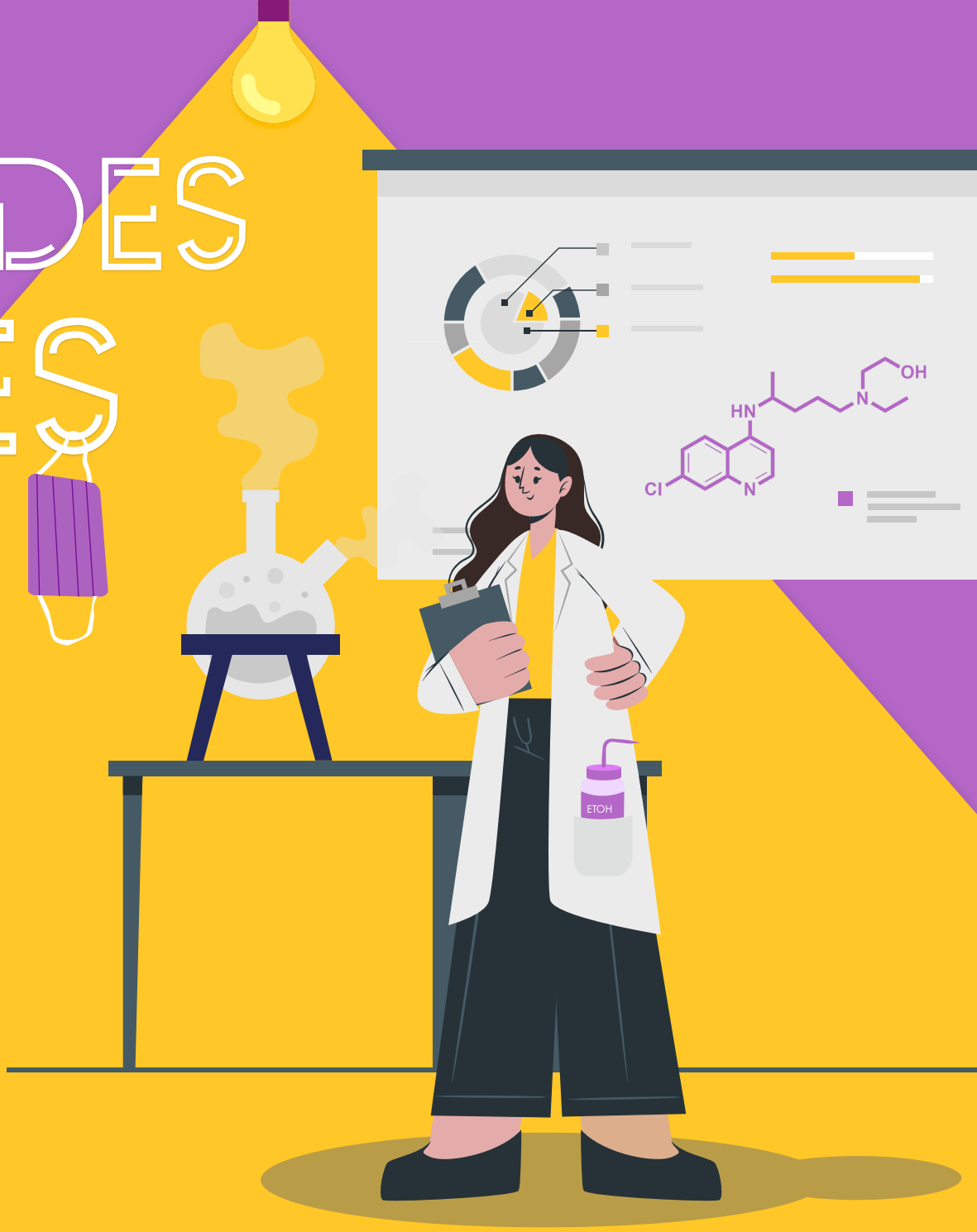
CONGRÈS DES CHIMISTES



Jeudi 10 septembre 2020

À partir de 9h - Salle Jean Jaurès
29 rue d'Ulm 75 005 Paris

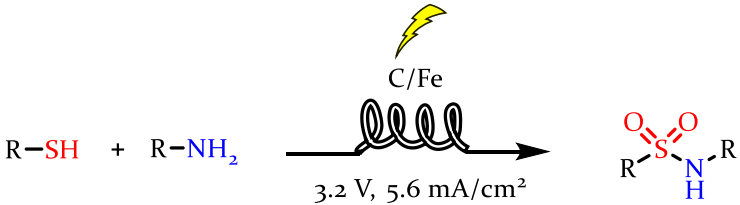
ENS Département de CHIMIE PSL

Design : La récréation d'Alya

9h30-9h50

BASICS IN ELECTROLYSIS APPLIED TO ORGANIC SYNTHESIS

Aude Salamé
University of Göttingen



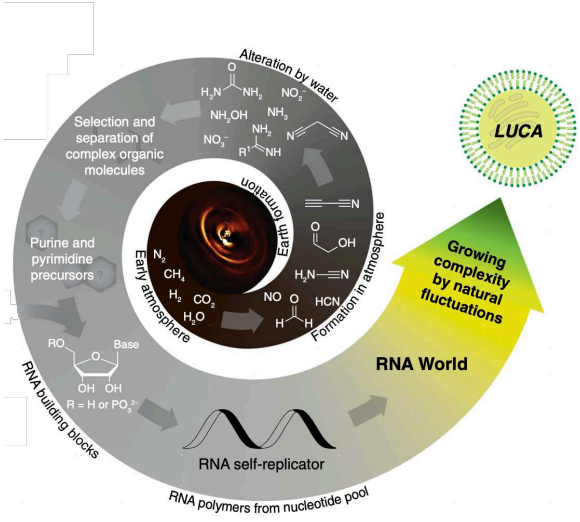
Optimal conditions for the synthesis of sulfonamides through the electrochemical oxidative coupling of amines and thiols

Electrosynthesis has known a great development these past decades and is now a very useful method in organic synthesis. The most powerful advantage of electrochemical reactions is the avoidance of chemical wastes and oxidising/reducing agents as well as the discovery of new and greener synthetic pathways. However, electrolysis is a very complex method and a broad range of parameters must be considered to optimize the reactional conditions and to ensure a high selectivity. In this presentation, we will take as example a recent article from literature to illustrate different aspects of electrosynthesis and try to understand its complexity.

9h50-10h10

Prebiotic pathways for the synthesis of canonical & non-canonical RNA nucleosides

