For Women in Science

FONDATION L'ORÉAL

FOR WOMEN IN SCIENCE

in partnership with

INSTITUT DE FRANCE
Académie des sciences

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MUSÉUM NATIONAL D'HISTOIRE NATURELLE

2020

L'ORÉAL - UNESCO

For Women in Science

French Young Talents

L'ORÉAL UNESCO

YOUNG TALENTS 2020
FRANCE

RESEARCH PROJECTS

SUMMARY

THE FUTURE OF SCIENCE

Created in 2007, the L'Oréal-UNESCO *For Women in Science* French Young Talents program aims to promote and support the involvement of young women in scientific research.
For this 14th edition, 686 candidates were evaluated by a committee of 87 experts representing the major research institutions in France and covering a wide variety of disciplines. Following this first phase of evaluation, 109 applications were submitted to a jury composed of leading researchers from the French Academy of sciences.
This Jury, composed of 20 members and chaired by Professor Laure Saint-Raymond, a mathematician and professor at the Ecole Normale Supérieure de Lyon, selected 23 doctoral and 12 post-doctoral students to encourage them to pursue a brilliant scientific career.

In the next following pages, you will discover the outstanding work of these 35 Young Talents 2020, who have joined the community of the 265 researchers rewarded by the French program since its creation.

MEDICINE

Group 1

MEDICINE

Dr Marianne Burbage

IMMUNOLOGY

Improving immune responses against cancer

Institut Curie

Paris, France

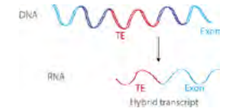
ROLE OF THE DARK GENOME IN MEDIATING IMMUNE RECOGNITION OF TUMOUR CELLS

INTRODUCTION

Efficient immune responses against cancer are hindered by multiple immunosuppressive mechanisms used by tumour cells[1]. The recent advent of immunotherapy provides means to partially restore immune control of tumours[2].

However, these approaches need to be further improved, as they are only effective in a fraction of patients. A major hurdle is the identification of targets expressed selectively by tumour cells[3].

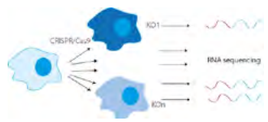
To be detected by the immune system, tumour cells need to present specific peptides on major histocompatibility molecules (MHC). We recently found that part of the dark genome (transposable elements) could be presented by tumour cells and induce an immune response.



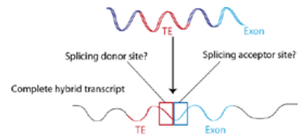
More precisely, we identified hybrid transcripts, with part coming from transposable elements and part from an exon. This project aims at better understanding the biology of these hybrid sequences.

MATERIALS AND METHODS

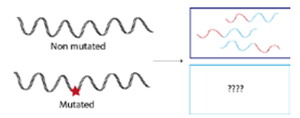
My first aim is to explore the epigenetic mechanisms controlling expression of the hybrid sequences. I will inactivate a panel of epigenetic regulators in tumour cells, and analyse hybrid expression by RNA sequencing.



My second objective is to investigate the role of the splicing machinery in hybrid generation. I will reconstitute the complete hybrid transcripts. Then, I will look for motifs (small nucleotide sequence) involved in splicing.

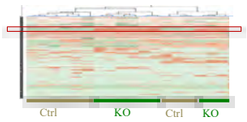


To validate these results, I will use the rich cancer patient database from The Cancer Genome Atlas (TCGA). In particular, I will test whether mutations in epigenetic regulators or splicing factors are associated to alterations in hybrid expression.



EXPECTED RESULTS

With Ares Rocanin-Arjo, we will use bioinformatics tools (like hierarchical clustering) to identify the pathways controlling hybrid expression (example below of KO-specific hybrids).



Such approaches will unravel:

- The contribution of the splicing machinery to hybrid generation and partial expression of the dark genome.
- The epigenetic regulatory network controlling hybrid expression.

I will then be able to select key regulators in this network, and characterise their contribution to the immune landscape of tumour cells.

Hence, this project will identify candidates that could be targeted to boost immune responses against cancer.

CONCLUSION

Immunotherapy has brought about a small revolution in cancer treatment. However, protocols need to be improved to further increase patient survival.

This project will provide a precise characterisation of how elements of the dark genome become expressed in a tumour context.

The results obtained here will be instrumental in instructing the design of combination strategies for improving immunotherapeutic protocols.

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Ms Astrid Chevance

PSYCHIATRY

On the trail of Renaissance humanists

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NEW METHODS FOR THE DEVELOPMENT OF CORE OUTCOME SET : THE EXAMPLE OF DEPRESSION

INTRODUCTION

Clinical trials are experimental studies which aim at evaluating the benefits and harms of treatments.

Outcomes are variables monitored during a trial to document the impact of a treatment.

Meta-analyses compare and combine the results of trials to hierarchize the different available treatments. They require the standardization of outcomes across trials of a given disease.

Core outcome sets (COSs) are agreed-on standardized sets of outcomes that should be minimally measured in all trials of a given disease.

Involving all relevant stakeholders (e,g,patients, clinicians, careers) in COSs development will help increase the selection of relevant and important outcomes, thus enhancing research value.

We propose new methods for the development of COS taking the example of depression.

The several layers of a Core Outcome Set

MATERIALS AND METHODS

Step 1: Identifying outcome domains
- International online survey of patients with depression, clinicians, carers
- Methodological review of outcomes of trials

Step 2: Selecting the outcome domains to be included in the COS
- International online survey to elicit the preferences of all stakeholders
- Final meeting involving all relevant stakeholders

First step:
Survey of 4 open-ended questions
- Available in French, English and German
- Qualitative content analysis
- Assessment of data saturation using a mathematical model

Methodological review of outcomes
- Depression trials of clinicaltrials.gov
- Extraction of domains and OMI
- Experts and patients will compare the domains of the review with the domains of the survey.

