light. While photocatalytic systems using carbon dots as sensitizers have been reported, transformations involving the production of high value-added chemicals are underexplored. These systems are based on the absorption of visible light by carbon dots followed by electron injection to either the metal oxide semiconductor or the targeted species in solution, which triggers a chemical transformation. The physical and electronic architecture of these nanohybrids is a crucial factor that will dictate some of their optical and catalytic properties. In this work, we evaluate the sensitization of zinc oxide nanowires with carbon dots for the α-heteroarylation of 1-phenylpyrrolidine with 2-chlorobenzothiazole under visible light illumination.

Developing Multi-Sensing Imaging Probes Using Carbon Dots

J.-R. Macairan*, R. Naccache

Concordia University

Fluorescent imaging probes serve as a unique diagnostic tool for bioimaging and nanomedical applications offering high sensitivity particularly in their ability to image cells and tissues, as well as for the study of biological processes. These tools are becoming crucial for early detection and disease diagnostics especially with an increase in numbers of an aging population and the requirement for more efficient health care. Recent advancements in the field of nanomaterials have propelled research groups into investigating these nanoparticles for various biological applications including drug delivery, biosensing and bioimaging. Indeed, several nanomaterials including polymer dots, quantum dots and lanthanide-doped upconverting nanoparticles have been investigated for these applications and more recently carbon dots, which have garnered significant attention. These carbon-based nanoparticles are interesting as they can be prepared from simple synthetic routes using inexpensive precursors, offer low cytotoxicity and good biocompatibility, as well as possess tunable optical properties. Their inherent fluorescent nature not only allows for fluorescence imaging, but also for sensing environmental changes (i.e. temperature and pH), which can provide additional insights in diagnostics. In this work, dual-fluorescing carbon dots are synthesized using a one-step microwave-assisted reaction. The carbon dots' physico-optical properties are thoroughly studied in order to shed light on their fluorescence mechanism. The fluorescence of the carbon dots is tailored through manipulation of key synthesis parameters to determine their underlying effect on the resultant optical signature. In addition, our results showcase that both the pH and the temperature of the media can be monitored through a ratiometric approach with the changes in fluorescence signatures in both the blue and red regions of the spectrum. We exploit these phenomena to develop a temperature- and pH-sensor inside living cells.

Molecular Biology

Brown and White Adipose from Hibernators Sense and Respond to Inflammatory Triggers Differently

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Carleton University

Inflammation is an energy intensive solution invoked to manage cellular stress caused infections, toxins, irradiation, physical trauma, biochemicals, cellular damage, and so on. How do some of the world's most metabolically coordinated species use (or suppress) inflammation as they naturally adapt to extreme environmental conditions? With limited energy stores available to fuel metabolism for the entire 6-9 months they lay dormant, fat-storing hibernators adapt to harsh winter conditions by suppressing metabolic rate and body temperature to near-zero levels. During torpor, these savvy species have molecular mechanisms in place to prevent cellular damage, but cell stress caused by fluctuations in ATP/oxygen/nutrient availability, ion flux, enzyme profiles and activities could still increase. It is still unknown if during torpor, various organs trigger inflammatory responses in response to cell stress. Curiosity-driven research focusing on how the innate immune system may be regulated in metabolically suppressed ground-squirrels revealed tissue-specific differences in the activity of the inflammasome. This multi-protein complex that forms in the presence of inflammatory stimuli, activates caspases and leads to the release of pro-inflammatory cytokines, was more active in brown adipose compared to white adipose of hibernating ground squirrels, which is important due to their secondary functions as endocrine organs.

Characterization of the Protein-Protein Interaction Between NS3 and NS5 Within the Replication Complex of West Nile Virus

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West Nile virus is a single-stranded RNA virus transmitted by mosquitoes. It belongs to the family of Flaviviruses that can cause serious neurological diseases and causes tens of thousands of deaths worldwide each year. Currently, there is no antiviral treatment available despite extensive research efforts to develop viral enzyme inhibitors. Flaviviruses have only two enzymes, NS3 and NS5. Both proteins have been shown to interact within the viral replication complex, and we hypothesized that this interaction is essential for effective viral replication. We therefore seek to better characterize the interaction between the NS3 and NS5 proteins in order to target this interaction for the discovery of new antiviral compounds. An interaction model between West Nile virus NS3 and NS5 proteins was created and subjected to a molecular dynamics simulation, and potential interactions between the two proteins have been identified. The residues involved in these interactions have been mutated in a West Nile replicon to measure the impact of these mutations on viral replication. A particular region on the surface of the NS3 protein has been identified as being important for efficient viral replication. This region will be investigated further to develop an inhibitor of the protein-protein interaction.

The Role of Alternative Splicing Modifications in Virally Induced Cancer

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Université de Sherbrooke

Viruses modify a multitude of cellular processes in an infected cell. Amongst others, it has been shown that certain viruses modulate the alternative splicing (AS) of their host cell. AS is a post-transcriptional RNA modification that allows for different proteins to be produced from a single gene. Changes in AS are also a hallmark of cancer cells. Furthermore, seven viruses are known to cause cancer such as the human papillomavirus (HPV). Those observations led us to investigate the impact of oncogenic viral proteins on the alternative splicing of cellular transcripts. Stable HEK 293 cell lines individually expressing a dozen oncogenic viral proteins from all seven oncogenic viruses are currently being generated using lentivirus infection. RNA sequencing will be performed on those stable cell lines to investigate the changes of AS in their transcripts. As a proof of concept, immunofluorescence of cells transfected transiently with the E7 protein from HPV showed its localization to the nucleus which is favorable to the modulation of AS. If the AS of genes involved in cancer is modulated upon expression of oncogenic viral proteins, this new function of viral oncogenes will lead to a better understanding of the role of AS in carcinogenesis.

Excised and Isolated Chromatin Rings, Containing the Entire rRNA Gene, Retain the Native Chromatin Structure: a Mass Spectrometry Analysis

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Cancer cells show a high division rate. This is sustained by an important rRNA production. Indeed, in active cells rRNA production represents more than 50% of total cell transcription activity. Thus, rRNA-genes (rDNA) transcription became a target for cancer therapies. Furthermore, rDNAs are also of interest in fundamental sciences: they are utilised to study DNA mechanisms in chromatin. Indeed, rDNAs are highly repeated genes, of which only a part is in transcription. This leads to the simultaneous existence of two chromatin conformations: an ‘open’ chromatin depleted of nucleosomes characterises transcribed genes, whereas a ‘close’ chromatin stands for inactive genes with DNA wrapped around nucleosomes. Thus, this allows comparing and determining the chromatin effects on DNA mechanisms. Among those mechanisms, nucleotide excision DNA repair (NER) is of interest when speaking of cancers, especially skin cancers. In the laboratory, the budding yeast is used as working model to study NER of rDNAs. For this purpose, engineered yeasts were made to allow rDNA excision from the chromosome and chromatin purification. The current study presents the effects of excision and isolation on native chromatin. Results show excision does not affect chromatin structure and accessibility. Isolated chromatin was submitted to mass spectrometry analysis.

Falloff of RNA Polymerases I at DNA Damage, and their Replacements by Nucleosomes, is Mirrored by the Inverse Activities of Transcription Coupled (TC-) and Global Genome (GG-) Nucleotide Excision Repair

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UV induced DNA damage obstructs the elongation of RNA polymerases. It is removed by the 2 nucleotide excision repair (NER) sub-pathways: GG-NER that repairs most of the genome, and TC-NER that only repairs the transcribed strand of active genes. The nucleolus forms around clusters of rRNA genes that are transcribed by RNA polymerase I (RNAPI). The number of rRNA genes varies among organisms, and they are ~150 in yeast. But at any given time, only a portion of rRNA genes is transcribed and has no nucleosomes, whereas non-transcribed rRNA genes are folded in nucleosomes. Previously, we showed that RNAPI encountering DNA damage falloff from the transcribed strand and are replaced by nucleosomes. To understand the interplays between UV induced DNA damage, NER and chromatin, in this study we employed a technique based on DNA-polymerase extension of DNA primers. We measured DNA damage and repair at nucleotide level, in both strands of rRNA genes. In agreement with the current knowledge, the rRNA gene non-transcribed strand is repaired by GG-NER. Remarkably and novel, the transcribed-strand is repaired by TC-NER at the 5'-end, but by GG-NER towards the middle and at the 3'-end of the gene, mirroring the replacement of RNAPI by nucleosomes.

Biochemistry

Responses of Porcupine and Wntless proteins to oxidative, hypoxic and endoplasmic reticulum stresses in HEK293T and HCT116 cell lines

R. Mohamed

Carleton University

Worldwide, colorectal cancer accounts for 10.2% of all reported cases of cancers and 9.2% of all cancer deaths (World Health Organization). Porcupine (PORCN) and Wntless (WLS) are factors that control the production of wingless-type MMTV integration site family (WNT); a protein involved in the early stages of gastric cancer development. The WNT proteins play a role in stem cell biology and cancer. We investigated how modifications PORCN and WLS result in changes in WNT expression including Wnt3a and Wnt5a and secretion from cells under physiological and chemical stresses. We quantified the mRNA expression of both PORCN and WLS and (WNT3A and WNT5A) and found that both mRNA expressions were significantly increased in human colon cancer (HCT116) cells. The expression of PORCN and WLS proteins increased with ER stressors and hypoxic mimetic treatments in both HCT116 and human embryonic kidney (HEK293T) cells. We performed electrophoretic mobility shift assay (EMSA) on promoter elements of PORCN and WLS to elucidate the activation of essential transcription factors (TFs), that include hypoxia inducible factor-1 alpha (HIF-1α) and nuclear factor (erythroid-derived 2)-like 1 and 2 (NRF-1 and -2). We demonstrated that HIF-1α and NRF-2, had altered promoter binding under physiological and chemical stressors in HEK293T cells.

Enhancing the Overall Profile of a Potent PACE4 Peptidic Inhibitor by the Formation of a Host-Guest Inclusion Complex with beta-Cyclodextrin.

P. Navals

Sherbrooke University

The proprotein convertase PACE4 has been validated as a new target to expand the range of prostate cancer (PCa) treatments. We previously described the design and synthesis of a potent peptidomimetic PACE4 inhibitor known as compound C23 (Ac-dLLLLRVK-Amba). C23 shows excellent anti-proliferative effect in different PCa cell lines (DU145 IC50= 25nM C23, LNCaP IC50= 45nM) and blocks tumor progression in vivo in LNCaP xenograft-bearing mice. However, C23 suffers from low stability facing most common biological degradations and from rapid renal clearance. In order to improve its profile and to facilitate its administration, we decided to test different formulation strategies. Here, we investigated the use of cyclodextrins (CDs) and their property to form “host-guest” inclusion complexes with a variety of molecules based on hydrophobic interactions. To allow the formation of such structures a series of C23 analogs have been formulated with the selected beta-cyclodextrin and evaluated in various biological assays. As a result, a new formulated lead compound has been identified named FC23bCD, which in addition to be more soluble and more potent towards PACE4 also showed an improved stability profile in different matrices. The encouraging properties of this analog make it an excellent candidate for further in vivo investigations.

Mechanoenzymatic Breakdown of Chitin into N-acetylglucosamine: Higher Activity and Reduced Waste in the Absence of Bulk Water

D. Therien*, F. Hammerer, T. Friščić, K. Auclair

McGill University

It is estimated that 6-8 million tons of crustacean shell waste is generated annually worldwide, with most of it being discarded into landfills or back into the ocean. Chitin is one of the major components of crustacean shells and is the most abundant nitrogen containing biopolymer found on Earth, consisting of repeating β-(1,4)-N-acetylglucosamine (GlcNAc) units. However, current methods to obtain GlcNAc from chitinous biomass typically employ harsh, aggressive chemicals (such as concentrated HCl and concentrated NaOH) at high temperatures and therefore lack sustainability. In contrast to the chemical route, enzymatic catalysis provides a significantly milder approach. Enzymes capable of hydrolyzing chitin, called chitinases, are produced across living organisms, from humans to bacteria and fungi. Our group has recently reported that some enzymes can be more efficient when used in the absence of bulk aqueous or organic solvent. This is possible thanks to a combination of ball milling and accelerated aging (static incubation) repeated over several cycles, which we call reactive aging (RAging). This presentation will highlight the development of a new method to hydrolyze various chitinous materials into GlcNAc using an inexpensive commercial chitinase in the absence of bulk solvent.

Anticancer Potential of GL13K Peptidomimetics: A Biophysical Assessment of their Activity Based on the Interaction with Model Membranes

J. Porro-Suardiaz*, C. DeWolf

Concordia University

GL13K is a selective broad-spectrum antimicrobial peptide that shows bactericidal and antibiofilm activity without lysing human erythrocytes, which makes it an attractive candidate for antibiotic applications. Many antimicrobial peptides have recently exhibited anticancer activity. Therefore, we present here the assessment of anticancer activity for both D- and L-GL13K enantiomers in cancer cell lines. It emerged that D-GL13K showed greater selective toxicity in cancer cells attributed to their resistance to proteolytic degradation. To probe the roles of membrane composition and peptide chirality, we studied the interaction of D- and L-GL13K with model membranes mimicking human cancer and erythrocyte cells using a combination of bulk and surface-specific biophysical techniques including circular dichroism, PM-IRRAS and X-ray scattering. The enantiomers showed differential interactions in agreement with their activity (in the absence of proteases) as evidenced in greater binding and insertion in the cancerous model membranes. However, both enantiomers of GL13K did not displayed a crystalline beta-sheet conformation in presence of the cancer cell model, even though crystallinity is present in more negatively charged models. The molecular origins and significance of these results will be discussed.