Clara TESTARD
Ludwig-Maximilian Universität
Munich



Possible emergence of nucleosides on the early Earth
Becker *et al. Nat Commun* **9,** 5174 (2018)

Regarding the question of the emergence of life on Earth, several models have been proposed and developed over the years by the scientific community. For chemists, the challenge is to find plausible pathways explaining how the crucial molecules of life could have formed, in early Earth environments. The RNA World hypothesis is a model stating that life could have originated from RNA molecules supporting both functions of information storage and catalysis. Such a system would require the presence of all RNA components in the same reservoir. Several prebiotically plausible syntheses of purine and pyrimidine ribonucleotides have already been proposed. Fewer studies address the question of nucleobase modifications, although there is a growing belief that non-canonical nucleosides could be molecular fossils of a pre-RNA species.

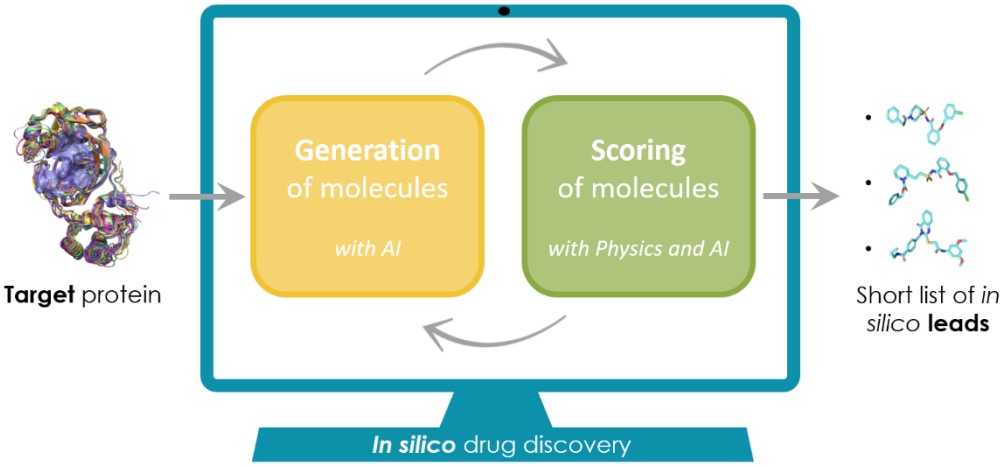
10h10-10h30

Towards synthesizability scoring for *de novo* drug discovery via generative models

Aubin RAMON

Aqemia

Paris, France



The general pipeline to generate *in silico* leads from a target protein via a scoring optimization.