Second step:
Survey involving a ranking task of the domains identified in step 1
- Adaptation of the Q-method for online and large sample
- Recruitement of patients with depression, clinicians, carers, researchers, regulatory authorities
- Data analysis using a logit model for sets of ranked items

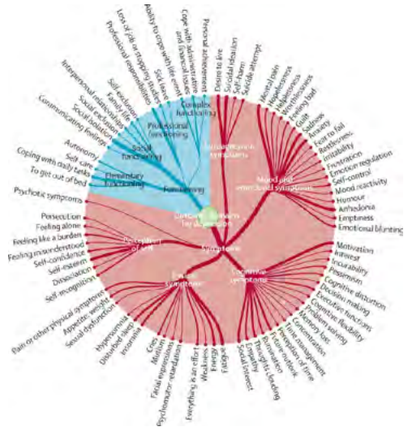
Final meeting using mediation to determine the 7 mandatory outcomes and the further layers of

RESULTS

First step: available results of the survey
1912 patients, 464 carers, 627 clinicians from 52 countries
8183 free-text answers
80 domains related to
- symptoms (64 domains) such as mental pain (523 [17%] of 3003 participants)
- functioning (16 domains) such as social isolation (541 [18%])

57 other outcome domains regarding safety of treatment, health care organisation, and social representation, such as stigmatisation (408 [14%]).

First step: expected results of the review
Poor match of outcomes measured in trials and outcomes that matter to patients, carers and clinicians.



Second step: expected results
Ranking of the domains by importance for each category of stakeholders.
Comparison of the rankings
COS for depression

Perspective:
Step 3: selection of the corresponding outcome measurement instruments

CONCLUSION

Involving all relevant stakeholders in the development of COS 1) proved feasible, 2) allows for more generalizable and credible COS, 3) ground outcomes in stakeholders' needs, enhancing clinical research value.

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Chevance A, Ravaud P, Tomlinson A, et al. Identifying outcomes for depression that matter to patients, informal caregivers, and health-care professionals: qualitative content analysis of a large international online survey. Lancet Psychiatry 2020; 7: 692–702.

Ms Elodie Hinnekens

SPORT & FITNESS SCIENCES

Making babies walk and fighting disabilities

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FONDATION ELLEN POIDATZ

Université Paris-Saclay
Fondation Ellen Poidatz

Orsay / St-Fargeau-Ponthierry, France

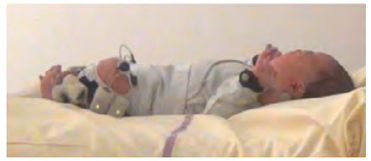
CHARACTERIZING THE CONTROL OF MOVEMENTS IN ATYPICAL DEVELOPMENT

INTRODUCTION

Babies are able to produce rhythmic behaviors involving their lower-limbs as soon as birth: stepping (step-like cycles when held upright) and kicking (spontaneous flexion and extension cycles when lying in a supine position)

Both behaviors are believed to be walking precursors as they help to build muscular synergies [1]

Stepping training can lead to an earlier walking onset in infants with atypical development, therefore the community suggests to also use kicking training in early therapy [2]



However the nervous command of kicking was never characterized and we do not know if rehabilitation should aim at enhancing the quantity of kicking movements only or should also imply qualitative modifications

MATERIALS AND METHODS

Material: electromyographic (EMG) surface electrodes and video cameras

- Small surface electrodes will be used to record the EMG signal of leg muscles during kicking practice
- Motion will we recorded thanks to 2D video cameras

Subjects: 3-to-6-month-old infants with typical development (TD) and atypical development (AD)

First objective: to characterize the command of AD infants

- The command of rhythmic behaviors can be studied with non-negative matrix factorization (NNMF) of EMG signals which allows to identify muscular synergies [3]
- Muscular synergies used by TD and AD infants will be compared to see if both behaviors are qualitatively different

Long-term objective: to build an early rehabilitation protocol based on kicking

- To design a mobile that works as a feedback (it moves and makes sounds when the infant kicks)
- This mobile will be controlled by an algorithm processing video recordings in real-time
- The command of the mobile will depend on the results of this study

RESULTS

Different hypothesis:

(1) Muscular synergies could be equivalent between groups →

(2) Muscular synergies could be different between groups →

(3) Muscular synergies could be less variable in infants with AD as suggested by kinematic studies [4] →

Effect on the long-term objective:

(1) The mobile will be commanded to enhance the quantity of movements

(2) It will be commanded to enhance the quantity of typical movements

(3) It will be commanded to enhance variability and motor exploration

CONCLUSION

This study will help building an early rehabilitation program for infants with atypical development

Early rehabilitation is highly recommended since cerebral plasticity is more important during the first year of life

Those data could also help with early diagnosis which is a major challenge to reduce disabilities

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For Women in Science
FONDATION L'ORÉAL

Ms Solène Marie

PHARMACOLOGY

From Marie Curie to radiopharmacy

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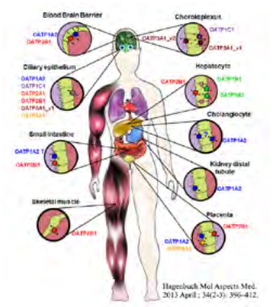
IMAGING DRUG DISTRIBUTION AND DRUG-DRUG INTERACTIONS IN HUMANS

INTRODUCTION

Glyburide (GLB) is an antidiabetic drug acting on pancreas by blocking the sulfonylurea type 1 receptors (SUR-1), thus stimulating insulin release. GLB is also investigated as a neuroprotective agent thanks to SUR-1 blockade in the brain tissue.

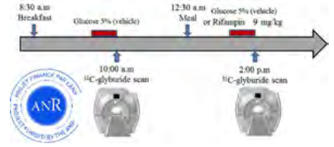
However, the brain and body distribution of GLB is unclear and may involve carrier-mediated processes, particularly Organic Anion-Transporting Polypeptide (OATP) transporters [1]. Many other drugs are transported by OATPs *in vitro*.



OATP transporters are highly expressed in the liver where they mediate hepatobiliary elimination of GLB. OATPs are also identified at many other tissue-interfaces where they could be involved in drug-drug interactions (DDI).
Innovative protocols are needed to address the impact of OATP function on pharmacokinetics and drug distribution to tissues in humans.
Our aim was first to label GLB with carbon-11 to study its distribution with positron emission tomography (PET) imaging. Then we developed OATP-inhibition protocols to assess their impact on GLB distribution in humans.