Development of Fluorescent tools to Study Cellular Lipid-Derived Electrophile Chemistry

A. Van Kessel*, G. Cosa

McGill University

Lipid-derived electrophiles (LDEs) are reactive degradation products of hydroperoxides formed during lipid peroxidation. While LDEs can act as important cellular signals, increased concentrations lead to undesired protein alkylation and are implicated in many pathologies. Several strategies have been developed to study the reactive targets of LDEs, but the mechanistic role of LDE reactivity and trafficking in disease states remains poorly understood. Our group is utilizing fluorescence microscopy to monitor both the cellular reactivity of LDEs and the influence of LDEs on cellular health. Towards this aim, we recently reported a fluorogenic LDE analogue (AcroB) bearing an acrolein moiety, the electrophilic LDE warhead, linked to a BODIPY chromophore. Upon reaction with a cellular nucleophile (protein thiol or glutathione), AcroB becomes fluorescent, allowing super-resolution mapping of probe reactivity and monitoring of adduct trafficking in healthy live cells. In this presentation, I will describe ongoing work conducted using both the originally reported probe and newly developed analogues with varied chemical reactivity and partitioning properties. Our results focus on the impact that different cellular metabolic states have on the spatiotemporal mapping of fluorogenic LDE analogue reactivity and trafficking.

Biosynthesis of Enterobactin in Escherichia coli – Adventures in Metabolon Mapping

S. Ouellette*, P. Pawelek

Concordia University

Most bacteria require ferric ions for their growth and survival. To obtain scarce iron from their environment, bacteria synthesize and secrete high affinity siderophores to chelate Fe3+. Enterobactin is a catecholate siderophore synthesized by Escherichia coli and Salmonella. Synthesized in the cytoplasm by the concerted action of seven enzymes, EntCBDAEF and EntH, enterobactin is then transported out of the cytoplasm by the inner-membrane protein EntS. We hypothesize that these Ent proteins assemble in a large multiprotein complex to enhance metabolic flux of the intermediates and prevent diffusion. Pairwise interactions between the biosynthetic enzymes have already been well characterized. Employing techniques such as bimolecular fluorescence complementation and in vivo chemical crosslinking, we will investigate high-order complexation between EntCBA as well as EntBAE. We also have evidence that these enzymes localize to the E. coli inner membrane. We therefore hypothesize that the proposed assembly interacts with the efflux transporter channel EntS. Interaction between biosynthetic enzymes and EntS will be probed by proximity labeling with biotin. Finally, we will pursue isolation and purification of EntS with a view to crystallize it, but also to deliver a tool that can be employed for further applications such as functional studies of this efflux transporter channel.

Organic Chemistry

Silver-promoted Synthesis of SF5-Containing Oxazolines and Lactones

A. Gilbert*, M. Roudias, X. Bertrand, J.-F. Paquin

Université Laval

On the one hand, the pentafluorosulfanyl (SF5) group has been attracting interest due to its unique properties, including high lipophilicity and hydrolytic stability, strong electron-withdrawing capacity and large dipole moment. On the other hand, oxazolines and lactones are attractive moieties in medicinal chemistry, in addition to being useful building blocks in organic synthesis. In that context, we envisioned that SF5-containing oxazolines and lactones could represent valuable SF5-containing heterocycles. Herein, we report the synthesis of SF5-containing oxazolines and lactones. Our methodology is based on a silver-promoted cyclization of SF5-containing acyclic precursors (either amides or acids) that can be prepared via the radical addition of SF5Cl on the appropriate alkenes. The synthesis of the substrates and the scope of these transformations will be discussed.

Stereoselective Synthesis of E-Tetrasubstituted Olefins via Dynamic Kinetic Resolution of Olefin Mixtures

J. Majhi[1]*, B. W. H. Turnbull[2], H. Ryo[3], J. Park[4], M.-H. Baik[3], P. A. Evans[1]

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The development of novel methods for the construction of pure and stereochemically complex compounds is an active area of investigation in modern synthetic organic chemistry. In this regard, the synthesis of geometrically defined tetrasubstituted olefins is a highly challenging endeavor. Nevertheless, this ubiquitous functional group is an important motif in pharmaceutical agents and materials research, where the geometry of the alkene often plays a critical role in the activity and properties of a specific compound. Despite the challenges associated with traditional olefination methods, many modern methods continue to employ the same general technique that involves the de novo installation of the carbon-carbon double bond. This strategy requires stereochemical control of the substituents within the newly formed olefin, a challenge that is often difficult to overcome and thus hampers the synthetic utility of these processes. Herein, we will describe a new approach that can prepare geometrically defined E-olefins through a novel dynamic kinetic resolution of olefin mixtures with excellent selectivity and broad substrate scope. Moreover, this presentation will outline the mechanistic origin of exquisite stereocontrol of this new transformation with DFT studies.

Development of Small-Molecule YAP–TEAD Inhibitors Derived from Flufenamic Acid

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Dysregulation of the Hippo pathway due to overexpression of its downstream effectors YAP (Yes-associated protein) or TEAD (Transcriptional Enhanced Associate Domain) has been reported in a wide range of cancers. Responsible for the expression of genes contributing to cell growth and proliferation, the functional transcription factor complex YAP-TEAD is a key target for the development of novel anti-cancers therapies. Flufenamic acid has been reported to bind in TEAD's central hydrophobic pocket, therefore preventing its palmitoylation and its binding to YAP. We report herein the design, synthesis and biological evaluation of flufenamic acid derivatives that bind to TEAD with micromolar potency, successfully inhibiting TEAD autopalmitoylation. Overall, the SAR on this series is now well-understood and demonstrates the importance of the central secondary amine as well as the acid for obtention of potency. Different substituents at various positions on both aryl groups have been optimized to improve potency and biophysical properties of the compounds.

Accessing Novel Thienoisoquinoline Analogues Through New Synthetic Modularity

A. Shafeii*, P. Forgione, C. Alphord

Concordia University

Chemotherapies are the leading treatment in late stage cancers. However, they are known for their harsh side effects caused by poor selectivity for cancer cells over healthy cells. For this reason, the development for molecular regulators of mechanisms solely found in cancer cells is crucial for improving chemotherapies. Thienoisoquinolines are known to be an estradiol mimic and can potentially be used in the regulation of inflammation response and treat related diseases. In preliminary studies, thienoisoquinolines show selective biological activity against cervical cancer cells. This activity is selective to cells of hard to treat cancers with aberrant centrosomes over healthy cells. However, the mitosis clusters are found to be multipolar after treatment with our current lead compound suggesting a novel target for which anti-cancer drugs have not currently been developed. Our goal is to produce a library of analogues for to confirm the target of the candidate drug and complete in cellulo structure-activity relationship studies. Limitations in the current synthetic pathway have hindered synthesis of a broader range of analogues. For this reason, new synthetic pathways are being developed to diversify the library of analogues.

Physical Chemistry

The Wavelength-Dependent Optical Properties of Weakly Absorbing Aqueous Aerosol: Model and Measurements

A. Bain*, T. Preston

McGill University

An accurate description of the propagation of light in the atmosphere requires an understanding of the scattering and absorption of light by aerosol particles. Both of these processes depend on the geometry and the complex refractive index of aerosol particles. While the real part of the refractive index for aqueous aerosol is straightforward to characterize, there is little data available for the imaginary part as its measurement is more challenging. Here, we model the complex refractive index of weakly absorbing aerosol using an effective oscillator in the far-UV and the causal connection between the real and imaginary parts of the refractive index described through the Kramers-Kronig relation. Utilizing cavity-enhanced Raman spectroscopy, we measure both the real and imaginary parts of the refractive index of atmospherically relevant aqueous solutions. We demonstrate that the effective oscillator model accurately describes both the real and imaginary parts of the refractive index of these solutions across a wide range of water activities and wavelengths. Finally, through a comparison with experimental measurements, we verify that mixing rule calculations utilizing oscillator parameters determined from solutions containing only a single solute in water can be used to predict the optical properties of aqueous solutions containing multiple solutes.

π-π Stacking in Models of Phenolic Surfactant Monolayers

J. Gaba*, C. DeWolf, H. Muchall

Concordia University

Lipid and surfactant assemblies at interfaces are important tools for studies of biological functions and molecular self-assembly; their structure and organization depend on their intermolecular interactions. Experimental work at the air-water interface has implicated both hydrogen-bonding and π-stacking interactions as major driving forces of the pronounced aggregation behaviour of phenolic surfactants and lipids. Grazing incidence X-ray diffraction (GIXD) studies have produced information on the lateral organization of these single- and double-chain surfactants, but the relative contributions of the non-covalent interactions at the molecular level are not yet understood. The use of electronic structure methods to predict model assemblies that concur with the GIXD data allows the determination of the non-covalent interactions driving two-dimensional phase behaviour. Results will be shown for monohydroxy and trihydroxy single- and double-chain ester model systems using density-functional (ωB97X-D) and semi-empirical (GFN1-xTB) methods. Experimentally, it has previously been found that phenol forms a hydrogen-bonded cyclic trimer in the gas phase. Our studies reveal that the cyclic trimer motif and its hydrogen-bonding network are abandoned both with substitution changes on phenol, and with the addition of an explicit water subphase. In larger assemblies of single-chain and double-chain systems, π-π stacking is observed instead in the long-range order.

Novel Pressure-Sensors Based on Luminescent Chromium(III) Complexes

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Luminescence spectroscopy has proved to be a very powerful technique to investigate the electronic and molecular structure of many different chromium(III) complexes. Such luminophores have been widely studied and exploited in cutting-edge technological applications such as the ruby laser. Recent work from the Heinze group has yielded new, strongly emissive chromium(III) complexes with high quantum yield and a potential for applications as sensors. We have studied the surprising pressure effects on luminescence spectra of a series of chromium(III) complexes and compare with the well-established properties of doped solids. Luminescence and Raman spectra and their variation with external pressure are presented. The pressure-induced red shift of -11 cm-1/kbar-1 in [Cr(bpy)3]3+ is slightly lower than reported for [Cr(ddpd)2]3+(-15 cm-1/kbar-1) , but higher by more than an order of magnitude than for chromium(III) doped oxides, widely applied as pressure sensors. Moreover, increasing pressure leads to a strong broadening of luminescence bands. This comparison enables us to discuss physical origins of different shifts.

A Methodology to Enhance Absorption of Thin Films on Ice Using Reflection-Absorption Infrared Spectroscopy (RAIRS)

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Université de Sherbrooke

The detection of adsorbed molecules on ice at surface coverage similar to those encountered in environmental conditions requires high surface sensibility that few techniques can afford. A methodology that exploits electric field standing wave (EFSW) effects intrinsic to grazing incidence Reflection Absorption Infrared Spectroscopy (RAIRS) will be presented that relies on optical interferences within thin films. As a case study, CH4 is used as a probe molecule and its adsorption on amorphous solid water (ASW) is studied using this methodology. An enhancement in absorption from 20 to 35 is achieved when destructive interference coincides with the absorption features of the adsorbate, that is the ν3 and ν4 modes of methane, respectively. Simulations using Fresnel transmission and reflection coefficients reproduce the film thickness dependant enhancement for CH4 absorption bands and reveal that it occurs when the square modulus of the electric field at the film's surface reaches its minimum. Exploiting the EFSW allows the limit of detection of molecules adsorbed onto ice to be reduced to 0.2 ML using CH4 as a probe molecule which opens interesting perspectives for spectroscopic studies of heterogeneous atmospheric chemistry at coverages that are more representative of those found in the natural environment.

A Theoretical-empirical Strategy for the Rational Design of Efficient Triplet Quenchers via Photoinduced Electron Transfer

J. Ramos-Sanchez*, Y. Gidi, L. Payne, G. Cosa

McGill University

Photostability is one of the main challenges in single-molecule fluorescence imaging. Triplet states and radicals are long lived reactive species that can lead to photodegradation. Oxygen is known to be an efficient triplet quencher; however, it has been associated with photodegradation. Removal of oxygen may increase the survival time of the fluorophores; however, it causes undesired blinking due to the persistence of long-lived triplet state and radical species. A Reducing and oxidizing (ROXS) strategy has been successfully used to decrease the triplet lifetime. In a ROXS scheme a reducing agent can undergo electron transfer with the fluorophore. The formed radical can be oxidized by a second species to recover the singlet ground state of the dye. While ΔG0 energies allow to predict electron transfer thermodynamics, they don't provide direct information on the kinetics of this process. Herein, utilizing transient absorption spectroscopy and DFT modelling, we describe a strategy to predict electron transfer rate constants. Within the framework of Marcus theory of electron transfer, we have computed activation energies and correlated them with experimental rate constants of electron transfer.

Crystal Engineering of Room Temperature Phosphorescence in Organic Solids: The Story of Carbonyl-bridged Triphenyl Amines (TANGOs)

E. Hamzehpoor*, D. Perepichka

McGill University

The biocompatibility, processability, synthetic tunability of optical and electronic properties of organic phosphors bring up exciting opportunities in the fields of biological imaging, sensing, LEDs, OPVs etc. However, organic phosphors are rare because of the general inefficiency of the intersystem crossing (ISC) in organic molecules. In this work we studied a series of highly emissive azatriangulenetrione (TANGO) solids in which the luminescent properties can be rationally controlled by engineering the molecular packing through adjusting the steric size of substituents. The co-alignment of the 'phosphorogenic' carbonyl groups within the columnar pi-stacks results in an almost pure triplet emission, while their rotational misalignment by ~60° in the sterically hindered derivatives turns off the phosphorescence channel leading to a pure singlet emission. Despite strong pi-pi interactions, aggregation-induced quenching and triplet-triplet annihilation are avoided in two of the derivatives which display efficient phosphorescence in the solid state.

Analytical Chemistry

Development of a Method for Quantification of Toluene Diisocyanate and Methylenediphenyl Diisocyanate Migration from Polyurethane foam Sample Surface by HPLC-UV-MS

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UQAM

The US Environmental protection agency (EPA) has published guidance that includes test procedures for evaluating indoor exposure to chemicals. One of the test procedures represents the migration test for evaluating potential dermal exposure from home furniture. The objective of this project was to develop and validate an analytical method for quantification of migration of 4,4'-methylenediphenyl diisocyanate (MDI), 2,6-toluene diisocyanate (2,6-TDI) and 2,4-toluene diisocyanate (2,4-TDI) from a polyurethane (PU) flexible foam that meets the recommendations of the EPA test protocol. Following the EPA protocol, six synthetic sweat solutions were prepared and used in evaluation of isocyanate recovery performance. The migration tests were conducted using five foam types that were chosen and supplied by PU foam manufacturers to represent the types most commonly found in commercial products, and with formulations anticipated to have the highest potential residual TDI or MDI. Migration tests were conducted using glass fiber filters (GFF) coated with 1-(2-methoxyphenyl)piperazine (1,2-MP) and analyzed using HPLC-UV-MS. The recovery tests on a Teflon surface for 5 of the 6 EPA-recommended synthetic sweat solutions indicate the recovery percentage was approximately 80% for diisocyanates and approximately 30% for the sixth. TDI and MDI migration was not observed when testing was conducted on foam samples.