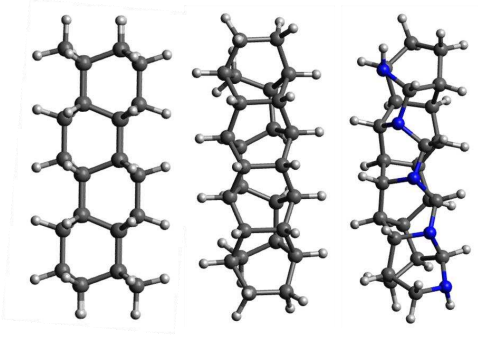
The emergency as known during the COVID-19 pandemic perfectly brings to light the lengthy delays to develop new drugs. It can last more than 10 years and cost 2.6 billion dollars to lead to a marketed drug. But advancements in computer-aided drug design techniques are made to speed up drug discovery. Molecular simulations are widely used to test the affinity of a molecule to a therapeutic target. And more recently, the rise of machine learning allows computers to learn how to generate potential drugs. However, designing in silico molecules is prone to unlearn their chemical reality: even if the generated molecules have great theoretical chances to inhibit a protein, they inevitably need to be synthesizable to be tested in vivo and to get a chance to become a drug. This presentation will describe a new way to predict the synthesizability of *in silico* compounds to guide generative models for *de novo* drug discovery.

11h-11h20

Theoretical study of hole mobility in carbon nanothreads,

where we show that charge transport properties of saturated molecules can have less holes than a Swiss cheese

Dune ANDRÉ
Laboratory for Computational Molecular Design,
École polytechnique fédérale de Lausanne



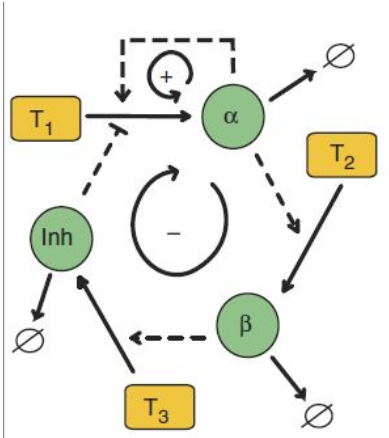
Three studied carbon nanothreads

Organic molecules can be used to design innovative electronic devices. Molecular structures are varied, from single molecule components to molecular materials, all constituting the field of Molecular Electronics. For electronic applications, good charge transport properties are required and can be evaluated with theoretical work. π-conjugated molecules have shown high theoretical and physical performances. Recently, computational studies found high conductivity results for saturated molecules in the case of single molecule junctions (SMJ). Besides, common behaviors were noticed between SMJ and molecular materials. These two results brought me to consider hole transport properties of saturated molecular materials, particularly in carbon nanothreads. Several hydrocarbonated wires were studied and designed to improve hole transport and reach promising hole mobility results.

11h20-11h40

About the Design of DNA-based Chemical Reaction Networks *in vitro*

Louis Bunel
Condé sur Noireau

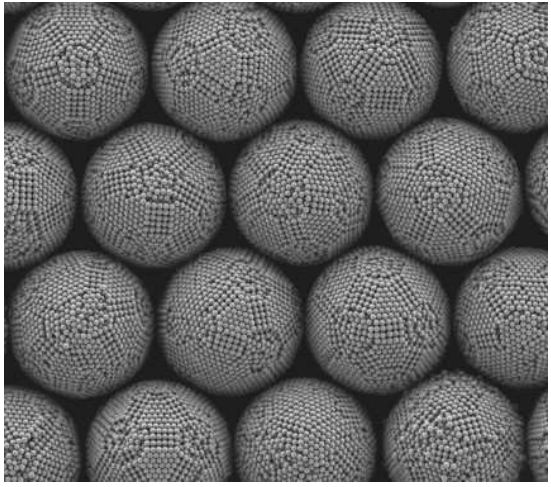


Topology of the Oligator a Chemical Reaction Network producing oscillations using only six DNA strands and three enzymes.