MATERIALS AND METHODS

A clinical trial was performed in healthy volunteers.



- Four young men underwent a [^{11}C]GLB PET scan to study the drug distribution.
- Three of them underwent a second [^{11}C]GLB PET scan after a premedication with the potent OATP inhibitor rifampicin (RIF, 9 mg/kg intravenously, IV).

RIF was previously validated as transporter-inhibitor in a preclinical study [2].

Pharmaceutical-grade [^{11}C]GLB was locally produced, purified and controlled to be injected to healthy volunteers.
Whole-body dynamic (4D) acquisitions were performed for 30 minutes after [^{11}C]GLB injection with a PET/MR camera (Signa®, GE Healthcare).
Images were reconstructed to quantify [^{11}C]GLB distribution to tissues before and after RIF.

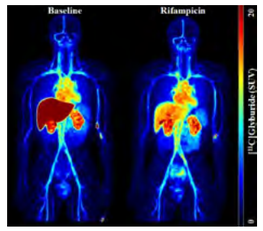
EXPECTED RESULTS

[^{11}C]GLB was predominantly distributed to the liver where OATP expression is important.

Negligible brain distribution was observed in healthy subjects [3]. This suggests that GLB only enters in damaged brain.

Inhibition with RIF dramatically decreased the liver distribution of [^{11}C]GLB.

This confirms the importance of OATP transport at this interface and their potential of DDI in hepatobiliary elimination.
A compensation was observed with an increase of [^{11}C]GLB in the urinary bladder in presence of RIF.
Inhibition of OATP significantly increased circulating [^{11}C]GLB in blood, thus enhancing exposure to tissues.



CONCLUSION

This first-in-man imaging protocol reveals the distribution of [^{11}C]GLB in the body, showing negligible brain uptake and predominant uptake in the liver.

The use if RIF revealed the importance of OATP transporters in controlling drug distribution to tissues, such as the liver. It also highlights the role of these transporters in mediating DDI between OATP substrates and inhibitors.

This whole-body 4D PET imaging approach gives new insights on mechanisms mediating drug distribution and DDI at the tissue level in humans.

REFERENCES

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[2] Marie and al. Validation of Pharmacological Protocols for Targeted Inhibition of Canalicular MRP2 Activity in Hepatocytes Using [99mTc]mebrofenin Imaging in Rats. Pharmaceutics. 27;12(6):486 (2020).
[3] Marie and al. 11C-glyburide PET imaging unveils the negligible brain penetration of glyburide in humans. Neurology. 23;92(17):813-814 (2019).

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Ms Johanna Mondesir

HEMATOLOGY

Mending the living

Dana-Farber Cancer Institute · HARVARD MEDICAL SCHOOL · institut cochin · Université de Paris

Harvard Medical School
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Boston, USA / Paris, France

MECHANISMS LINKING CELL DEATH AND IMMUNE STIMULATION UPON AMPK ACTIVATION IN ACUTE MYELOID LEUKEMIA

INTRODUCTION

Acute Myeloid Leukemia (AML) is an aggressive blood cancer caused by the deregulated proliferation of immature myeloid cells (Fig1A).

Current treatments are based on chemotherapy and hematopoietic stem cell transplantation (HSCT) with a cure rate of less than 25% due to relapse/refractory disease.
AML is sensitive to the antineoplastic effects of the immune system as attested by the activity of HSCT.

However, results of immunotherapies currently evaluated in cancer such as immune checkpoint blockade are disappointing in AML. Preliminary data suggest that activation of AMPK (AMP activated protein kinase, Fig1B), a key regulator of cellular energy balance, may trigger immunogenic cell death (ICD) as illustrated in

Fig1A. *1B.*

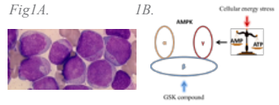


Fig2.

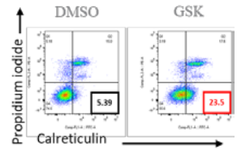


Fig2 by the surface exposure of Calreticulin, the main mediator of ICD, Fig2)[1].Our goal in this project is to assess the ability of AMPK activators cells to potentiate the anti-leukemic activity of immunotherapy in preclinical models of AML.

MATERIALS AND METHODS

To test our hypothesis *in vivo* we will work with two murine models of AML (the murine C1498 AML cell line or murine myeloid progenitors transduced with the human oncogene *MLL-AF9*) in immunocompetent hosts (C57BL/6 mice). In a first set of experiments called 'vaccination assays'

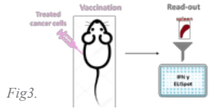


Fig3.

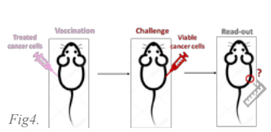
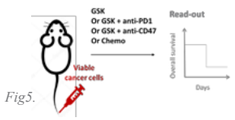


Fig4.

we will inject subcutaneously AML cells prior treated *in vitro* by AMPK activators, then evaluate the immunologic response by measuring Interferon gamma (IFNγ) production by mice splenocytes (IFNγ ELISposts) or by measuring the ability of the hosts to prevent tumor growth when challenged with viable AML cells in the contralateral flank (Fig4). In a second set of experiments we will address the translational impact of our findings by evaluating the therapeutic efficacy of AMPK activator alone or in combination with immune therapies compared to standard chemotherapy[2].

Fig5.

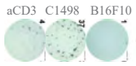


EXPECTED RESULTS

In a first vaccination assay we found that the injection of C1498 cells pretreated *in vitro* by an AMPK activator (GSK621) had a vaccination effect in mice as shown by a delayed tumor growth after rechallenge with live tumor cells.

This effect was associated with an immune response measured by IFNγ ELISpot from cellular suspension isolated from the mice spleens (Fig6).

Fig 6.



IFNγ ELISspot from a mouse vaccinated with GSK treated AML cells. Each spot is an IFNg producing splenocyte after exposure ex vivo to aCD3: positive control, B16F10: melanoma cell line (negative control), C1498: AML cells.