Analytical Workflow in the Era of the Opioids Crisis: Screening for Novel Synthetic Opioids

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The opioids crisis has been a fixture in North America for several years. In 2017, 72% of deaths related to opioids involved fentanyl and novel synthetic opioids (NSO). To achieve extended screening of these compounds, a comprehensive, flexible and responsive screening method for 54 NSO was developed and successfully validated under ISO 17025:2017 requirements. Extraction was carried out by protein precipitation, where 100 µL of blood or urine was mixed with 10 µL of internal standard solution (fentanyl-D5 0.1 µg/mL), and diluted with 100 µL of MeOH:0.2% formic acid (50:50 v:v). Precipitation was achieved by adding 400 µL of an acetonitrile:acetone (70:30 v:v) solution and vortexing for 5 minutes. The extract was injected on an Agilent 1200 HPLC coupled to a Sciex 5500 QTRAP operated in ESI+ mode with multiple reaction monitoring (MRM). Most analytes (n = 40) exhibited an LOD ≤ 0.1 ng/mL. Presence of carryover was monitored, with only cis-3-methyl norfentanyl being problematic. Specificity and absence of interference from 175 exogenous compounds were confirmed. Emergence or disappearance of NSOs in the population dictates dynamic addition or removal of compounds. This new screening tool allowed detection of NSO in >10 cases, demonstrating its importance in the forensic toxicology context.

Développement de méthodes de conservation, d'extraction et de quantification du 4,4'-MDA dans les sols

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Le 4,4'-méthylènediphenyl diisocyanate (4,4'-MDI) est une substance souvent utilisée dans la fabrication de mousses de polyuréthnane, de colles ou comme revêtement d'engrais ou de pesticides qui peuvent s'appliquer au sol. La dégradation de produits à base de MDI, par hydrolyse ou photolyse peut mener à la formation du 4,4'-méthylènedianiline (4,4'-MDA). Bien que le MDA réagisse avec la matière organique présente dans le sol, il est intéressant de surveiller sa présence dans l'environnement. Un méthode existante développée, optimisée et validée pour l'extraction du MDA dans les sols a été améliorée par l'ajout d'un standard interne et d'un surrogate afin de corriger les pertes lors de l'échantillonnage, la stabilisation, la conservation, l'extraction et l'analyse des échantillons de sols. La rétention du MDA dans des sols à textures et compositions organiques différentes a permis le développement d'une méthode d'imprégnation. L'imprégnation, la stabilisation, l'extraction et la quantification du MDA dans le sol a été validé en utilisant 1 g d'échantillon de sol allant de 2.5 à 10 % de matière organique. Il a également été démontré que le MDA était à la fois stable dans un sol sec ou un sol immergé dans du méthanol.

Characterization of the Human Tear Proteome by LC-MS/MS

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Université du Québec à Montréal

Eye diseases are widespread in the population. It is essential to quickly diagnose different ocular diseases and choose the appropriate treatment. The composition of tears proteins is important. A change in the quantity and quality of specific proteins in the ocular surface can correlate with disease. The comparative analysis of proteins from tears could identify a list of biomarker proteins for the diagnosis of ophthalmological diseases. Our goal is to develop a robust and sensitive method for the determination of tears proteins composition. An eventual application of this work would be to help diagnose certain eye diseases, and their progression. To properly analyse tears proteins, we need to optimize a sample preparation method and proteomic analysis by liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS). Digested tears samples were analysed on two high-resolution LC-MS/MS quadrupole-time-of-flight hybrid systems. Preliminary data has shown that the microflow-6600 platform separation gives a greater possibility of identifying low-abundant proteins than the regular flow-5600 platform. We will be looking at normal variation in protein distribution from several healthy volunteers, to ascertain which proteins may be better candidates as biomarkers of eye disease. We will also study variation in the same individuals at different times of day.

Untargeted LC-MS/MS Based Metabolomics to Decipher Metabolic Changes upon Acetaminophen Treatment in Rats

M. Mireault*, V. Prinville, L. Ohlund, L. Sleno

UQAM

Acetaminophen (APAP) is a common analgesic used worldwide. Unfortunately, this drug is also the main cause of acute liver failure in the western world. Studying the perturbation of endogenous metabolites can be used to understand modes of action and side effects. An untargeted metabolomics approach was employed to study the effects of different doses of acetaminophen in rat, related to its hepatoxicity.
Metabolites were extracted from rat plasma treated at four different doses of APAP. Extracts were analyzed with two liquid chromatography methods, one using a PFP fully porous column and the other using a solid-core C18 column. Liquid chromatography coupled with high-resolution tandem mass spectrometry on a quadrupole-time-of-flight platform was employed to look at changes in metabolite features with APAP dose. Data was treated with an untargeted workflow and the metabolites were identified. The distinguishing features in both workflows were compared. The PFP column was found to show good overall coverage of metabolites, however the optimized separation on the C18 column was necessary to see all many changes occurring for features related to bile acid isomers. Both methods enabled us to differentiate between low and high doses of acetaminophen based on known (and unknown) metabolite peaks.

In vitro Metabolism of Butylated Hydroxytoluene (BHT) by LC-HRMS/MS

O. Ousji*, L. Ohlund, L. Sleno

UQAM

Environmental contamination by xenobiotics is a worldwide phenomenon as a result of human activities such as the industrial production of plastics, additives in food, the pharmaceutical industry, etc. The exposure to these environmental xenobiotics can induce adverse effects on human health. BHT is one of the most widely used preservatives in food, cosmetics and pharmaceutical industry to inhibit lipid autoxidation. The metabolism of BHT, and several of its analogs, has been studied in vitro to investigate the formation of stable and reactive metabolites. Metabolites were formed using in vitro incubations with microsomes and S9 fractions and profiled using a newly developed LC-HRMS/MS method. Positive and negative mode data were processed to probe the formation of oxidative metabolites, as well as glutathione, glucuronide and sulfate conjugates. High resolution MS/MS data was employed to elucidate fragmentation pathways and for the structural elucidation of metabolites.

Inorganic Chemistry

In Depth Study of the Electronic Properties of NIR Emissive κ3N Terpyridine Rhenium(I) Dicarbonyl Complexes

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Université de Montréal

The structure-properties relationship in a series of carbonyl rhenium(I) complexes based on substituted terpyridine ligands of general formula [Re(κxN-Rtpy)(CO)yL]n+ is explored by both experimental and theoretical methods. In these compounds, the terpyridines can adopt both bidentate (κ2N) and terdentate (κ3N) coordination modes associated with three or two carbonyls, respectively. Conversion from the κ2N to the κ3N coordination mode leads to large change in the absorption spectra and oxidation potentials due to destabilization of the HOMO level. The κ3N complexes absorption profiles cover the whole visible spectra with lower maxima around 700 nm, tailing till 800 nm, while no emission is observed with Br- as axial ligand L. When the axial ligand is modified from the native halide to pyridine or triphenylphosphine, the lowest absorption band is blueshifted by 60 and 90 nm, respectively. These cationic complexes are near-infrared emitter with emission maxima between 840-950 nm for the pyridine compounds and 780-800 nm for the triphenylphosphine ones.

Spectroscopie Raman d'un complexe du nickel(II) commutable à ligand azoture

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Université de Montréal

Des études sur un composé à deux centres nickel(II) montrent qu'un ligand pontant N3- mène à une bistabilité magnétique avec un comportement hystérétique. Ce changement du moment magnétique se produit entre 205 et 230 K. Cette affiche vise à apporter plus de précision par rapport aux études précédentes sur les propriétés de ce ligand quant à la variation de la température et de la pression. Des spectres Raman ont été mesurés pour une gamme de température comprenant les seuils de transitions observés dans la précédente recherche. Les résultats montrent un changement abrupt du maximum Raman caractéristique de la torsion angulaire du N3-. L'élongation symétrique ne semble pas être affectée par le changement de la température. En parallèle, une recherche a souligné deux transitions de phase du ligand azoture en augmentant la pression. Des spectres Raman ont aussi été mesurés afin de vérifier si la pression induisait des effets similaires. Les pressions utilisées se situent entre 1 et 25 000 bars. Une première transition de phase se voit clairement à 1,1 kbar, comme attendu par la recherche précédente, mais la deuxième transition reste indétectable. Remerciements spéciaux à Guido Leibeling, Serhiy Demeshko, Sebastian Dechert et Franc Meyer.

Rare-earth Based fcu Metal-organic Framework for Aqueous Contaminants Degradation

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Concordia University

Metal-organic frameworks (MOFs) are a family of structurally diverse materials made up of both inorganic and organic components. the permanent existence of pores in their structures and their low density makes their potential for applications wide ranging. The formation of a hexanuclear rare-earth (RE) based cluster opens up the door for a diverse class of robust functional MOFs. it is possible to use these clusters as metal nodes and, through the use of organic linkers that are linear and ditopic, obtain a framework with fcu topology. Antibiotics are amongst the most successful treatments for improving human, animal and plant health. nonetheless, the ubiquitous use of antibiotics has led to their release in natural ecosystems. their most detrimental effect is the development of mutagenic, multi-antibiotic resistant bacterial strains that can produce non-treatable infections that affect mainly aquatic life.
This presentation will discuss the synthesis and full characterization of RE-MOFs with fcu topology and their potential for use in the catalytic breakdown of antibiotics in water.

One-pot Synthesis of Orgaoruthenium(II) Complexes bearing N,O-donor Ligands Under Microwave Irradiation: Isolation of a Rare Aldehyde Intermediate Complex

H. Elasmy*, A. Castonguay, M. M. Haghdoost, C. Cotton

INRS

Ruthenium(II) bearing a N,O-donor Schiff base ligand have attracted attention in the last few years due to their numerous applications in catalysis1 and biology2. Their success is partly due to their ease of synthesis and versatility. In the course of our ongoing efforts to prepare series of Ru(II)-arene drug candidates with various substituents3-5,we initially encountered difficulties for the preparation of Schiff base ligands bearing a maleimide group using the traditional amine-aldehyde condensation method, leading to very poor yields. Herein, we report an efficient one-pot synthetic method for the preparation of a maleimide-containing organoruthenium(II) Schiff-base complex derived from N-(2-aminoethyl)maleimide and 2-hydroxynaphthaldehyde.This strategy is simpler and more efficient than our previous multistep synthesis procedure involving the isolation of a Schiff-base ligand prior to its reaction with a Ru(II) precursor and a tedious work-up, especially under microwave irradiation. An optimization of the reaction conditions improved the overall reaction yield by 30% compared to the multistep synthetic pathway initially attempted. Moreover, this new microwave-assisted one-pot strategy does not require high temperatures nor long reaction times. Interestingly, a very rare air-stable organoruthenium (II)-naphthaldehyde intermediate was successfully isolated after the first 30 min of the reaction and its solid-state structure was established. Our preliminary results regarding the biological activity will be discused

Synthesis and Characterization of Ru(II) Complexes Bearing Triazole Containing Ligands for Potential Antifungal Applications

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INRS-Centre Armand Frappier Santé Biotechnologie, Université du Québec

Triazole-containing compounds are widely used as antifungal therapeutics. The mode of action of these compounds involves their interaction with various enzymes, notably fungal CYP51, which catalyses the production of ergosterol. Since ergosterol plays an important role in the regulation of fungal membrane fluidity and structure, enzymes catalyzing the production of this hormone is commonly targeted for therapeutic purposes. Fungal CYP51 comprises an iron porphyrin co-factor, which is the site at which triazole rings interact and inhibit the catalytic activity of this enzyme. In recent years, several ruthenium complexes have been studied for their potential pharmaceutical applications including their antifungal properties. Several ruthenium species have been reported to be active against various types of fungous strains that cause tropical diseases. In the course of this study, we have been interested in the design of novel ruthenium complexes bearing triazole-containing ligands for which both the metal and the ligand can mutually interact with biomolecules. This strategy can lead to drug candidates with enhanced therapeutic properties and contribute to the prevention of the development of treatment resistance. Herein, we report the synthesis and the characterization of Ru(II) complexes containing a triazole ring within their structure and discuss their preliminary antifungal properties.

A New Cyclohexyl-Based Catalyst for Hydrogen Generation

V. Picard*, O. Schott, G. S. Hanan

Université de Montréal

Since 1980, facing the global warming is an upcoming challenge for every scientist. we face the challenge of making a new way to live, according with nature, by producing and waste less, in order to maintain an acceptable environment and try to reverse the climatic changes that cause a slowly extinction of every species on earth. In this awesome challenge, one of the most interesting solution that has been found to replace combustible fuels was to use solar energy to produce clean combustible, like hydrogen or electricity. The hydrogen is an interesting fuel because in the same mass as combustible fuel, we have almost 4 times more energy produced when we burn it. Furthermore, it can be produced from water and regenerate it when it is burn. The main issue right now is that this energy is too expensive to produce, versus the hydrogen that is produced from petrol oil. A new promising catalyst has been discovered to make progress in the artificial water splitting reduction process, reducing hydrogen production price. His properties make him one of the most useful catalyst that is known today and pave a way to obtain a new molecule that would fit our needs.

A New Family of Isostructural Rare Earth Metal-Organic Frameworks synthesized from a Tetratopic Linker

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Metal–organic frameworks (MOFs) are porous crystalline materials that have been intensively studied in the last two decades due to their potential for application in gas adsorption, catalysis, and water remediation, amongst others. The structures and properties of MOFs are driven by the composition and geometry of the organic linkers (L) and metals (M) used to build the framework. In this work, we describe the solvothermal synthesis of new yttrium, terbium, and erbium based MOFs comprised of metal cluster nodes bridged by tetratopic organic linkers. The MOFs have been characterized by powder X-ray diffraction, single crystal X-ray diffraction, 1H-NMR spectroscopy, single crystal X-ray diffraction, thermogravimetric analysis, diffuse reflectance infrared Fourier transform spectroscopy and nitrogen adsorption-desorption analysis. Ongoing work includes testing the stability of the MOF in aqueous conditions, including chemically challenging acidic and basic environments, as well as testing the MOF for applications in organic contaminant removal from water.