Reproducing living-like molecular behaviour with a bottom-up approach has been a chemists' dream since Belousov discovered his famous reaction forming temporal and spatial chemical oscillations. In the last decade, DNA has proved to be an efficent material for the design of chemical reaction networks in order to obtain complex behaviours like oscillations, formation of patterns or to be used as an interface with the living. In this talk we propose an overview on this topics from the systems using enzymes able to interact with living organisms to the enzyme-free systems able to perform computation like molecular computers.

11h40-12h

Magic numbers and superparticles



Crystallized superparticles

From Wang, J.*et al* Magic Number Colloidal Clusters as Minimum Free Energy Structures. *Nat. Commun.* **2018**, *9* (1), 5259. https://doi.org/10.1038/s41467-018-07600-4

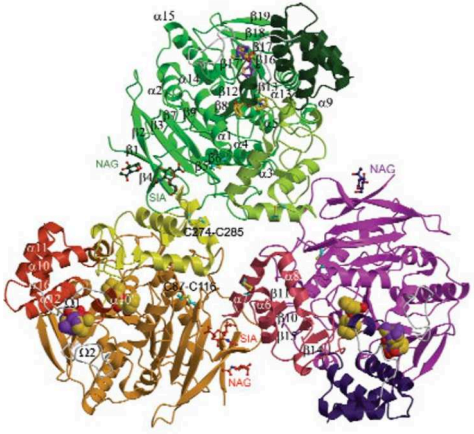
Théophile Gaichies
Friedriech-Alexander Universität Erlangen

Superparticles can be formed when a drop of a solution containing colloids is let to dry in a solvent. Some superparticles are more stable than others. The numbers of particles inside these objects are called magic numbers. These magic numbers also exist in very different systems. I will present some of these systems, containing nucleons, molecules or even millimeter-sized magnetic disks !

14h-14h20

Prodrugs activation by human esterases

Manon Fleszar, Ecole Fédérale Polytechnique de Lausanne

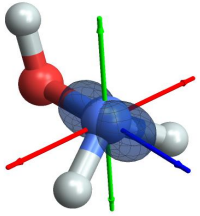


Overall Structure of Carboxylesterase 1
Bencharit and al, *Nat. Struct. Mol. Biol.* **10**, 349–356 (2003)

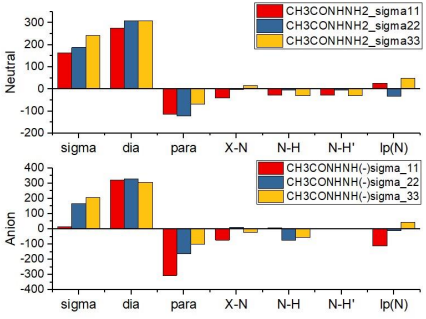
Prodrugs are pharmaceutically inactive compounds that are bioconverted *in vivo* into their active form. Understanding the processes of prodrug metabolism is essential to the design of effective new therapeutic agents. Esterases are one of the most important group of enzyme involved in the activation of prodrugs. In this presentation, based on a literature review, we will analyse their activity in the human body in terms of biology and biochemistry, to examine their substrate specificities, as well as other factors that may influence prodrug bioconversion. Some substrates proved to be highly selective to a type of esterase, which could be helpful in the process of prodrug design with enhanced specificity and pharmaceutical properties. Further studies about esterases and further clarification about classification, should be conducted in order to allow better understanding of drug metabolism.

14h20-14h40

Chemical Shift Tensor Analysis: A Tool to Understand the Alpha Effect



Alban SIMONNOT
ETH Zürich



Projection of Chemical Shift Tensor on hydroxylamine (up) and Natural Localized Molecular Orbitals contributions for two compounds

The alpha effect is an enhancement of the nucleophilic properties of some compounds containing adjacent atoms with lone pairs. The simplest compounds of this kind are hydrazine (H_2NNH_2) and hydrogen peroxide (HOOH). First reported in 1948, in a study of the mechanism of the alkaline cleavage of some pyridinium salts, this effect was never completely understood from a theoretical perspective. The effect has been ascribed to various features, most prominently ground-state destabilization, transition-state stabilization, solvent effects, and product stability.

Solid-state NMR spectroscopy and computational methods, such as DFT, can give access to the chemical shift tensor (CST) of nuclei. The CST contains considerable information on the electronic environment of nuclei and can hence be a sensitive probe of their reactivity.