To demonstrate the specificity of ICD induction upon AMPK activation, we will repeat this vaccination assay with cells knocked out for Calreticulin, the main mediator of ICD *in vivo*.

To evaluate the therapeutic gain of this novel strategy we expect to measure a survival benefit in AML-bearing animals treated with AMPK activators in combination with innate or adaptative immune check point inhibitors (anti-CD47 and anti-PD1 respectively) compared to single agents. Establishment of a specific immune response will be demonstrated by the ability of survivors to reject tumor cells in a subsequent challenge.

CONCLUSION

Our project is exploring an innovative approach to enhancing therapeutic anti-tumor immunity. By combining our expertise on signaling pathways, metabolism, and immunology, our strategy could prevent relapses and increase survival of patients with AML. Beyond AML, activation of AMPK could sensitize additional solid and hematologic cancer to immunotherapies for therapeutic gain.

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Ms Nadine Serhan

IMMUNOLOGY

Towards a treatment for atopic dermatitis

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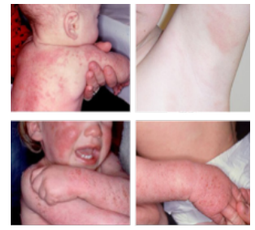
HOUSE DUST MITES ACTIVATE NOCICEPTOR-MAST CELL CLUSTERS TO DRIVE TYPE 2 SKIN INFLAMMATION

INTRODUCTION

Allergic skin diseases, such as atopic dermatitis (AD), are characterized by **severe itching** and **type 2 immunity-associated hypersensitivity** to widely-distributed allergens[1].

Mast cells are innate immune cells involved in allergic diseases[2], including AD, that specifically express **MRGPRB2**, a receptor from the Mas-related G protein-coupled family that binds cationic molecules such as the neuropeptide **Substance P** encoded by the gene *Tac1* and mainly produced in the skin by nociceptive sensory neurons, known as **nociceptors**[3,4].

Do neuro-immune interactions play a role in the development of allergic skin inflammation?



MATERIALS AND METHODS

A/ Mouse model of an AD-like skin allergic inflammation

***Tac1*$^{-/-}$**
Substance P-deficient

Resiniferatoxin-treated
TRPV1^{+} nociceptor-deficient

***Cpa3-cre*$^{+}$*; Mcl-1*$^{fl/fl}$**
Mast cell-deficient

***Mrgprb2*^{mut}**
Non-functional MRGPRB2

Repeated epicutaneous exposures to :

SEB
Exotoxin from *Staphylococcus aureus*

Dermatophagoides farinae *(Der. f)*

→ Study of the development of allergic skin inflammation

B/ *In vivo* two-photon live microscopy of living mice

Intradermal injection of Avidin sulforhodamine → 1 week →  Intradermal injection of Vehicle or Stimuli → 15 min →  3D image acquision using a 2-photon microscope

Image processing and analysis of fluorescence
Collagen
Avidin sulforhodamine (mast cells)
Pirt-GCaMP3 (calcium tracer in neurons)

EXPECTED RESULTS

A/ TRPV1^{+} Tac1^{+} nociceptors and MRGPRB2^{+} mast cells are required for the development of AD-like pathology

Substance P-deficient, TRPV1^{+} nociceptor-deficient, mast cell-deficient and *Mrgprb2*^{mut} mice were all protected from the development of AD-like allergic skin inflammation.

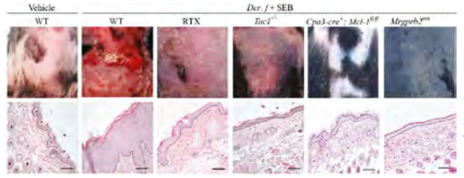


Figure 1*. Representative photos (upper panel) and H&E staining (lower panel) of vehicle- and Der. f + SEB-treated areas of WT, resiniferatoxin-treated, Tac1*$^{+}$*, Cpa3-cre*$^{+}$*; Mcl-1*$^{fl/fl}$*, Mrgprb-2*^{mut} *mice and controls.*

B/ House dust mites induce calcium flux in neurons and subsequent mast cell degranulation in vivo

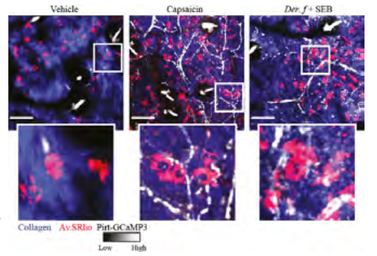


Figure 2*. Representative high-resolution 3-D images of the dermis; merged fluorescence of Av.SRho (red), GCaMP3 calcium tracer (pseudocolor intensity scale) and collagen structures (blue). White lines identify magnified areas shown in lower images. Bars = 100 µm. *Capsaicin is a strong TRPV1 agonist.*

CONCLUSION

Here we found that: **(1)** House dust mites directly activated peptidergic **nociceptors** to **(2)** produce **substance P. (3)** Activation of **MRGPRB2 on mast cells** induces **(4)** mast cell degranulation **(5)** driving the development of **allergic skin inflammation**.

Activation of **TRPV1^{+}-*Tac1*$^{+}$ nociceptor–MRGPRB2+ mast cell sensory clusters** represents a key early event in the development of allergic skin reactions and can thus be identified as a new therapeutic target to treat atopic dermatitis.

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Dr Ralitsa Todorova

NEUROSCIENCES

Understanding how memories are born

Collège de France

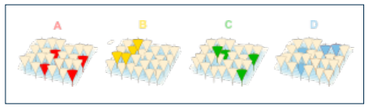
Paris, France

REACTIVATION AND REORGANISATION: THE DANCE OF THE SLEEPING CEREBRAL CORTEX

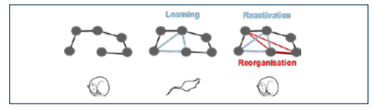
INTRODUCTION

In sleep, the cerebral cortex communicates with the hippocampus in order to integrate new memories and stabilise them[1] – but how?
One of the main mechanisms of cortical computation is the formation of cell assemblies, groups of neurons that are active together to encode emergent information[2].
We know that cell assemblies formed during learning get reactivated in sleep to consolidate the memory.