Rare-Earth Metal-Organic Frameworks (RE-MOFs) as Potential Fluorescent-Based Chemical Sensors for Applications in Detecting Contaminants in Water

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Recently, a new subset of metal-organic frameworks (MOFs) that implement rare-earth (RE) metals have emerged as exciting new candidates for various potential applications in gas adsorption and separation, catalysis, drug delivery and storage, and chemical sensing. These RE-MOFs are assembled with a plethora of various RE metals, due to their intriguing electronic, optical and coordination properties, alongside commercially available organic linkers. Herein, we report a RE-MOF produced by a rare-earth hexanuclear metal cluster, yttrium (Y+3) and a tritopic linker, benzene-1,3,5-tricarboxylic acid (H3BTC) to form a 3,6-connected MOF with spn topology reported as CU-45 (CU = Concordia University). CU-45 displays permanent porosity and high thermal stability, with the ability to remove capping ligands and expose open metal sites (OMSs) on the Y6-cluster node. The OMSs accessibility is observed by the adsorption of salicylic acid (SA) in water. These results demonstrate the prospect to design and synthesize stable, RE6-MOFs with open metal sites, as a blueprint for a library of new RE6-MOFs used as potential applications as fluorescent sensors in the detection of contaminants in water.

Photon to Chemical Bonds : TON and TOF for Supramolecular Ir-Co and Ru-Co Systems

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Université de Montréal

Molecular artificial photosynthesis aims to mimic nature by extracting electrons from water and reducing protons or others organic compounds (CO2...) in order to store solar energy in chemical bonds [1]. Since the combustion product of hydrogen is water, this chemical conversion acts as a promising solution for renewable energy. Tuning the properties of molecular photocatalytic center by the design of metal-ligand interaction shows infinite possibilities of creation [2]. Here, we highlight the high photocatalytic activity of supramolecular Ru-Co and Ir-Co system for hydrogen generation. The electronic distribution of heteroleptic and homoleptic bidendante amide Ru complex [3] is investigated trough new derivatives for red-shift absorption, photoredox-reversibility and efficiency. Unstudied macrocyclic cobaltoxime derivatives prove high robustness for hydrogen evolution. Under various wavelengths of irradiation, the behavior of photo-catalytic activity is discussed to develop mechanistic advances.

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Coordination Polymers Based on Linear Terpyridine Ditopic Ligands

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Terpyridine ligands are well known for their high affinity to metal ions and their resulting metal complexes have been widely studied in the past. Linear polytopic ligands can form rod-type macromolecular assemblies when complexed with metal ions, eg. ruthenium or iron. A possible application is their use as photosensitizers, or as a combination of photosensitizer and catalyst in one structure. In this study, tertbutyl groups are introduced to a ditopic terpyridine ligand to increase the solubility of long metallo-supramolecular assemblies in organic solvents. The ditopic ligand is complexed with ruthenium or iron. The complex' absorption and redox potentials are studied. Furthermore, a monotopic terpyridine ligand with tertbutyl substituents was synthesized and complexed with ruthenium or iron. The absorption and electrochemistry of this complex are used as references. Future work will be to combine light absorption and hydrogen production in one macromolecule.

Partial Hydrogenation of Nitro to Hydroxylamine Group Tethered to Asymmetric Salen-type Ligands and Their Complexation with Metal Ions

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Reduction of nitroarenes (ArNO2) to the corresponding amines (ArNH2) is through intermediate states including ArNO and ArNHOH compounds via sequential 2e transfer processes. Herein, our primary goal is to perform this reaction with the highest selectivity in NHOH. We are also interested in studying the behaviour of this functional moiety upon interaction with the metal ions. In our project, asymmetric salen-type ligands with a nitro-containing sulfonamide group were synthesized. Substitutions on the salicylimine aromatic ring afford various structural and electronic modifications. To carry out the partial hydrogenation of NO2 to NHOH functionality on coordinating ligands, two different approaches were used for synthesis. The partial hydrogenation of imine ligands (LItBu-NO2 and LI-NO2) was carried out catalytically using Pd/C (10 wt.% Pd) catalyst poisoned by thioether to maximize the quantity of NHOH species thereby precluding it to fully reduced to NH2 whereas the reduction of amine-based ligands (LAtBu-NO2 and LA-NO2) was accomplished employing more facile, cheap and Zn/NH4HCO2 system.
Subsequent reaction with metal ions such as copper(II), nickel(II) and zinc(II) may trigger a reaction with the redox-active NHOH function, such as coordination, oxidation and/or disproportionation. A few examples of well-characterized complexes will be presented.

Physical Chemistry

Component Exchange for Multiple Property Tailoring

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Component exchange is the change of constitutional components of a compound. The exchange is enabled by reversible bonds, which can either be supramolecular or covalent bonds. The component exchange can be triggered with external stimuli such as heat, a catalyst or mechanical forces. It will be shown that covalent imine bonds can sustain dynamic component exchange. While component exchange typically involves the change of a unique property, multiple property tailoring such as both fluorescence and electroactivity will be demonstrated by component exchange.

Dynamic NMR Study of Thiobencarb (S-4-chlorobenzyl N,N-diethylcarbamothioate)

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Sharif University of Technology

Variable-temperature 1H NMR spectroscopy are used to investigate barrier of C–N rotation in Thiobencarb (S-alkyl thiocarbamate). Experimental ΔG‡298 value was calculated 63.22 and 66.36 kJmol-1 in chloroform and acetone solvents respectively. All the spectra were taken at different temperatures, and then by simulation of band shape broadening pattern, rate constants for all temperatures were calculated. The obtained rate constants were used to calculate the thermodynamic parameters of activation (ΔG‡, ΔH‡, ΔS‡ and Ea). The computational calculations were studied in various levels and basis sets.

Synthesis and Characterization of Polyaniline Capped Silver Nanoparticles to be Used in Dye Sensitized Silver Nanoparticles

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The efficiency enhancement of dye sensitized solar cells (DSSCs) has been a major challenge. The performance of DSSC could be improved by enhancing the absorption cross-section of dye which could be achieved by utilizing the unique surface plasmon (SP) property of metal nanoparticles. But bare metal nanoparticles suffer from surface etching when brought in direct contact with cell electrolyte. This may undermine the plasmonic effect of metal nanoparticles. In order to overcome this limitation, we have synthesized polyaniline (PANI) capped silver (Ag) nanoparticles. XRD diffraction pattern confirmed the presence of silver nanoparticles with average particle size of 27.58 nm. UV-Vis spectra shows the SP resonance band of Ag. From TEM images, shell like structure can be seen surrounding the silver nanoparticles with mean particle size of 28.16 nm. FT-IR spectra shows the shift in characteristic peaks of polyaniline indicating the attachment of silver nanoparticles with polyaniline. These PANI capped Ag nanoparticles can be used for enhancing absorption cross-section of dye molecules, which is the heart of DSSC.

Formation of Ion Pairs and Charge-Transfer Complexes in the Doping of Organic Semiconductors

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The two known charge-transfer mechanisms in the molecular doping of organic semiconductors (OSCs) are the formation of ion pairs (IPA) and ground-state charge-transfer complexes (CPX), where the latter is typically regarded as detrimental to doping efficiency. Various molecular properties promote one or the other, where small OSCs tend towards CPX formation while polymers usually yield IPA. In our work we used X-ray scattering (GIXRD) and spectroscopic techniques (FTIR, UV/vis/NIR) combined with thermal de-doping to study the prototypical OSC polymer P3HT, p-doped with F4TCNQ. We observed the dopants alternatingly stacked with the backbone as well as dispersed in the polymer sidechain region – two spatial arrangements thought to favor CPX and IPA, respectively. Further, we probed the influence of the dopant electron affinity (EAdopant) with respect to the OSC ionization energy (IEOSC) by substituting F4TCNQ with its less-fluorinated derivatives of reduced EA. As expected, the case of IEOSC ≤ Eadopant results in IPA. However, at high doping concentrations (additional) CPX occurred for all cases. Finally, we investigated F4TCNQ doping of oligothiophenes of varied length, synthesized in-house by Liu, Forgione et al., to approach the number of thiophene repeat units necessary to shift from the small-OSC CPX regime into that of IPA.

Reconstructing the Parallel Folding Pathways of Guanine Quadruplexes by Thermal Hysteresis

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G-quadruplexes (GQs) are four-stranded, guanine-rich nucleic acid structures that are implicated in regulating biological processes such as gene expression and chromosome stability. GQs are structurally heterogeneous, often existing as ensembles of interconverting conformers. The coexistence of different folded conformations suggests that there may be multiple parallel pathways leading from the unfolded to the folded state, potentially modulating folding rates and biological activity. We have developed a thermal hysteresis approach that quantitatively measures the rates of individual pathways for conformationally heterogeneous GQs, and applied it to the Pu22 GQ that is found in the promoter region of c-myc and has been shown to regulate expression of this oncogene. We find that in this case, the presence of four parallel folding pathways leads to a two-fold acceleration in folding, i.e. the wild-type folds twice as rapidly as its fastest individual pathway. Interestingly this leads to transient population of a folding intermediate whose conformational ensemble resembles that of the wild-type but with a redistribution of populations among the different conformers. This folding acceleration through pathway multiplicity likely occurs for many other biological GQ sequences that can adopt twelve or more distinct folded conformations, with potential acceleration of an order of magnitude or greater.

Quantum Chemical Simulation of Thermal-Mechanical Coupling in High Pressure and Temperature Materials Synthesis

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Concordia University

The diamond anvil cell (DAC) now allows experimental studies of phase transitions in materials under much higher pressure (700GPa) and temperature (5000oC) then previously feasible. Individually, increasing pressure and temperature often have opposite effects on materials, as the former contracts and the latter tend to expand the crystal lattice. The exact nature of the thermal-mechanical coupling inside the DAC necessary for the chemical transformation to take place is still poorly understood and difficult to decipher experimentally. We propose a simulation technique mimicking pressure jumping experiments yielding reaction energy, stress and shear profiles necessary to examine thermal-mechanical coupling effects. In addition to reaction profiles, pressure vs temperature phase transition diagrams can also be generated. The simulation methodology is applied to cubic carbon nitride (c-C3N4) and cubic boron nitride (c-BN), both superhard materials with available experimental data for high pressure and temperature phases. The simulated pressure vs temperature curve agrees well with experimental results. The reaction profiles exhibit multiple bond breaking and forming steps during phase transition; shear flow is shown to be associated with bond breaking and forming processes at the onset of mechanical work coupling with thermal heat, while the stress profile is not significantly perturbed in the process.

Quantification of Molecular Orientation in Polymeric Nanomaterials Using Raman Spectroscopy

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Electrospun nanofibers (NFs) are unidimensional nanostructures formed upon the solidification of a thin electrified jet drawn from a viscous polymer solution. They have previously demonstrated remarkable properties such as high toughness, strength and modulus, making them promising candidates for a wealth of applications related to fields such as sensing, actuation, and energy harvesting. However, grasping how polymer chains alter their conformation and orient themselves during the electrospinning process is crucial for understanding the effect of various processing parameters on the resulting properties of the fibers. Therefore, experimental quantification of molecular orientation is essential for the development of optimized nanomaterials. Using Raman spectroscopy, our group has developed characterization methodologies enabling orientation studies at the individual-nanofiber level, which have refined the understanding of NFs' structure-property relationships. This poster highlights the application of these Raman methods for investigating the influence of multiple parameters involved in the preparation of NFs on their molecular orientation and on their properties. Special emphasis is placed on our recent spectroscopic characterization of polyoxymethylene and poly(ethylene oxide) nanofibers, spun using various solvents and collected with multiple experimental setups. This study provides valuable knowledge on the structural effects of the medium from which these nanomaterials are drawn and collected.

Intramolecular Hydrogen Bond Directed Conformation Stability in N,N'-(pyridine-2,6-diyl)dibenzamide derivatives. Extensive NMR Investigations Supported by X-ray Studies and DFT Computations

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The combined utility of Nuclear Magnetic Resonance (NMR) and Quantum-Mechanical calculations using DFT based Computations permitted the detection of intramolecular hydrogen bond (HB) in all synthesized N,N'-(pyridine-2,6-diyl)dibenzamide derivatives. In fluorine substituted molecule the detection of the cross-correlated peak in two-dimensional 1H−19F HOESY experiment established their spatial proximity. Long-range coupling of substantial strength between two NMR active nuclei, where the spin polarization is transmitted through HB, further confirmed the participation of organic fluorine in intramolecular HB. Density Functional Theory (DFT) based computations indubitably confirms the NMR experimental findings. The molecular structures of the substituted N,N'-(pyridine-2,6-diyl)dibenzamide derivatives could be derived by various one and two dimensional NMR experiments that were unambiguously ascertained by the single-crystal X-ray diffraction data.

Protocol for Probing the Free-state Behaviour of Drugs and Their Tendency to Self-associate into Nano-entities

V. Roux

INRS IAF

Each drug adopts a unique multi-phase equilibrium in aqueous solution with some potential phases such as fast-tumbling lone molecules, a solid precipitate phase and intermediate self-association aggregates (or nano-entities). Moreover, due to this multi-phase equilibrium, each compound has its own unique properties. Literature reports have only begun to assign distinct properties to nano-entity states. This includes some undesirable properties such as in vitro off-target activity, false-positives in screens and toxicity. On the other hand, other beneficial attributes have also been noted such as enhanced drug oral bioavailability and the potential for drug encapsulation and delivery. Assigning these properties has been seriously hampered by the lack of appropriate protocols for detecting nano-entities. Here, we establish a holistic protocol to enable and simplify their detection. An overview and sub-protocols are described for the NMR Dilution Assay, NMR T2-CPMG Assay, NMR Detergent Assay, and subsequent Orthogonal Assays. In conclusion, our protocol provides new opportunities to explore drug multi-phase equilibria and expose the fascinating world of nano-entities and opportunities.