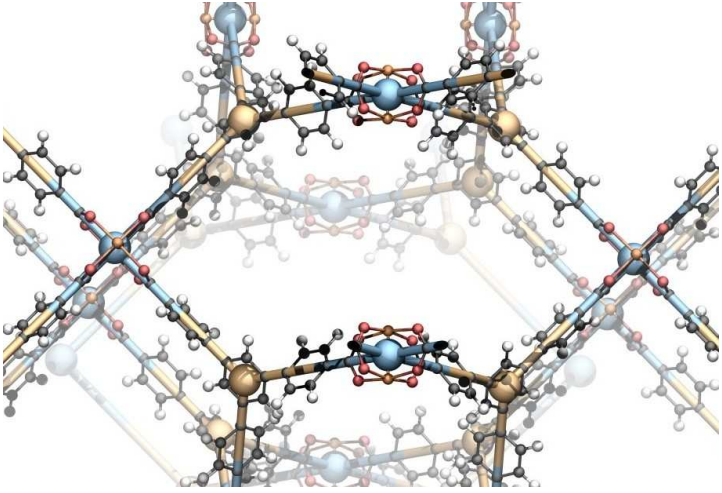
In this brief presentation, we will discuss the alpha effect from an NMR point of view, by analyzing the electronic structure of compounds that exhibit this effect.

14h40-15h

Automatic identification of crystal topologies

Lionel ZOUBRITZKY

Chimie ParisTech



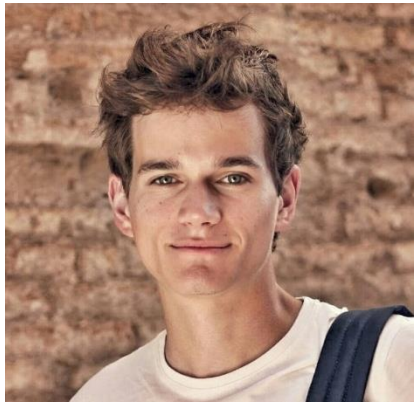
MOF-14 atomic structure superposed with its underlying topological net

Crystalline materials can be classified according to their topological structure, called a net. Although the net lacks information on the position and the nature of the different atoms, it is known to impact the physical properties of the crystals. However, determining the underlying net of a crystal and describing it in a concise representation is difficult.

This presentation will illustrate the concept of a net and detail how the existing Systre algorithm solves the problem of identifying the net underlying a crystal. Some improvements of the algorithm will be discussed as well.

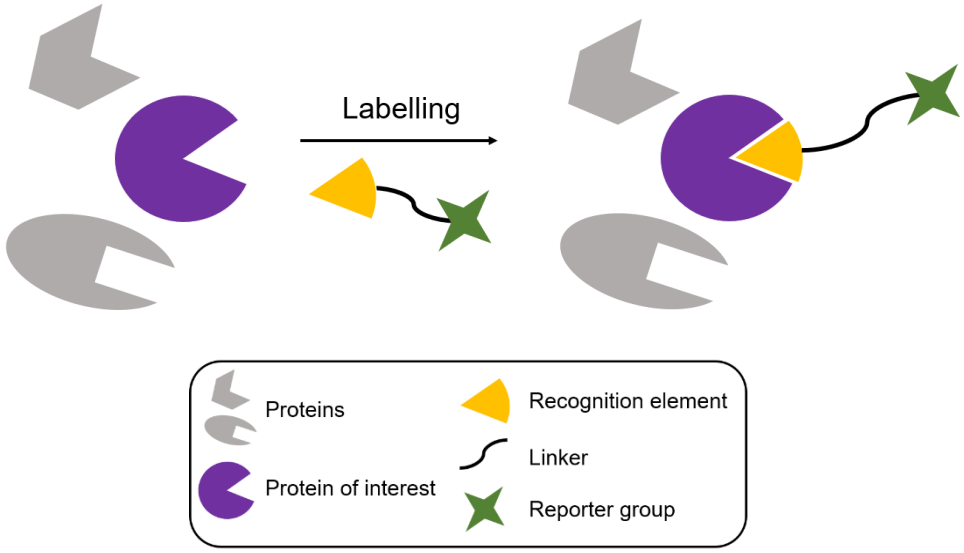
15h30-15h50

In vivo activity-based protein profiling (ABPP): some challenges to design adequate fluorogenic



Aubin RAMON

Withers group, University of British Columbia, Vancouver, BC, Canada



A typical experiment using an ABPP.
A proteome from a cell lysate or live cells is treated with the activity-based probe.