However, in studying long periods of sleep, I have discovered completely new assemblies, which were present neither in the learning task nor even before. This unexpected discovery suggests that two processes happen in parallel:

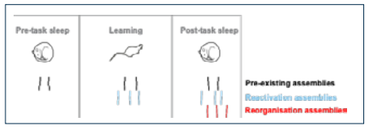


on the one hand, reactivation of assemblies formed in learning, in coordination with the hippocampus, and the reorganisation of cortical circuits to form new links between memories. The goal of my project is to test this hypothesis.

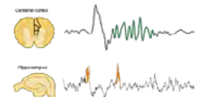


MATERIALS AND METHODS

I will analyse data recorded from rats in a model of post-traumatic stress disorder (PTSD). To detect the cell assemblies, I will use a method (SSA) I recently developed to detects groups of neurons active synchronously.

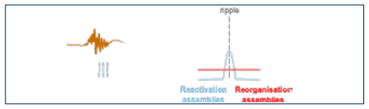


The detected assemblies will be divided into three groups: pre-existing assemblies already active in pre-task sleep; rreactivated assemblies formed during the task, and reorganisation assemblies formed for the first time in post-task sleep.
The activity of these groups of assemblies will be studied with respect to known sleep rhythms. Notably, their dynamics relative to hippocampal ripples, which are known to occur synchronously with reactivated assemblies.

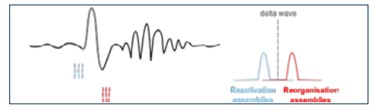


RESULTS

Our hypothesis states that reactivation and re-organisation would have different dynamics in relation to sleep rhythms.
In particular, we expect reactivated assemblies to closely follow hippocampal ripples and replay. The information encoded in the hippocampus would thus be communicated to the cortex. On the other hand, we expect reorganisation assemblies to either precede ripples or fire independently from ripples.



With regards to cortical delta waves, we predict reactivated assemblies activity to take place preferentially before cortical delta waves, where most reactivation takes place[3].



In contrast, we expect that reorganisation assemblies would form preferentially after the delta wave, where the network state is favourable to synaptic plasticity. Both of these effects will be compared to the dynamics of pre-existing assemblies.

CONCLUSION

This work will have important implications as it brings forth the view of memory consolidation in cortical networks as an interplay of two dynamic processes (reactivation and reorganisation) happening in parallel, orchestrated by the hippocampo-cortical dialogue of sleep rhythms.

How the dynamics are impacted in the different stages of the rat PTSD model may also lead to insights into PSTD mechanisms and thus inspire potential treatment strategies.

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Group 2

BIOLOGY

Dr Najate Ait-Ali

BIOCHEMISTRY & MOLECULAR BIOLOGY

Eyes wide open on innovation to prevent blindness

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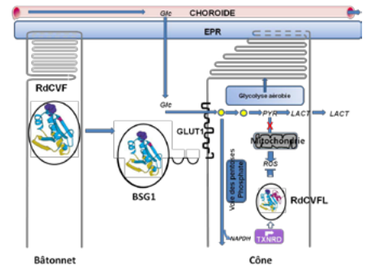
DOES A PEPTIDE INCLUDING BOTH THE RDCVF INTERACTION SITE AND THE CATALYTIC SITE HAVE A THERAPEUTIC POTENTIAL? COULD IT BE A NEXT GENERATION TREATMENT FOR RETINAL DISEASES?

INTRODUCTION

The bifunctional NXNL1 gene encodes for two proteins by an alternative splicing:
Rod-derived Cone Viability Factor (**RdCVF**), secreted by rod photoreceptors and protecting cone photoreceptors and the enzyme RdCVFL. The mechanism of action and the signalization of RdCVF and **RdCVFL** have been identified and integrated into a model system. RdCVF stimulates the renewal of cone outer segments and RdCVFL protects cones against oxidative damages[1,2].



A preclinical proof of concept based on a metabolic and redox treatment of retinitis pigmentosa (RP) is now ongoing. Preservation of visual acuity in the *rd10* mouse by subretinal injection of recombinant adeno-associated viral vector **AAV-RdCVF-RdCVFL**.

Scientific rational: RdCVF (109 amino-acids), the allotsteric activator of glucose transport into the cones is an intrinsically disordered protein (IDP). This indicates that only part of RdCVF sequence is required for its biological activity, so RdCVF would be a propeptide. RdCVF activity is mediated by its binding to its specific receptor, basignin-1 (BSG1), that presumably triggers an oxidation of extracellular cysteines of the glucose transporter GLUT1. The chemical oxidoreduction of the oxidized form of the catalytic site of RdCVF (CPQC) resulted to reduction of the cysteines of GLUT1. This finding opens novel therapeutic perspective.
In my project; I will develop a new preclinical form of RdCVF (**RdCVFp**) relying on peptide synthesis. In order to define the shortest active amino-acid sequence to produce, I will test the properties of a series of candidates RdCVFp. All of them will include the catalytic site $C_{44}PQC_{46}$ and the glutamic acid at position 64 of RdCVF that is required for the interaction with the immunoglobulin domain 0 (Ig0) of BSG1 with a length compatible with standard peptide synthesis. After chemical synthesis of these peptides, they will be tested *in vitro* for their capability to protect the cones. The active ones will then be tested *in vivo* for their therapeutic potential in the rd10 mouse model of the RP disease. The delivery of this synthetic peptide will bypass the use of an viral vector.