Second-Order Many-Body Perturbation Theory Exchange-Correlation Hole

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Hybrid density functionals, which combine wave function-based methods with density functional theory (DFT), usually rely on empiricism to achieve high accuracy. On the other hand, in the correlation factor approach recently developed in our group, the exchange-correlation (XC) hole is modeled. This allows to use the many known physical constraints on the XC hole to reduce the degree of empiricism needed for the development of hybrid functionals. Our objective is to develop a novel formulation that allies perturbation theory with DFT. As a first step, we propose correlation factor models for the XC hole in the second-order perturbation theory approximation. We then apply corrections to the obtained XC hole using constraints known from DFT. The potential of the method is showed for the description of a variety of chemical systems, including single-bonded, multiple-bonded, and Van der Waals molecules.

Dual Electrochromic and Electrofluorochromic Role of a Red Emissive Fluorophore

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Electrochromism (EC) is the change in color with applied potential. Typically, the color of the redox state is significantly different than its neutral state. Triphenylamine (TPA) is an ideal electrochrome. This is because it can be reversibly oxidized. It also undergoes a visible color change when it is oxidized. Both its color enhancement and fluorescence in the visible region are possible when the electron rich TPA is conjugate with the electron withdrawing benzothiadiazole. Its absorbance can be extended into the visible/NIR region by coupling a strong electron donor and an acceptor into the pi-conjugated framework. In this study, we present the electrochromic properties, in both solution and a device, of a dual responsive electro- and fluorochrome that is based on the TPA framework.

Organic Chemistry

Synthesis of NSC14778 and evaluation of its DNMT inhibitory activity

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UQAM

DNA methylation is a stable epigenetic modification that leads to the installation of a methyl group at the C5-position of cytosine. In cancer cells, dysregulation of DNA methylation processes was observed, with silencing of promoter regions of tumor suppressor genes. This change can be reversed by targeting DNMTs. Although the commercial NSC14778 has been reported as an DNMT inhibitor, it was demonstrated that pure material is inactive, leading us to hypothesize that its activity comes from intractable impurities that it contains. In this work we synthesized NSC14778 using different protocols from the literature with the objective of reproducing the activity that was observed with commercial NSC14778. The reaction crudes obtained were analyzed by spectroscopic techniques and their DNMT inhibitory activity was measured using a fluorescence assay. Our results indicate that the inhibitory activity of crude NSC14778 is highly dependent on the method of synthesis.

Toward a Greener Approach to the Deoxofluorination Reaction Using XtalFluor-E®

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Université Laval

Developed by OmegaChem in 2009, XtalFluor-E® is an aminodifluorosulfinium fluorinating reagent which is safer than those typically employed for the deoxofluorination reaction (DAST, DeoxoFluor® and their counterparts). Indeed, its crystalline structure and its thermal stability make it easier to handle in comparison to the other reagents. In addition, when used with an external source of fluoride, XtalFluor-E® shows excellent reactivity toward a wide range of alcohols and carbonyl derivatives. However, the conditions generally employed for this type of transformation are far from being ideal as they imply the use of dichloromethane, a carcinogenic solvent, and low temperature, which are not ideal for industrial applications. Therefore, this project aims at developing greener conditions for the deoxofluorination reaction using XtalFluor-E®, especially for the synthesis of acyl fluorides which are excellent intermediates for medicinal chemistry.

Synthesis of Aryl Cyclopropyl Sulfides via Copper-Catalyzed S-Cyclopropylation of Thiophenols using Tricyclopropylbismuth

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UQAM

Aryl Cyclopropyl Sulfides are found in numerous biologically active compounds, mainly in their oxidized form. These compounds are also highly useful synthons for organic synthesis. Current methods to access this class of compounds suffer from severe limitations such as low yields, poor scope and the requirement for harsh conditions. We developed conditions for the direct S-cyclopropylation of thiophenols using tricyclopropylbismuth. The reaction is catalyzed by copper(II) acetate, operates under simple conditions, tolerates substitution at all position of the aryl ring and affords the corresponding aryl cyclopropyl thioethers in good to excellent yields. The conditions were applied to benzethiol, a non-aromatic thiol. The S-cyclopropylation of thiophenols was also accomplished with cyclopropylboronic acid and potassium cyclopropyl trifluoroborate, two commercially available cyclopropylating agents. These S-cyclopropylation reaction represent the first example of C(sp3)–bond formation using organobismuth and organoboronic acid reagents.

Bulk Heterojunction Photovoltaics with Improved Efficiencies Using Stem Leaf, Shish-Kebab and Double-Fibrillar Nano-Hybrids Based on Modified Carbon Nanotubes and Poly(3-hexylthiophene)

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For improving the photovoltaic efficiencies, the conductive ordered and disordered nano-hybrids were developed as morphology mediator based on multi-walled carbon nanotubes (CNTs), their chemically surface-modified derivatives, regioregular poly(3-hexyl thiophene) (RR-P3HT) and non-regioregular poly(3-dodecyl thiophene) (PDDT). In unmodified CNTs and their derivatives functionalized with 2-hydroxymethyl thiophene (CNT-f-COOTh, FCNT) and grafted with poly(3-dodecylthiophene) (CNT-g-PDDT, GCNT), double-fibrillar, shishkebab, and stem-leaf nanostructures were decorated. When the pre-developed FCNT/P3HT and GCNT/P3HT nano-hybrids were applied in thin active layers, a progress was detected in photovoltaic characteristics, in particular for P3HT: GCNT/P3HT devices via larger phase separations. The current density (Jsc), fill factor (FF), and power conversion efficiency (PCE) values ranged in 8.14–8.66 mA/cm2, 49–51%, and 2.55–2.78% for P3HT: GCNT/P3HT systems, respectively. The best photovoltaic features were detected for P3HT: GCNT/ P3HT:phenyl-C71-butyric acid methyl ester (PC71BM) devices (Jsc = 9.91–10.22 mA/cm2, FF = 57–59%, and PCE = 3.50–3.74%). The peak values around 69–71% and 52–54% in the external quantum efficiency (EQE) curves were detected at about 550 nm for P3HT: GCNT/P3HT: PCBM and P3HT: GCNT/P3HT devices, respectively.

Total Synthesis of Ananatosides as a Novel Class of Biosurfactants

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INRS - Centre Armand-Frappier Santé Biotechnologie

Microbial glycolipids possess a variety of therapeutic activities owing to their ability to form pores and destabilize biological membranes. Our group has recently reported that the proteobacterium Panteoa ananatis produces novel biosurfactants, named ananatosides A and B. These atypical biosurfactants are composed of a β-D-glucose moiety to which is attached a dilipidic side chain. Ananatoside A additionally features an unprecedented scaffold consisting of a 13-membered macrodilactone ring formed through the intramolecular lactonization of ananatoside B, its opened form congener. Noteworthy, various glycolipids featuring di- and trilactones of different macrocycle sizes produced by plants and microorganisms are known to exhibit potent antiviral activities. We have therefore hypothesized that ananatosides A and B, as well as their non-natural derivatives, represent potential therapeutic agents. Thus, we have designed a high-yielding multi-step synthetic route involving a late-stage intramolecular glycosylation step which allowed us to prepare ananatoside A. We also showed that the latter could be prepared through enzyme-catalyzed macrolactonization of ananatoside B. (1-->2)-, (1-->3)- and (1-->4)-Macrodilactone-containing rhamnolipids were prepared via our optimized late-stage intramolecular glycosylation approach. With the new interest of macrocyclic compounds in a therapeutic context, this project could lead to the identification of new biologically active glycosidic macrolactones.

Synthèse totale d'anthocyanes et anthocyanidines naturelles à visée thérapeutique pour la prévention du déclin cognitive

E. Delar*, C. Ramassamy, C. Gauthier

INRS Armand Frappier Santé Biotechnologie

La maladie d'Alzheimer (MA), maladie neurodégénérative progressive liée à l'âge, a affecté 47 millions de personnes dans le monde en 2015. Les stratégies thérapeutiques actuelles ne sont que palliatives. L'une des explications viendrait de la nature multifactorielle de la maladie ainsi que la faible perméabilité de la barrière hémato-encéphalique (BHE). Une formulation spécifique d'anthocyanidine (ACND) et anthocyanines (ACNs), connues pour passer la BHE, appelée MAF14001 développée par le Pr Ramassamy a montré des résultats prometteurs dans la prévention de la MA. Ici, nous investiguons la synthèse des ACNs et ACND comme alternative à leurs extractions. L'annélation de Robinson, condensation aldolique entre un aldéhyde phénolique côté Ouest et un arylcétone côté Est, représente l'approche de synthèse privilégiée. Le côté Ouest sera obtenu par formylation puis acylation régiosélective du phloroglucinol. Diverses acétophénones donneront les côtés Est après acylation du phénol, formation d'un éther d'énol silylé et époxidation suivie d'une hydrolyse. Le D-glucose servira de précurseur pour le glycoside qui sera estérifié et activé avec un trichloroacétimidate ou un thioglycoside. Par la suite des tests de glycosylation et de condensation aldolique seront réalisés. Ce projet de recherche devrait permettre l'accès à grande échelle aux ACNDs et ACNs ainsi que leurs métabolites et dérivés.

Exploring the Scope of the Mechanochemical Friedländer Synthesis

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The Friedländer reaction is used to synthesize quinolines, heterocyclic aromatic organic compounds that can be found in many natural and synthetic products. Quinoline derivatives often have important pharmacological properties, thus encouraging the discovery of new routes for their synthesis. Typically, the Friedländer reaction consists of the condensation of a 2-aminocarbonyl with a carbonyl having a reactive a-methylene group which is followed by a cyclodehydration to form the quinoline motif. While this reaction is readily carried out in solution under acid- or base-catalyzed conditions, there are only a few investigations of the Friedländer condensation reaction carried out under solvent-free mechanochemical conditions. Mechanochemical reactions offer the potential advantages of shorter reaction times, milder reaction conditions, and compatibility with a greater number of functional groups – thereby avoiding many of the limitations often present in solvent-based Friedländer reactions. Insofar, the aim of this research is to expand the scope of mechanochemical Friedländer reactions through systematically derivatizing the 2-aminocarbonyl and its ketone condensation partner. A long term goal is to utilize this newly acquired knowledge to build scaffolds that can be pharmaceutically relevant.

Copper Acetate-Promoted S-Cyclopropylation using Cyclopropylboronic Acid

A. Fnaiche

UQAM

Aryl cyclopropyl sulfides are highly valuable synthons in organic synthesis. Cyclopropylation of thiophenols through SN2 reaction with cyclopropyl bromide and SNAr reactions between aryl fluorides and cyclopropanethiol are the most frequent synthetic routes used to access these compounds. However, these approaches usually require harsh conditions such as the presence of a strong base and high temperatures. In light of the relevance of aryl cyclopropyl sulfides in medicinal and synthetic organic chemistry, we developed conditions for the direct S-cyclopropylation of thiophenols using cyclopropylboronic acid under copper(II) catalysis. The procedure operates under simple conditions to afford the corresponding aryl cyclopropyl sulfides in good to excellent yields. The reaction tolerates substitution in ortho, meta and para position as well as electron-donating and electron-withdrawing groups.

Cyclization Cascade Followed by Non-usual Indoline Formation Towards the Synthesis of Enantioenriched Aspidospermatan Alkaloids

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Indole and its bioisosteres are recognized as biologically active functional groups and are found in a wide variety of alkaloids and drugs. The strategy generally used for the synthesis of aspidospermatan indole alkaloids is to begin with the indole portion and then construct the rest of the molecule around it. Over the last years, our research group developed a one-pot sequence of Vilsmeier-Haack cyclization and non-stabilized azomethine ylide intramolecular (3+2) cycloaddition to rapidly increase the molecular complexity. We have already applied this strategy to effectively synthesize an advanced tricyclic intermediate for the synthesis of racemic tubotaiwine and congeners. A major advantage of cyclization cascades resides in the control of the absolute configuration of all stereogenic centers, induce by only one stereogenic center on the cascade precursor. Recently, different approaches have been successfully explored to allow a non-racemic synthesis of this key step precursor using Evans auxiliaries. Another objective of this project is the incorporation of indoline at the end of synthesis. Because of ring strain, known methods based on thermodynamic enolization (e.g. Fischer) are not suitable. To address this problem, we proposed an approach consisting of an oxidative radical decarboxylation and trapping with an adjacent aniline.

Synthesis of Imino Sugar Analogues of Kdo as Potential LPS and EPS Biosynthesis Inhibitors in Gram-Negative Bacteria

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INRS-Institut Armand Frappier

Antibiotic resistance has become a major worldwide health problem. Governments and international health organizations like WHO have issued several warnings concerning the rational use of antibiotics in order to avoid the proliferation of new strains of the so called “super resistant” bacteria. However, the development of new antibiotic treatments remains as an important research priority. 2-Keto-3-deoxy-D-manno-octulosonic acid (Kdo) is an essential and highly preserved monosaccharide found in most of the Lipopolysaccharide (LPS) and Exopolysaccharide (EPS) structures of Gram-negative bacteria. As LPS and EPS are crucial components to guaranty cellular survival, the inhibition of the enzymes involved in the synthesis and introduction of Kdo could represent an interesting target for the development of new antibiotic therapies. In this project, imino sugar analogues of Kdo are being synthetized as potential inhibitors of LPS and EPS biosynthesis. 2-deoxy-α-imino Kdo was firstly synthetized in 12 steps starting from D-mannose. The critical reactions, mainly NaN3 insertion, HWE reaction and ring closure by an intramolecular nucleophilic addition of an amino group to a carbonyl group opened a new way to the syntheses of 2-deoxy-β-imino Kdo and glycosyl imino Kdo derivatives. These works are currently in progress.

Gold-Catalyzed Hydrofluorination of Internal Alkynes Using Aqueous HF

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Université Laval

The gold-catalyzed hydrofluorination reaction of alkynes represents a practical method for the synthesis of monofluoroalkenes. However, all the systems developed so far use amine-complexed hydrogen fluoride sources (Et3N·HF, DMPU·HF or pyridine·HF) as the HF source. Herein, we report the gold-catalyzed hydrofluorination reaction of internal alkynes using hydrofluoric acid. Notably, those conditions use one of the most economical sources of HF and are free of additional additives. Both symmetrical and unsymmetrical internal alkynes can be utilized, and the use of alkynes bearing a fluorinated group at the propargylic position as substrates allowed for a regioselective hydrofluorination reaction.