Genomics provides a lot of knowledge on evolution, physiology, and medicine, but still a lot of biochemical processes that rule organisms are regulated by post-translational modifications and epigenetic factors. One major way to by-pass the indirect genetic information is to directly see the activity and mechanism of the living processes. “Seeing is believing” becomes the guideline of activity-based protein profiling (ABPP) which is based on fluorescent probes to enlighten the in vivo activity of proteins in biological systems. Yet, the design of ABPP probes has to face a lot of constrains such as biological viability, sensitivity, or selectivity. This presentation will report the advancements made to tackle the aroused challenges through notably click-chemistry and quinone methide chemistry.

15h50-16h10

A brief overview of stainless steel science

Charles FAYOLLE

Max-Planck-Institut
für Eisenforschung
Düsseldorf

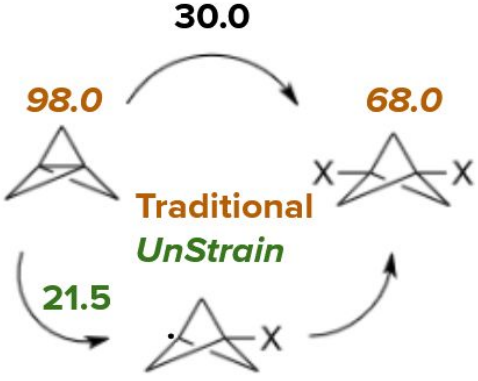
Microstructure of a duplex stainless steel grade observed by metallography
Outokumpu Stainless Steel Handbook, p.12

Stainless steel is a particular type of steel which contains a significant amount of chromium. This particularity permits the existence of a regenerative chromium oxide layer on the metal surface which protects against corrosion. The corrosion resistance property, even in rough environments, accounts for the wide use of stainless steel today, for instance in household appliance, in oil extraction, in chemical and food industry… There are hundreds of different stainless steels which have various corrosion properties, diverse mechanical behaviors and also different costs. To adapt the material to the application, a specific chemical composition, but also a particular microstructure are needed. This last one is controlled by the manufacturing process. To design a new grade, it is therefore necessary to understand the role of the microstructure in the macroscopical behavior, but also the influence of the making process on the microstructure.

16h10-16h30

A new procedure for the calculation of reactivity-correlated strain energies: *unStrain*

Miguel DE LA PUENTE
University of Oxford



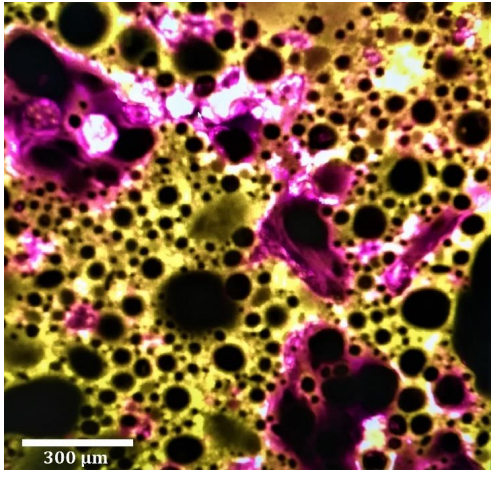
*Strain energies obtained with **unStrain** and a traditional method for [1.1.1]propellane in kcal/mol*

Strain refers to the energy change introduced in a molecule by geometrical deviations from a given state and is often an indicator of the stability and reactivity of molecules. However, if traditional values of strain are good global stability indicators, they have a limited use for predicting reactivities. Thus, a self-consistent computational methodology for the evaluation of the strain released when forming reactive intermediates, ***unStrain***, was developed by the group. We identified an efficient and accurate computational DFT-methodology to be used in the procedure and tested its robustness and its potential for deriving the strain-relief reactivity of small organic molecules. ***UnStrain*** has proven to be a promising technique for predicting strain correlated reactivities under thermodynamic control