MATERIALS AND METHODS

1. Design of the RdCVFp collection by bioinformatic analysis.
2. Vectorization of the RdCVFp sequence in an alkaline fusion protein.
3. Test the interaction of the RdCVFp constructs with Ig0 by cell transfection.
4. Measurement of the affinity content of the positive RdCVFp peptide by isothermal titration calorimetry.z
5. Screening for the chemical synthesis of the collection of RdCVFp peptides.
6. Analysis of chemical properties of these RdCVFp peptides by biophysical methods (mass spectrometry, circular dichroism,…).
7. Biological activity of the synthetized RdCVFp using cone-enriched culture from the retina of chicken embryo1, then using cone cultures from human induced pluripotent stem cells.
3. Test of the active RdCVFp peptides of mouse models of RP using the reference model, the *rd10* mouse[3].
4. Increasing doses of the *in vitro* active RdCVFp will be subretinally injected and the benefit for cone vision will be monitored over time after RdCVFp administration by optokinetic head tracking (cone visual activity), cone electroretinography ,cone electrophysiological function and cone density (cone survival)[1].

EXPECTED RESULTS

A novel small molecular drug, **RdCVFp** for the treatment of all genetic forms of the inherited blinding disease, retinitis pigmentosa

CONCLUSION

The gene therapy approach currently under development relies on the delivery of RdCVF using a recombinant associated-adeno virus (AAV)[4] is promising therapy, however, given the aversion for viruses resulting from the current pandemic5, the development **RdCVFp**, a synthetic peptide, is justified.

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Ms Charlotte Canet-Jourdan

CELL BIOLOGY

When a rather atypical path leads to excellence in oncology research

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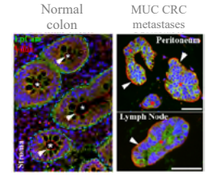
TUMOR SPHERES WITH INVERTED POLARITY, A NEW MODE OF COLORECTAL CANCER DISSEMINATION

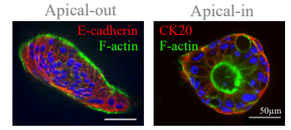
INTRODUCTION

With more than 2 million new cases and nine thousand deaths in 2018, colorectal cancer (CRC) is the 2nd cause of cancer-related death worldwide[1]. Our team demonstrated that in patients with a mucinous (MUC) CRC, metastases arose from tumor spheres displaying an inverted apicobasolateral (A/B) polarity. We called them TSIPs for Tumor spheres with inverted polarity[2].

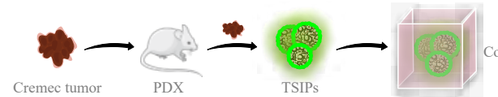
It was the first time that cohesive structures that i) preserved their epithelial features throughout the metastatic cascade, ii) maintained their apical pole in contact with their surrounding extracellular matrix (ECM) and iii) had a proper metastatic ability were described[3,4,5]. All TSIPs present an inverted polarity in suspension like in peritoneal fluids where we first identified them.



Once in contact with the stroma, two topologies can be observed: they either stay in this inverted conformation with the apical pole at their surface (called "Apical-out"), or they reorganize their polarity, putting their apical pole away from the ECM by forming a lumen (called "Apical-in").

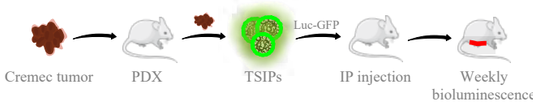


MATERIALS AND METHODS



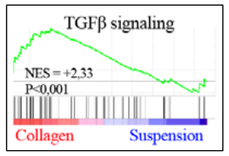
I also developed a mouse model of peritoneal carcinomatosis by injecting spheres into their peritoneal cavity, allowing me to decipher their metastatic abilities *in vivo*.

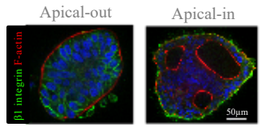
Using a well characterized Patient-derived xenografts (PDXs) bank[6], I am able to reform TSIPs that conserve all the patients' characteristics. Then, I study their behavior in 3D collagen-I gels to mimic their physiological environment.



RESULTS

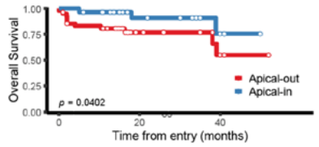
By comparing the expression profiles of Apical-out vs. Apical-in spheres, I could show that their was a downregulation in the TGFβ signaling.





This induces a defective ECM-sensing machinery (β1 integrins are basolaterally sequestred) causing Apical-out spheres to be « blind » to their environment. Using the mouse model described before, I demonstrated that Apical-out spheres are more efficient at forming metastases.

Moreover, using patient's data, I could identify a strong topology-dependent expression signature which has a predictive and a prognostic value. Indeed, Apical-out spheres correlate with a decreased overall survival.



CONCLUSION

TSIPs represent the main tumoral intermediate in hypermethylated CCR patients but they also have been found in other types of cancer (e.g. breast cancer).
They could represent a useful tool for both diagnosis and patient care improvement. Indeed, their inverted topology suggests that the intake and outtake drug receptors are misplaced, with more outtake receptors at the Apical-out spheres surface.

This could imply that Apical-out spheres are more resistant to treatment and their presence could facilitate early patients' stratification.

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Dr Stéphanie Jacquet

EVOLUTIONARY BIOLOGY

Adding your own piece to the puzzle of viruses and hosts' relationship

Laboratoire de Biométrie et Biologie Evolutive (LBBE) et Centre International de Recherche en Infectiologie (CIRI)

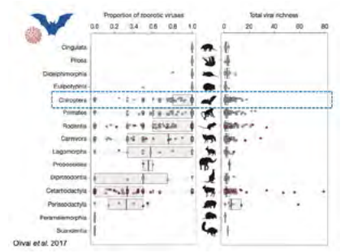
Lyon, France

GENETIC ADAPTATIONS OF BAT ANTIVIRAL IMMUNITY AGAINST VIRUSES

INTRODUCTION

Bats harbor a high number of viruses with potential to spill into human populations. Intriguingly, they appear asymptomatic to most viral infections that are pathogenic to other mammals. One hypothesis is that bats have evolved a unique balance between immune resistance and viral tolerance. Yet, the underlying mechanisms are currently misunderstood.

Here, we investigate how bat's innate immunity has adapted to viral pathogens, and deciphered unique mechanisms underlying bat-virus interplays.