Organocatalyzed Amination of Benzylic Fluorides

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Université Laval

Simple alkyl fluorides are generally regarded as poor electrophiles in nucleophilic substitution reactions, mainly because of the strength of the carbon-fluorine bond. Over the years, we have described the activation of C–F bonds using hydrogen-bond donor. In all cases, the donor was either the solvent or present in a stoichiometric amount. Herein, we describe, to the best of our knowledge, the first hydrogen-bond-based organocatalyzed activation reaction of a C–F bond in benzyl fluorides. Precisely, the amination of benzylic fluorides using a catalytic amount of a thiourea as the hydrogen-bond donor will be presented.

Towards Organic Stretchable Conductive Films

M. Lerond

Ecole Polytechnique de Montreal

It will be presented how a macromonomer consisting of poly(dimethylsiloxane) (PDMS) and 3,4-propylenedioxythiophene (ProDOT) can be prepared. It will be shown how the macromonomer prepared can be polymerized by chemical oxidation involving the thiophene termini. The elastomeric properties of the cross-linked polymer and its mechanical properties will be presented. The conductive properties of the cross-linked polymer when doped with additional ProDOT monomer prior to the polymerization will be presented.

Biacenaphthylene-based Molecules: A Novel Building Block for n-type Organic Field-Effect Transistor (OFET)

Y.-H. Liu

McGill University

pi-conjugated organic semiconductors (OSCs) have attracted much attention for their optoelectronic application, like organic field-effect transistor (OFET). In this regard, the development of n-type (electron transport) OFET is the key to achieve the promising properties, for example, low-power consumption and high switching speed, which, however, is still limited by few candidates for air-stable unipolar n-type materials. In this work, the building block with well-delocalized conjugation system, biacenaphthylene (BAN), is introduced and its derivatives with electron withdrawing groups (Cl, Br, and CN) lower HOMO/LUMO energy level as potential n-type OSCs. Their electronic properties for OFET devices are investigated. With four Cl atoms on the terminals, Cl4-BAN-O results in head-to-head sheet packing crystal. This denser structure has access to intermolecular charge transfer, increasing efficient charge transport in solid state. Furthermore, with the stronger electron withdrawing group, CN, the low-lying LUMO of CN4-BAN-O is -4.03 eV, which meets the requirement of air-stable unipolar n-type OFET.

Iodine(III)-mediated Method to Access Polysubstituted γ-Butyrolactone Derivatives

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Université de Sherbrooke

Hypervalent iodine reagents have emerged as versatile and powerful tools in organic synthesis over the last 25 years. For example, the iodine(III)-mediated α-tosyloxylation of ketones derivatives has been an active field of research, giving rapid access to useful synthetic precursors. Our group has made numerous contributions to access α-substituted ketones derivatives using iodine(III)-reagents. We now report the application of this methodology in the diastereoselective contraction of 3,4-dihydropyran-2H-ones to access polysubstituted γ-butyrolactones. The starting materials (i.e. 3,4-dihydropyran-2H-ones) can be obtained from simple starting material using numerous methods, including NHC organocatalysis. The developed methodology tolerates a wide range of functional groups to give access to γ-butyrolactones that would be difficult to access through known methodologies. The products accessed by this methodology are important pharmacophores and motifs often found in natural products. The effect of the reaction conditions, as well as the nature of the iodine(III) reagent, will be discussed. The current reaction scope and limitations, as well as preliminary insights on the reaction mechanism, will be presented.

Development of Antibiotics with a High Selectivity for N. gonorrhoeae and N. meningitidis

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INRS - Centre Armand-Frappier Santé Biotechnologie

There is a need to develop novel avenues to selectively treat bacteria that are becoming increasingly resistant to currently used antibiotics. For instance, antibiotics are currently preventing a devastating global epidemic, but some bacterial strains of Neisseria gonorrhoeae are rapidly evolving to escape these types of human interventions. In collaboration with microbiologists, we recently found that organoborates are highly effective at selectively killing Neisseria gonorrhea and Neisseria meningitidis. Our aim is then to develop antibiotics with a comparable or higher activity than currently used therapeutics for the treatment of infections caused pathogenic bacteria from the Neisseria family but importantly, that do not alter the activity of other bacteria that constitute the normal flora in healthy individuals and prevent other potential infections. In this presentation, strategies adopted for the preparation of a variety of organoborates will be reported. Moreover, results from their preliminary structure-activity screening against the two pathogens of interest will be discussed, including the influence of their respective lipophilicity on their ability to internalize bacteria, as determined by logP. Results emerging from this study could lead to the development of novel strategies for the design of highly selective treatments for these pathogens that are becoming serious human threats.

Direct Hydrofluorination of Methallyl Alkenes Using a Methanesulfonic acid/triethylamine Trihydrofluoride Combination

X. Bertrand*, J.-F. Paquin

Université Laval

This presentation describes the use of a methanesulfonic acid/triethylamine trihydrofluoride combination for the direct hydrofluorination of methallyl-containing substrates. Under those metal-free conditions that use readily available, cheap and easy to handle reagents, a range of methallyl alkenes could be converted to their corresponding tertiary fluoride in up to 78% yield. Finally, a promising result for the adaptation of this chemistry to continuous flow conditions will be discussed. This work represents a straightforward method for the incorporation of a single fluorine atom.

Molecular Biology

Holding back Jumonji: OCT-1 induced epigenetic changes combat oxidative stress

A. Gupta*, K. B. Storey

Carleton University

Wood frogs (Rana sylvatica) show a remarkable ability to survive extreme winter conditions. They can endure the freezing of ~70% of their body water with full survival after thawing. Freezing combines stresses including dehydration, anoxia and hyperglycemia as well as potential physical damage from ice crystals; all be combated for freezing survival. Episodes of freeze/thaw or anoxia/reoxygenation are known to cause oxidative stress with potentially destructive pathways consequences such as apoptosis. To combat these challenges, numerous genes are differentially regulated to induce pro-survival proteins. Octamer Transcription factor 1 (OCT1) is a highly conserved gene regulatory factor that directly senses cellular stress and interacts with DNA dependent protein kinases. Phosphorylation of OCT1 at serine and threonine sites promotes binding to Jumonji domain containing 1A (Jmjd1a) or KDM3A gene promoters and regulates their expression. Jmjd1a is a hypoxia-responsive regulatory histone demethylase that has specificity for H3K9Me2 and H3K9Me1, and is associated with gene activation in oxygen deficient conditions. Our results show inactivation of JMJ1A under anoxic conditions, indicating that this enzyme might play a role in epigenetic regulation of under stress.

Towards Increasing the Chemical Diversity of Aptamers

D. de Rochambeau, H. Sleiman, M. McKeague, S. Hirka*, D. Saliba

McGill University

Aptamers are synthetic DNA/RNA affinity ligands that bind specifically and with high affinity to a given target. They present a molecular recognition alternative to antibodies thanks to their greater stability and ease of synthesis. When coupled to an appropriate transducer, they produce robust biosensors. Despite aptamer versatility, nucleic acids lack diversity in terms of chemical functionality. To overcome these limitations, we are exploring two different approaches for introducing new functional groups into aptamers. Specifically, we are concentrating on a method called “click-SELEX”. In this method, one nucleoside is switched to a base-modified version carrying a bioorthogonal handle that can be decorated with one modification at a time, retaining its ability to amplify. In another approach we are exploring the ability to introduce numerous modifications into an existing aptamer sequence, but with the drawback that in vitro selection is not possible due to the inability to amplify the modified nucleotides. Here, we present our progress towards developing model thrombin-binding aptamers with modified residues. We show that several modifications to the original aptamer sequence result in high-affinity binding. In the long-term, both of these approaches will be employed to discover new aptamers with high affinity to diverse targets.

Fat but Fit: How Hibernating Ground Squirrel Adipose Tissue Regulates pro-inflammatory Signaling Pathways

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Both the advanced-glycation end product (AGE) receptor (AGE-RAGE) signaling pathway and the inflammasome pathway are important signal transduction pathways that influence the immune/oxidative stress responses and are dysregulated in patients with obesity/diabetes. To uncover novel protective mechanisms against inflammation in a natural model of obesity, we studied how obese "fat but fit" hibernating ground squirrels regulate these pathways in two kinds of adipose (WAT and BAT) as they transition into and out of torpor, a state of metabolic suppression. Surprisingly, RAGE levels increase during torpor and as animals arouse from hibernation, but the relative levels of RAGE ligands either don't change or decrease in both WAT and BAT. Inflammasome components were more expressed at the mRNA level in BAT but not WAT, suggesting that ground squirrel WAT may suppress inflammasome component expression to prevent obesity-induced inflammation and associated chronic diseases. BAT may increase inflammasome activity as hibernators emerge from torpor due to an associated influx of ROS. These studies are the first of their kind that show hibernators may use coordinated mechanisms to regulate inflammation as they enter and arouse from torpor and could help elucidate novel points of inflammatory regulation for disease prevention in obese mammals.

Excised and Isolated Chromatin Rings, Containing the Entire rRNA Gene, Retain the Native Chromatin Structure: a Mass Spectrometry Analysis

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Cancer cells show a high division rate. This is sustained by an important rRNA production. Indeed, in active cells rRNA production represents more than 50% of total cell transcription activity. Thus, rRNA-genes (rDNA) transcription became a target for cancer therapies. Furthermore, rDNAs are also of interest in fundamental sciences: they are utilised to study DNA mechanisms in chromatin. Indeed, rDNAs are highly repeated genes, of which only a part is in transcription. This leads to the simultaneous existence of two chromatin conformations: an 'open' chromatin depleted of nucleosomes characterises transcribed genes, whereas a 'close' chromatin stands for inactive genes with DNA wrapped around nucleosomes. Thus, this allows comparing and determining the chromatin effects on DNA mechanisms.
Among those mechanisms, nucleotide excision DNA repair (NER) is of interest when speaking of cancers, especially skin cancers. In the laboratory, the budding yeast is used as working model to study NER of rDNAs. For this purpose, engineered yeasts were made to allow rDNA excision from the chromosome and chromatin purification. The current study presents the effects of excision and isolation on native chromatin. Results show excision does not affect chromatin structure and accessibility. Isolated chromatin was submitted to mass spectrometry analysis.

Investigating Novel Targeted Therapeutics Against Acute Myeloid Leukemia Stem Cells

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Acute myeloid leukemia (AML) is an aggressive form of blood cancer. The 5-year survival rate remains low despite the aggressive standard of care drugs used. In addition, patients often relapse and succumb to the disease. This is partially driven by the chemo-resistant nature of the leukemic stem cells (LSCs), which evade therapy and sustain the disease. Thus, novel therapies are needed to preferentially target LSCs while sparing hematopoietic stem cells (HSCs). Through the use of our established LSC and HSC gene signatures, we have used in silico and screening approaches and have identified 12 candidate compounds that can eliminate LSCs when tested in vitro in a human primary AML, while sparing HSCs. One main class are the FDA-approved glucocorticoids. We found these to induce the terminal differentiation of LSCs to leukemic blast cells in some human AML. Differentiating as a mode of treatment is successful in one subtype of AML, acute promyelocytic leukemia (APL), using all-trans retinoic acid. Following this paradigm, glucocorticoids are potentially important candidates for further investigation. Our goal is to investigate these compounds ex vivo and in a panel of genetically defined primary AML samples to establish their efficacy, safety for clinical use and mechanism of action.

Selective Targeting of HDAC8 Using Novel Small Molecule Scaffolds for Cancer Treatment

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Histone Deacetylases (HDAC) are a class of enzymes that regulate the expression and activity of several proteins associated with cancer initiation and progression. Thus, several cancers such as leukemia, breast, and colorectal cancer have been associated with elevated levels of HDACs, suggesting inhibition of HDACs to be a viable approach to chemotherapy.1 Furthermore, HDAC8 knockdown studies have identified the crucial role HDAC8 in the progression of neuroblastoma. There are currently four FDA approved HDAC inhibitors, all of which show pan-inhibition of HDACs resulting in a wide range of side effects and host-toxicity. The use of selective HDAC inhibitors is hypothesized to maintain antitumor efficacy while reducing pan-HDAC inhibition associated side effects. Our lab has synthesized a library of hydroxamic acid-based HDAC inhibitors that display selectivity for HDAC8. We have invented small-molecules with structural components that are essential to potency and selectivity agains HDAC8, as well as metabolic stability in vitro, in cellulo, and other stability assays for treatment of neuroblastomaas

Biochemistry

Characterization of the Role of Position 64 in Saccharomyces cerevisiae tRNA Nucleotidyltransferase

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The enzyme ATP(CTP): tRNA nucleotidyltransferase (tRNA-NT) adds the cytidine-cytidine-adenosine (CCA) sequence to the 3' ends of all eukaryotic tRNAs. This 3' tag is required on the tRNA for aminoacylation and delivery of the amino acids to the ribosome. A temperature-sensitive (ts) mutation was mapped to the Saccharomyces cerevisiae CCA1 gene encoding tRNA-NT. This mutation converts glutamic acid (negatively charged) at position 189 to lysine (positively charged) in the protein, reducing enzyme activity and thermal stability. Subsequently, a second-site suppressor with arginine (large and positively charged) at position 64 converted to tryptophan (large and hydrophobic) was identified. We used site-directed mutagenesis experiments to explore the significance of position 64. Replacing R64 with phenylalanine (also large and hydrophobic) or alanine (small and hydrophobic), but not proline (hydrophobic but rigidifies polypeptide backbone) resulted in viable cells. While only the R64F suppressed the ts phenotype. Our data highlight the importance of the relative orientations of conserved motifs A (containing R64) and motif C (containing E189). In the E189 variant, a hydrophobic residue at position 64 allows for a change in the orientation of motif C to suppress the ts phenotype. However, R64P locks motif C from any structural alteration, and the enzyme cannot function.