17h-17h20

Mixing well controlled oil-based foams and aqueous foams

Antoine BREZAULT
University of Edinburgh

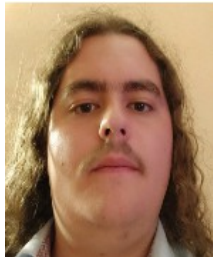


Mixed water-based (pink) and oil-based (yellow) foams observed with confocal microscopy

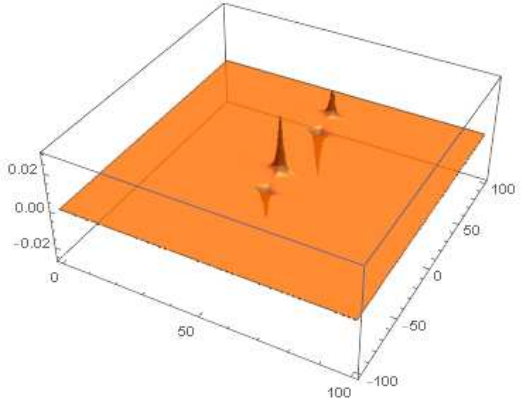
Scientists have already succeeded into making long-lived water-based foams and oil-based foams stabilised by particles. The later fix at the liquid-air interface and reduce the shared area between the two fluids. Nevertheless, these two types of foams have never been mixed. Here we first make long-lived aqueous foams and long-lived oil-based foams separately. We use particles as stabilising agents. We obtain a good control on the volume of foam, the size of the air bubbles, and the proportion of residual liquid. To do this, we vary the shaking time, the particle concentration and the initial volume of liquid and we explain their effect on the foams' properties. Then, we mix the aqueous and the oil-based foams. To study the effect of the mixing on both foams we use well-chosen dyes to separately label the oil-based foam and the aqueous foam for fluorescence confocal microscopy. This is the first step in understanding the complex mechanisms involved in the cooking of buttercreams for instance.

17h20-17h40

Simulating NMR experiments: basic theory and exemples



Léonardo Rico
University of Southampton



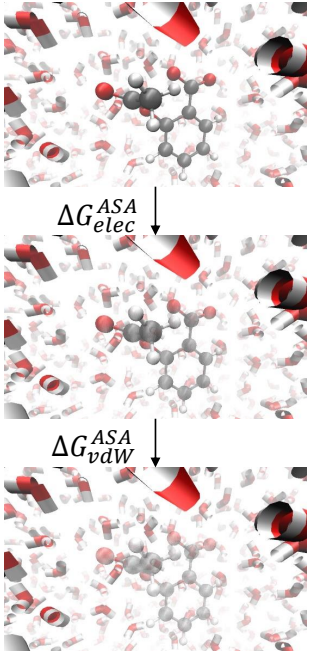
A simulated 2D spectrum resulting of simulating an INADEQUATE experiement on a two ½ spins system

Nuclear Magnetic Resonance (NMR) is a spectroscopic technique widely used in organic chemistry because of its wide range of uses, and its precision. However, the different protocols actually used were well refined over time, mainly using experiment as the base of its betterment. In order to make this time-consuming task easier, and less consuming of spectrometer time, simulating the developing protocol with a precise enough theory can be of use. Therefore, codes allowing such simulations must be created, with different conditions in mind, such as machine-time consumption, user-friendly functions, etc... In this presentation, we will discuss the basics of NMR theory, in order to understand the SpinDynamica code developed at the University of Southampton

17h40-18h

Modern alchemy: correcting finite-size artifacts in binding free energy calculations of charged ligands

Juliette FENOGLI
University of Edinburgh



Scheme of alchemically transforming aspirin to a dummy molecule

A reliable computational prediction of binding affinities of ligands to proteins remains a major objective of drug design that would decrease the number of molecules synthesized to identify a compound for clinical developpement. Alchemical free energy calculations estimate free energies of binding from molecular dynamics simulation trajectories. The approach consists in progressively transforming atoms of the simulated compounds to another atom type, just like medieval alchemy intended to ! Here, a fully interacting ligand is alchemically perturbed into a dummy molecule exempt of any interaction. This is possible thanks to the use of state functions and thermodynamic cycles. In realistic biological systems, the electrostatic interactions between ligands, proteins and solvent act in a macroscopic environment. But due to limited computational power, simulations are often performed neglecting these interactions beyond a certain distance. This introduces a systematic finite-size error particularly when simulating a charged ligand. We focus here on a recent methodology that evaluates the correction terms to apply to the charging free energies in a post-simulation step.