1. Proportion of zoonotic viruses and total viral richness per mammalian order (from Olival et al. 2017)

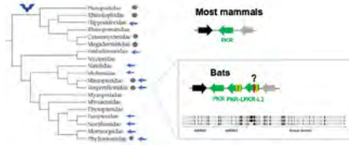
We focus on the Protein kinase R (PKR) - a major antiviral effector in mammals that inhibits viral replication by shutting down protein synthesis. Combining evolutionary analyses and functional assays, we characterize the evolution of bat PKR.

Protein Kinase R, PKR (EIF2AK2 gene)

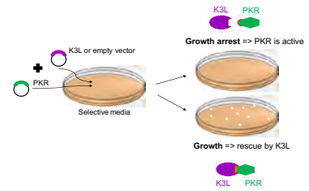
2. Structural representation of PKR

MATERIALS AND METHODS

First, we have conducted an extensive sampling of bats and de novo sequenced PKR from 13 additional species, spanning 60 million years of divergence.



3. Bat phylogeny indicating the families sampled (arrows) or retrieved from public databases (circles), n=21 species.

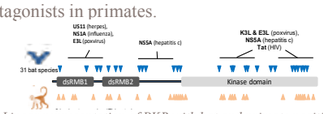


Second, we carried out in-depth phylogenetic and genomic analyses on bat PKR coding sequences and publicly available genomes.

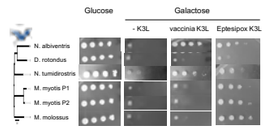
Finally, we functionally characterized the genetic adaptations observed in PKR, using a heterologous yeast system in which we assessed bat PKR basal functions and its counteraction by two poxvirus antagonists, K3L and E3L (which have been well studied in primates) issued from different host species, including bats.

EXPECTED RESULTS

- PKR has undergone major duplication events in some bat lineages, while it is conserved as a single copy in all mammals studied to date.
- Bat PKRs exhibit signatures of positive selection. Several positively selected sites overlap with known sites of interaction with viral antagonists in primates.



5. Linear representation of PKR with bat and primate positively selected sites and known viral interacting sites in primates.



6. Yeast assays showing PKR sensitivity to poxviral antagonism.

- All tested bat PKRs, including the duplicated copies, encode for functional proteins that inhibit protein synthesis.
- PKR variants are differentially capable of evading viral antagonism by K3Ls, which may be the result of adaptive changes.

What are the implications of such genetic adaptations in bat antiviral response?

Expected results should bring new insights into:

- Functional advantages of PKR duplication
- Genetic determinants of species-specificity of poxviruses, and other targeted viruses (ex. influenza virus)

CONCLUSION

Altogether, our results show that sustained exposure to pathogenic viruses may have led to the rapid evolution of bat PKR.

These adaptations of PKR may account for specific antiviral immune responses in bats, and may impact the biological interactions between modern viruses and bats.

Our ongoing work aims at deciphering the costs / benefits of PKR duplication and diversification. Overall, our study should extend our understanding on some aspects of bat antiviral response.

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Ms Coline Monchanin

ENTOMOLOGY & BEHAVIORAL SCIENCES BIOLOGY

From bees to corals: between passion and commitment

Université Paul Sabatier
Macquarie University

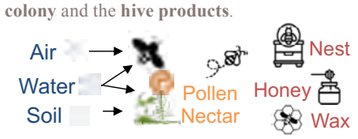
Toulouse, France / Sydney, Australia

IMPACT OF HEAVY METALS ON HONEY BEE BEHAVIOR

INTRODUCTION

Heavy metals are **ubiquitous and persistent contaminants** of the environment. **Human activities**, such as mining, smelting, combustion of fossil fuels, industrial productions, have considerably increased **environmental concentrations, far above natural baseline levels** [1].
Particularly, the WHO [2] stated that the widespread use of lead resulted in significant contaminations, with **no safe levels for organisms**.

Pollinators, such as honey bees are i**n the front line** [3]. Bees can encounter metal particles while flying and may bring back contaminated water, nectar and pollen to their colony nest, thus ultimately **contaminating the whole colony** and the **hive products**.



While pollinators provide **crucial ecosystem services** for crops and wild plants and ensure **food security** and **human welfare** [4], virtually **nothing is known** about the effects of heavy metal pollution on honey bees, while the current permissible levels are **not restrictive enough for insects**.

MATERIALS AND METHODS

Whole honey bee colonies were exposed for 10 weeks **to field-realistic concentrations of lead** (Pb) in food. Those doses fell below the level authorized in food and irrigation water.

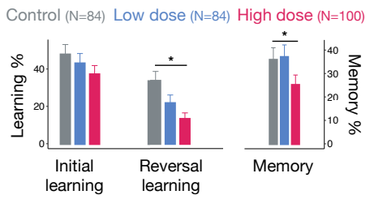
I monitored **impacts on cognition** of individuals bees. Bees were submitted to a reversal learning task, a two-task assay assessing the cognitive flexibility of bees in response to changes in flower rewards.

I also evaluated the effects on **morphological development** by weighting and measuring new-born bees (head, wing, leg).

RESULTS

Honey bees **bio-accumulated** significant amounts of lead throughout the experiment, which ranged within the measurements from bees in natural conditions [5].

I found no effect of lead exposure on colony dynamics (brood production, food stores). While lead exposure did not affect the bee motivation, bees exposed to the highest concentration had **reduced learning and memory performances**.



In addition, bees exposed to lead **were shorter, with smaller heads**.

I also showed that control bees learning performances were correlated to head size. Therefore, lead exposure during larval development may have impaired brain development, thus **constraining honey bee cognitive functions**.

CONCLUSION

Our results raise the concern for pollinators exposed to **environmental metallic pollution**. Bees foraging on contaminated flowers may exhibit **cognitive and developmental impairments**. Ultimately, these effects can alter **colony function**.
Our results show that lead pollutants can have **dramatic effects on honey bee health** and may contribute to the the widespread decline of pollinators. More generally, this study calls for a better assessment of the contribution of heavy metal pollutants to the **global decline of insects**.

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Dr Laure-Anne Poissonnier

ENTOMOLOGY & BEHAVIORAL SCIENCES BIOLOGY

Addressing mental health issues in the field of research

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Toulouse, France

COGNITION IN INSECTS

INTRODUCTION

A) Traffic organisation

Can ants maintain smooth traffic on their trail, without the existence of external control and enforcement of traffic rules? Or do they, like us, suffer from traffic jams?