Preparation and characterization of recombinant Plasmodium falciparum glyceraldehyde-3-phosphate dehydrogenase

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GAPDH is a glycolytic enzyme with many moonlighting functions. In Plasmodium falciparum, hemoglobin degradation produces toxic free heme, and the antimalarial drug, chloroquine, inhibits heme detoxification. Parasite proteins binding heme, like GAPDH are of interest since they may function in heme detoxification and/or utilization by the parasite. However, GAPDH-heme interaction is obscure with no heme-bound crystal structure available. I aim to purify P. falciparum GAPDH (PfGAPDH) and characterize its heme binding to inform antimalarial development. A pET-15b vector encoding N-terminally His6-tagged PfGAPDH from strain 3D-7 was transformed into E. coli BL21(DE3) cells .The overexpression of soluble His6-PfGAPDH was confirmed by SDS-PAGE analysis prior to protein purification. Purified enzyme was highly active with activity of 70 U/mg. As His-rich sequences bind heme, it is critical to prepare tag-free PfGAPDH for our studies. We present a rapid method to remove the His6-tag by brief exposure to trypsin, and trypsin removal with immobilized benzamidine. Q-ToF MS confirmed tag removal (< 1 min) with no GAPDH digestion. Ongoing studies include PfGAPDH titration with heme by spectroscopic methods to determine heme-binding stoichiometry and affinity (KD). The heme-binding pocket(s) in PfGAPDH will be identified by heme-mediated H2O2 oxidation of nearby residues and identification by mass spectrometry.

Probing P450 3A4 Allosteric site via the Bioconjugation of Ligand Analogues

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McGill University

P450 enzymes (P450s) consist of a large family of hemoproteins catalyzing oxidation reactions essential to the biosynthesis of endogenous substances (steroids, lipids, vitamins) and natural products, as well as the metabolism of drugs and xenobiotics. P450 3A4 has the particularity to bind multiple substrates at once leading to complex cooperative behaviors which challenge the current paradigms in enzymology. Moreover, many substrates are also known to be allosteric activators of P450 3A4. The location of this allosteric site is still debated and is likely to depend on the specific effector involved. In order to investigate this allosteric pocket, we covalently attached ligand analogues at several positions on the enzyme to permanently activate it and probe the location of the allosteric site. The impact of the labeling was evaluated by monitoring the changes in enzyme kinetics with and without allosteric effectors. Our method allowed to narrow down the location of the P450 3A4 allosteric site by effectively mimicking the allostery observed with progesterone. Our results are of considerable interest not only in the fields of biocatalysis and enzymology, but also in the area of drug metabolism and for the prediction of drug interactions.

Lymphocytes Implications in Osteoclastogenesis Modulation

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Objectives: Two million Canadians suffer from osteoporosis. This disease is the result of a very active osteoclastogenesis, which depends on RANKL expression by osteoblasts. Host immune responses may also play a key role in promoting bone resorption since lymphocytes express RANKL. The aim of this research is to evaluate RANKL expression in lymphocytes in proinflammatory conditions, and its implication in osteoclastogenesis.
Methods: Cell lines Hob and Jurkat were treated with LPS [100 ng/mL], TNFalpha [10 ng/mL] and dexamethasone [10-8 M] to stimulate RANKL expression which was analyzed by Western Blot, ELISA and flow cytometry. Cells were then cocultured with PBMC extracted from blood donors to induce osteoclastogenesis measured by TRAP coloration and Western Blot.
Results: Expression of membrane-bound RANKL increases significantly ($p<0.05$) with a 1.9-fold in HOB and Jurkat with LPS and TNFα combined. Treated lymphocytes cultured with PBMC allow an increase of mature osteoclasts with a 1.7-fold, whereas treated osteoblasts allow a 1.3-fold increase.
Conclusion: Membrane-bound RANKL seems more implicated in osteoclastogenesis than its soluble form. Lymphocytes results reveal that they may be as important as osteoblast in the recruitment and activity of osteoclasts. This leads to a new pathway of pathophysiology and therapy of osteoporosis.

Development of ROS-Activated Dormant Photosensitizers with Theranostic Capabilities

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McGill University

Photodynamic therapy (PDT) is an established therapeutic technique for the treatment of diseases including cancer and bacterial infections. PDT employs photosensitizers which, upon photoexcitation, sensitize singlet oxygen (1O2), a cytotoxic reactive oxygen species (ROS). A risk of PDT is damage to surrounding healthy tissues when light is applied. Activation of a dormant photosensitizer by reaction with a chemical cue would mitigate undesired activity in healthy tissues. In 2016, our group reported a dormant photosensitizer that activates upon scavenging ROS to deliver 1O2 specifically in cells under oxidative stress associated with increased ROS generation, i.e. bacteria after treatment with antibiotics. The dormant photosensitizer combines a boron-dipyrromethene (BODIPY) photosensitizer with the antioxidant chromanol ring of α-tocopherol as a trap which quenches the excited photosensitizer via intramolecular photoinduced electron transfer (PeT), preventing the sensitization of 1O2. ROS-mediated oxidation of the trap prevents quenching, activating the photosensitizer. Upon activation, our second-generation dormant photosensitizer sensitizes 1O2 and also exhibits fluorescence. Thus, we may simultaneously monitor the level of ROS using fluorescence microscopy and produce lethal 1O2 under oxidative stress conditions. We aim to better understand ROS production in bacteria upon treatment with antibiotics and harness this oxidative stress to selectively induce a PDT effect.

Formulation of a Peptidomimetic PACE4 Inhibitor for the Administration of a Potential Prostate Cancer Treatment

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University of Sherbrooke

The proprotein convertase PACE4 has been validated as a new target to expand the range of prostate cancer (PCa) treatments. We have developed a potent peptidomimetic inhibitor of this enzyme named compound C23 that blocks tumor progression in LNCaP xenograft model of PCa. However, C23 suffers from low stability facing most common biological degradations. In order to improve its profile and to facilitate its administration, we decided to test different formulation strategies. Here, we investigated the use of cyclodextrins (CDs) since they can form “host-guest” complexes based on hydrophobic interactions. A series of C23 analogs have been formulated with the selected beta-cyclodextrin and evaluated in various biological assays. As a result, a new formulated lead compound has been identified named FC23bCD, which in addition to be more soluble and more potent also showed improved stability profiles. The encouraging properties make it an excellent candidate for further in vivo investigations.

In Vitro Reconstitution of the Salmonella Itaconate Degradation Pathway: an Immune System Evasion Mechanism and Antibacterial Target

J. Pierscianowski*, D. Duncan, K. Auclair

McGill University

There is a need for alternative treatment strategies to combat the antibiotic resistance crisis. One such method involves the resensitization of intracellular bacterial pathogens to our immune system by inhibiting the bacterium's defence machinery. During an infection, macrophages will engulf bacteria and expose them to antimicrobial molecules. Itaconate is one such molecule that blocks a metabolic pathway that is required for bacterial survival within macrophages, thus killing them. Some pathogens such as Salmonella enterica have evolved to express itaconate degrading enzymes that allow them to survive intracellularly. There are three enzymes in this pathway that convert itaconate into pyruvate and acetyl-CoA. Previously, the Auclair group has described a molecule that is able to inhibit this pathway and resensitize S. enterica to itaconate using a bacterial growth assay. This presentation will summarize the cloning of these three enzymes from S. enterica and reconstitution of the itaconate degradation pathway in vitro.

Détermination de la sensibilité de biomarqueur, suite à une contamination au Palladium chez Lemna minor

S. Jmii*, D. Dewez

UQAM

Les éléments du groupe du platine (EGP), sont des métaux lourds, identifiés comme polluants émergeants. Trois d'entre eux, le Platine, le Rhodium et le Palladium (Pd) entrent dans la fabrication des pots catalytiques, élément obligatoire des véhicules routiers permettant de convertir les gaz d'échappements en gaz non polluants. L'usure du pot catalytique libère ces métaux dans l'environnement. En parallèle, Le Pd devient progressivement majoritaire dans la composition du catalyseur, c'est le EGP le plus soluble et donc le plus mobile dans les écosystèmes. Il a d'ailleurs déjà été illustré comme contaminant dangereux car il peut être facilement absorbé et accumulé dans les tissus des producteurs primaires et intégrer la chaine alimentaire. Lemna minor est un modèle adéquat pour étudier la toxicité des contaminants car c'est un bioindicateur efficace à la base de plusieurs chaines alimentaires. L'objectif principal est d'étudier des biomarqueurs sensibles aux différents niveaux de bioaccumulation du Pd chez ce producteur primaire. Pour cela nous avons quantifié les niveaux de métal dans les tissus par ICP-EOS et dosé plusieurs biomarqueurs, capables de caractériser la toxicité au niveau cellulaire (stress oxydatif) et au niveau photosynthétique (inhibition du transport des électrons).

MondoA is a Master Regulator of Sugar-Induced Gene Expression and Link to Circadian Rhythms in Frozen Wood Frog

G. Singh*, K. Storey

Carleton University

Wood frogs can survive freezing up to 70% of their total body water during winter and return to full functions, unharmed, after thawing. As a cryoprotective measure and to maintain osmotic balance, blood glucose rises from 5 to ~300mM during freezing, and this requires the coordination at molecular levels. Mondo A, is an important glucose responsive transcription factor that interacts with its binding partner MLX to induce the expression of numerous genes involved in glucose metabolism and circadian rhythm. Previous literature suggests a strong link between these processes, and perturbance in either process is associated with type-2 diabetes risk. Our results show higher protein expression and DNA binding of MondoA and MLX in liver and brain of wood frog which correlate with expression of downstream targets. Also, circadian targets, BMAL1 show a general rise in expression in liver as compared to CLOCK which show higher expression in brain suggesting expression of targets in a tissue specific manner. KLF-10 and PFKFB3 downstream of MondoA, also controlled by circadian machinery decrease in expression during wood frog's freeze thaw cycle in liver suggesting role of MondoA in regulating glucose metabolism partly by modulating circadian rhythm.

Environmental Chemistry

Biotransformation of 8:2 Monosubstituted Polyfluoroalkyl Phosphate in Rat Liver, Intestinal, and Fecal Suspensions

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Polyfluoroalkyl phosphates have been used in a variety of commercial and industrial applications owing to their thermal stability and surfactant properties. However, these chemicals are precursors to metabolically labile fluorotelomer alcohols and bioaccumulative and persistent perfluoroalkyl carboxylic acids, making them a concern to humans and the environment. To further establish the mechanistic fate of polyfluoroalkyl phosphates, this present work focuses on the biotransformation of 8:2 monosubstituted polyfluoroalkyl phosphate (8:2 monoPAP) in rat via in vitro incubations with liver and intestinal S9 fractions and fecal suspensions. The hydrolysis product of 8:2 monoPAP, the 8:2 fluorotelomer alcohol, was monitored by GC-EI-MS. The maximum velocities (Vmax) for 8:2 monoPAP in the liver, intestinal and feces were (11 ± 2.1) ×10-2, (6.4 ± 0.7) ×10-2, and (2.0 ± 0.21) ×10-4 nmol/min mg, respectively. Michaelis constant (KM) values were (4.0 ± 1.5) ×103, (1.2 ± 0.3) ×103, and (6.4 ± 1.2) ×103 nM, respectively. These results indicate that ester hydrolysis activity for 8:2 monoPAP is two-fold higher in the intestinal compared to the liver. Fecal suspensions showed a lower activity rate presumably due to the aerobic microbial environment. Nevertheless, the current study demonstrates fecal microorganisms as contributors for environmental toxicant metabolism via phosphate ester hydrolysis activity.

Indium Recovery in a Leachate Produced from Spent Liquid Crystal Displays (LCD) of Computers and Laptops

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Electronic waste is generated in large quantities every year. This waste contains several critical or strategic metals, including indium (In), that can be recovered. The recovery of In from this secondary source is attractive because of it's high economic value, it's low availability as a primary resource and it's significant consumption for the production of indium tin oxide (ITO) used in LCD screens. Previously, we have successfully leached up to 99% of the In contained in LCD screens of computers and laptops. The present project aims to optimize the recovery of In leached from these LCD screens. The percent removal of In from a simulated leachate solution using selective precipitation and ion exchange will be presented. Further work will include a techno-economical study of the complete leaching and recovery process in order to develop a cost-effective method for recovering In from LCD screens.

Mechanisms of Chemical Bonding Between Organic Matter and Sulfidic Sediments in the Saint Lawrence Estuary - A Protecting Role

A. Tétrault, Y. Gélinas

Concordia University

Marine sediments present the principle sink for organic matter across geological timespans, i.e. millions of years. Evidence of strong associations between iron oxide minerals and organic matter reaching the seafloor has been known for some decades now. These associations are believed to explain the persistence of organic matter in the face of microbial degradation as it is slowly buried in the sediment layer. Despite the importance of this protective mechanism in the grand scheme of the global carbon cycle, virtually nothing is known of the fate of organic matter as it traverses the redox gradient into the reducing layers of sediment nor the exact mechanism(s) by which this occurs. This study presents a work-in-progress in probing the binding mechanisms between organic matter and iron sulfides with an eye to better understanding the shuttling mechanism and its potential impacts on the sequestered organic matter pool as it leaves the oxidative zone. This approach involves studying model compounds through an artificial redox shutttle, computer modeling, and an interpretation grounded in the electronic theory of chemical bonding.

Computational Chemistry

Electronic Structure Analysis on the Effects of Purine Hoogsteen Edge Hydration on Sugar Edge H-bonding

P. Archambault*, H. Muchall, G. Peslherbe

Concordia University

Non-covalent interactions, such as hydrogen bonding and pi-stacking, are the driving force for folding and stabilizing nucleic acid structures. These interactions between bases govern structural properties and have been considered a core of nucleic acid research. The conformational flexibility of nucleic acids arises largely due to interactions with the aqueous surrounding. Not only does water play an important role in their stability, but also their functionality. For instance, solvent effects significantly influence complex biochemical processes, such as DNA replication and biomolecular recognition, by modifying hydrogen bonding interactions within base pairs. With small changes to nucleobases, caused by protonation or hydration, capable of causing substantial changes to the stability of the base pair, it therefore becomes vital to understand the nature of non-covalent interactions to therapeutically target DNA and RNA appropriately. In this work, density-functional theory is used to examine Watson-Crick and non-Watson-Crick base pairing motifs with water included as explicit molecules or as a solvent field. The effects on the hydrogen-bonding interactions in the base pairs are characterized from the calculated electron densities with the Quantum Theory of Atoms in Molecules; changes in orbital interactions are quantified using Natural Bond Orbital analyses.

The Exchange-Correlation Factor Model in Density Functional Theory

É. Cuierrier*, Y. Zhou, M. Ernzerhof

Université de Montréal

Density Functional Theory (DFT) is the most widely used approach for electronic structure calculations. In the Kohn-Sham scheme, only the exchange-correlation energy Exc needs to be approximated; to this end, we model the spherically averaged exchange-correlation hole $\rho xc(r,u)$, which represents the reduction of the electronic density at a distance u from a reference electron at a position r . Previously in our group, an exchange factor $fx(r,u)$ was developed to approximate the exchange hole $\rho x(r,u)=fx(r,u)\rho(r,u)$. In this expression, $\rho(r,u)$ is the angle average of the electron density over all possible orientations of u : $\rho(r,u) =d\Omega u 4\pi\rho(r+u)$. This method is a variation of the Weighted Density Approximation and it has the potential of being one-electron, self-interaction error (SIE) free. Furthermore, our group developed a correlation factor ansatz in which the exchange hole yielding the exact exchange-energy per particle is multiplied by the correlation factor $\rho xc(r,u)=fc(r,u)\rho x(r,u)$. Our previous models of fc were not SIE free, however. To rectify this problem, we are developing an exchange-correlation factor to approximate the hole $\rho xc(r,u)=fxc(r,u)\rho(r,u)$. The exchange-correlation factor is constructed non-empirically by satisfying physical and mathematical constraints. Preliminary results for atomization energies obtained with simple models of $fxc(r,u)$ are encouraging.

Linear Polymers Heterogeneity and Dynamic seen by Simulation

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Université de Sherbrooke

A lot of complex phenomena happen within the glass transition. Even if glassblowers take advantage of it since many centuries, a lot of unanswered theoretical questions are still opened in the scientific community. This is mainly because the atoms dynamic is characterized by many time scales (from several picoseconds to years!). Our research aims to bring a chemist's vision to this phenomenon.
Linear polymers have been the subject of this study. Backbone dihedral movements have been correlated with the glass transition temperature. The effective activation energy is computed by an Arrhenius plot of the dihedral movement frequency logarithm as function of 1/temperature. Results on many polymers show that the effective activation energy is correlated to the glass transition temperature by the equation Ea (kcal/mol) = 0.01 Tg (K) + 0.44 kcal/mol. Moreover, the intramolecular cooperativity has been analyzed at the dihedral no. n+1, n+2, … to n+10. Also, the intermolecular cooperativity has been revealed by the computation of Q(t) and $\chi 4(t)$.

Estimating Reaction Energy Barriers with Machine Learning

H. Ji*, R. Fournier

York University

The prediction of transition states (TS) of reactions is one of most significant problems of quantum chemistry. As we all know, minimization is an easy mathematical problem. However, transition states are saddle points, which could be the maximum along one coordinate and the minimum along all others. So mathematically, they are much harder to locate. Hence, obtaining energy barriers (Eb) and locating TS are still difficult and time-consuming. We are exploring faster ways of obtaining approximate reaction energy barriers by machine learning (ML). We surveyed the literature and collected 100 energy barriers known to high accuracy and different properties of the reactants and products ("features") that are expected to correlate with these energy barriers from the literature. We are using ML techniques to help discover nontrivial relations between features (independent variables) and energy barrier (the dependent variable). There are hundreds of small molecules in the interstellar medium (ISM) and circumstellar envelopes (CSE) which can react in a myriad of ways. A fast screening method that helps reject every reaction with a predicted nonzero barrier would be very helpful for astrochemistry. Therefore, the anticipated significance of the work is to provide reasonable applications to astrochemistry.

Balancing act Between the Orthogonality and Locality of One-electron Orbitals

Z. Luo*, R. Khaliullin

McGill University

Spatially localized molecular orbitals are of tremendous importance in the electronic structure theory as they are widely used to describe chemical bonding and speed up calculations. Nonorthogonal localized molecular orbitals (NLMOs) are known to be noticeably more localized than their conventional orthogonal counterparts. Unfortunately, the existing methods to obtain NLMOs must pre-determine and freeze the localization center of each NLMO before its spread is minimized. This is done to avoid the "collapse" of the occupied subspace – a problem of NLMOs becoming linearly dependent. In this presentation, we describe an unconstrained black-box method to localize nonorthogonal orbitals that determines the position of their centers automatically during the optimization process. The key to the new procedure is to construct and impose a penalty function which prevents the orbital "collapse". An algorithm is proposed to adjust the strength of the penalty and produce the right balance between orthogonality and locality of NLMOs. The resulting method produces NLMO fast, without requiring good understanding of bonding patterns in the system (i.e. "chemical intuition") and is demonstrated to work well a variety of molecules and materials (gamma-point only) including large systems with non-trivial bonding patterns.

Construction of Self-Interaction-Corrected Exchange-Correlation Functionals Within the Correlation Factor Approach

R. Wang*, Y. Zhou, M. Ernzerhof

Université de Montréal

Despite the great success of the Kohn-Sham method in calculations of molecular properties, the self-interaction error remains a large challenge for approximate exchange-correlation functionals. Recently, Přecechtělová et al. constructed accurate, non-empirical correlation factor models based on exact exchange. In this approach, the exchange-correlation hole is written as a product of the correlation factor and an exchange-hole model. In particular, we address the one-electron, self-interaction error and introduce a modified correlation factor model which is constructed such that it reduces identically to one in one-electron regions of a many-electron system. This self-interaction corrected exchange-correlation hole is then used to generate the corresponding exchange-correlation energy functional. The new functional is implemented into a Kohn-Sham program and assessed by calculating various molecular properties. We find that, overall, a significant improvement is obtained compared to previous versions of the correlation factor model.

Nanochemistry

Synthesis and Characterization of a Chemically Modified Parallel-Stranded poly(A) RNA Duplex for Applications as a Stimuli Responsive Nanomaterial

K. Duke*, A. Noronha, C. J. Wilds

Concordia University

The need for structurally and functionally diverse nanomaterials is rapidly expanding due to their applications in fields spanning medicine, agriculture, and biotechnology. Nucleic acids, in particular, are attractive candidates for nanomaterials due to their structures and propensity for molecular binding. RNA has been gaining recognition as a potential nanomaterial due to its ability to engage in various non-canonical binding interactions and adopt numerous structural motifs. Polyadenylate (poly(A)), forms a parallel-stranded duplex at pH 4, or pH 7 in the presence of NH4+, through Hoogsteen base-pair interactions. Previous work has demonstrated that duplex stability occurred with the incorporation of either 2'-O-methyl or 2'-fluoro functionalities, whereas, the incorporation of 2'-deoxyribose or arabinose sugars was found to be destabilizing. In this work, the influence of 2'-O-propargyl functionality on poly(A) RNA duplex stability will be explored via Tm and CD analysis. These findings will provide insights to guide future chemical modifications to the duplex including the incorporation of aromatic systems to the exterior of the duplex, allowing π-stacking stabilization, to enhance the applications of this duplex as a pH and NH4+ responsive nanomaterial.

Photoactive Nanofiber with Upconverting Nanoparticles for Wound Healing

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Electrospun fiber mats have been considered as advanced wound healing bandages due to their ability to absorb fluid and the potential for drug release. The incorporation of nanometer-sized structures, such as quantum dots, carbon materials or oxide nanoparticles into nanofibers provide such fibers with fluorescence, conductivity, or antibacterial properties. Only few reports describe upconverting nanoparticle (UCNP)-containing nanofibers for would healing. The project began with the synthesis of LiYbF4: Yb3+, Tm3+/ LiYbF4 UCNPs with a narrow size distribution (31±3 nm by TEM) and subsequent characterization of their luminescent properties. Important processing parameters for electrospinning were optimized using aqueous poly(vinyl alcohol) (12% PVA). The successful synthesis of a photo-cleavable o-nitrobenzyl derivative via a four-step procedure was confirmed by 1H- and 13C-NMR spectroscopies. To preliminarily demonstrate the versatility of our concept, fluorescent molecules, as easily detected surrogates for wound healing drugs, will be conjugated to this photolabile derivative. Subsequently, the photo-releasing properties, triggered by NIR illumination of the UCNPs, will be investigated. By incorporating these different components into our electrospun nanofibers, a prototype wound-healing system that can be triggered by NIR light will finally be investigated.

Molecular dynamics simulation of noble gases adsorption on homogeneous and heterogeneous Carbon nanotube bundles

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We have used molecular dynamics simulations to investigate the application of single-walled carbon nanotube (SWCNT) bundles as noble gas storage materials. Adsorption of He, Ne, Ar, Kr and Xe have been studied. We have performed simulations using one model of bundles consisting of nanotubes having all the same diameter (homogeneous) and two different configurations of bundles of carbon nanotubes of different diameters (heterogeneous). The adsorption coverages were calculated. The results indicate that adsorption takes place both in the internal pore volume and at the external surface of the open-ended carbon nanotubes. It is also found that small gases such as He and Ne can adsorb in interstitial channels (ICs) between three adjacent tubes of bundles, but Ar, Kr, and Xe gases adsorb only in the (ICs) of one of the models of heterogeneous SWCNT bundles. These results demonstrate that the configuration of the bundle has a considerable effect on the adsorption capacity and (SWCNT) bundles have desirable characteristics as an adsorbent.

Carbon Dot-Catalyzed Biodiesel Production

A. Macina*, T. de Medeiros, R. Naccache

Concordia University

Global energy demands will grow to staggering numbers in the near years to come and will continue to increase as fossil fuel dependency rises. This has called for a seriousaccelerated the search to find alternative energy sources, . An abundant amount of research is going into the production of biofuels such as biodiesel. as an alternative to fossil fuel derived oil. Presently, biodiesel is produced through the transesterification of vegetable oil using an alcohol and a strong base. Although this method achieves high biodiesel conversion yields many challenges persist such as high production costs due to tedious purification processes and the inability to recover and reuse the catalyst ultimately leading to unsustainable practices. To address these drawbacks, heterogenous catalysts derived from metal oxides, carbon-based materials and mesoporous supported materials have all been consideredbeen investigated. , and aAlthough such systems they offer the possibility for catalyst recoveryability and reusability, they often require high catalyst loading, have the potential for metal leaching, the use ofneed for large excess amounts of alcohol, as well as and more complicated synthetic procedures. In order to circumvent these limitations, we propose prepareda citric acid-based glycine and citric acid derived carbon dots with via a simple one pot hydrothermal synthesis procedure. Our system requires low catalyst loading and maintained the catalyst reusability can be maintainedfor up beyond five reaction cycles. Using carbon dots as heterogenous catalysts can permit biodiesel production to become an a more environmentally-friendly, cost-efficient and sustainable practice and allow future global energy demands to be met.process that can meet future energy demands.

First Steps to Nanomedicine: Assessing Interactions Between Polystyrene Nanoparticles and Albumin Proteins

S. Osman

Ryerson University

Nanoparticles have gained traction for drug-delivery because they can overcome limitations associated with free drugs. When nanoparticles are injected into complex biological mediums, they procure a protein "coat", which affords them a new identity that affects their fate in vivo. To ensure nanoparticles can be used to their full potential, an understanding of protein-nanoparticle interactions needs to be established. This research aims to answer: What are the kinetics and thermodynamics of association between bovine serum albumin (BSA) and fluorescent polystyrene nanoparticles (fluorospheres), and what intrinsic and extrinsic parameters affect association? This research will assess the interactions between 100nm or 200nm diameter fluorospheres and BSA using two-photon excitation fluorescence cross-correlation spectroscopy (TPE-FCCS). This technique allows for direct, in situ measurement of fluorescently-labeled species and their binding interactions. TPE-FCCS will be used to measure the kinetic and thermodynamic parameters of albumin-fluorosphere interactions and to gain an understanding of forces that dictate protein coating. Thus far, results suggest low binding ratios (~ 18 proteins/sphere) and on-rates on the order of 10-4 s-1 for fluorospheres of 100nm diameter. These findings challenge the current understanding of the formation of a protein monolayer, or "protein corona" and highlight the need for further study of nanoparticle-protein systems.

Sequence-defined (DNA-oligomer)-based 2-D Nanostructures

M. G. Rafique*, D. Bousmail, H. Sleiman

McGill University

Two-dimensional supramolecular architectures comprise topologically planar macromolecules resembling planar sheets. Such structures have potential for applications in the fields of materials science and nano-diagnostics. One method of accessing such 2-D architectures is through self-assembled DNA-oligomers obtained through rational sequence design. Our group has previously shown the morphological tunability of supramolecular architectures comprising self-assembled DNA-oligomer amphiphiles leading to nano-spheres (0D), nano-rods (1-D), and nano-sheets (2-D). A detailed study of such 2-D architectures, however, has not previously been performed. Here we report the morphological analysis of nano-sheets obtained through the self-assembly of synthetic amphiphilic DNA-oligomers bearing π-conjugated chromophores. The dimensionality and structure of such architectures is explored, as well as the effect of the sequence and length of the hydrophilic and hydrophobic constituents of individual oligomeric strands on the overall self-assembly. The goal is to extend these self-assemblies to include diversified functional cores and surfaces which can be precisely modified. This would enable the creation of synthetically accessible two-dimensional structures that are viable for practical applications.

Immune Response of Small Drug-like Molecules: Influence of Self-aggregation

F. Shahout*, S. LaPlante

INRS

Many small drug-like molecules currently used to treat cancer can spontaneously self-assemble into aggregates in aqueous solution at micromolar concentrations. These small-molecule aggregators can have detrimental effects on drug safety, efficacy, and pharmacokinetics. The immune response of small-molecule aggregators is, therefore, an important issue. There is an evidence that aggregation of biotherapeutic proteins and nanoparticles has the potential induce an immunogenic response; however, immunogenicity of small molecule aggregators has not been yet reported. Here, we show that colloidal anticancer drugs, formed at 37 °C, can enhance the in vitro immune response of a murine macrophage (RAW 264.7) cells and human peripheral blood mononuclear cells (PBMCs) compared to non-colloidal forming drugs and inherent immunogenicity of the monomer form. This response depended on the aggregate type and size of colloids. We propose a cytokine signature including IL-6 and TNF-α as a potential biomarker of the in vitro murine macrophage and human (PBMCs) cells response to aggregates. Large colloidal aggregates including lapatinib and erlotinib induced the highest response compared with intermediate colloidal aggregates and non-colloidal and monomer forms. With an increased understanding of small-molecule aggregation enhanced immune responses, it may be possible to develop improved manufacturing and screening processes to avoid.

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The CBGRC Organizing Committee

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