B) Regulation of nutrition

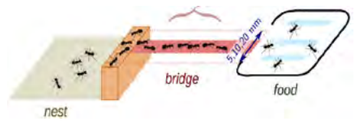
In insect colonies, only a small proportion of the colony collects the food for the group. Can they adapt their food collection to other colony member needs?

C) Integration of available options

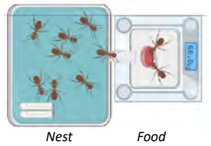
Can Drosophila modify their decisions according to available options? We want to investigate this question in the case of the choice of a sexual partner, which is crucial for fitness.

MATERIALS AND METHODS

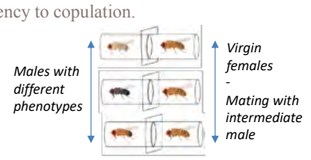
A) Ant groups of varying sizes have to cross bridges to access a platform with food. Recorded all ants crossing.



B) Ant and termite foragers have to feed a varying number of colony members. Measured food collected.

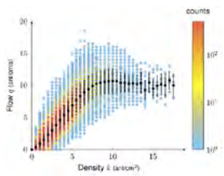


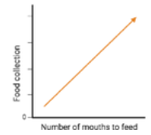
C) Drosophila females observe males of different quality before having the opportunity to mate with a male of intermediate quality. Measure latency to copulation.



RESULTS

Ant traffic flow does not decrease under very high densities but stays at a plateau.

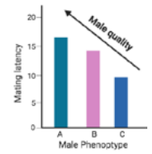




Ants and termites increase food collection with the number of individuals to feed. Ants also change food type according to colony needs, but termites don't.

PRELIMINARY RESULTS

Females appear to delay copulation after seeing a better male, and accelerating it after seeing a male of lower quality.



CONCLUSION

Ants regulate traffic along their trail efficiently, and do not appear to experience traffic jams.

Ant and termite foragers are able to modify food collection according to the needs of their colony. Ants are better at balancing macronutrient intake.

Flies might be able to integrate information from their environment to make accurate decisions.

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Figures made with the help of biorender.com

Ms Joanna Wandzik

MOLECULAR BIOLOGY

Using cryo-electron microscopy to better combat the influenza virus

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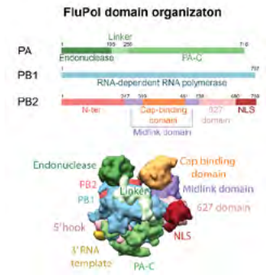
Université Grenoble Alpes (UGA)

Grenoble, France

STRUCTURAL STUDIES OF INFLUENZA TRANSCRIPTION BY MEANS OF CRYO-ELECTRON MICROSCOPY (CRYO-EM)

INTRODUCTION

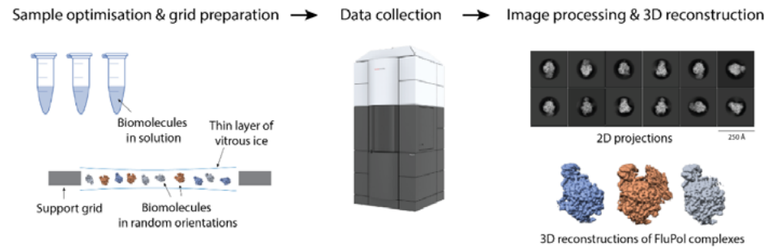
Influenza virus causes seasonal epidemics of respiratory disease that have enormous socio-economic impact worldwide.
Existing vaccines and drugs have only a moderate effectiveness in tackling the disease.
It remains primordial to develop alternative therapies in preparedness for the next possible pandemic, which could be as devastating as the current COVID-19 crisis.



During infection, transcription of viral RNA (vRNA) represents an essential step in virus amplification, production of viral mRNA and subsequent synthesis of viral proteins. Transcription is performed by the virally encoded RNA-dependent RNA polymerase (FluPol), which is a validated drug target. Atomic structures of FluPol were determined previously (1) and gave insights into global architecture and polymerase function. However a detailed mechanism of complete transcription cycle, information crucial for targeted drug design, is still lacking.

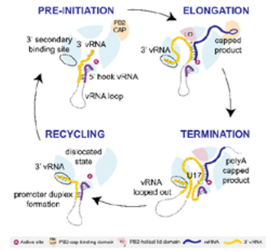
MATERIALS AND METHODS

Recombinantly expressed and purified FluPol was incubated with native-like vRNA templates to perform RNA synthesis *in vitro*. The reactions are stalled at different stages of transcription in order to capture various conformations of FluPol (2,3).
Once optimized, samples were applied to cryo-EM grids, data were collected on a 300 kV Titan Krios microscope, cryo-EM image processing and structure modelling was done to yield multiple high-resolution structures corresponding to distinct states of transcription cycle.



RESULTS

We obtained nine distinct cryo-EM snapshots of various functional states of FluPol from pre-initiation, elongation, termination until product dissociation and template recycling, enabling us to describe the complete cycle of influenza transcription.
The 2.4 Å termination structure reveals the template trajectory and provides strong rationale for the secondary 3' vRNA binding site, which plays an important role in template recycling.



The termination structure provides detailed mechanistic insight into the polyadenylation by stuttering which is unique for this class of RNA viruses.
After product dissociation, the template remains threaded through the FluPol interior with both 3' and 5' docked in their respective binding sites. Upon significant conformational rearrangement, the 3' end of vRNA is flipped into the active site for another round of transcription.

CONCLUSION

Our cryo-EM structures provide evidence for a secondary binding site that is conserved amongst other negative sense RNA viruses suggesting a common mechanism for template recycling, explains efficient multi-round transcription on a single vRNA as well as how both vRNA ends are protected from cellular nucleases.

Finally, methodology developed during my project allows structures to be determined at unprecedented resolution (up to 2.4 Å) and to capture viral polymerases « *in action* » enabling drug discovery projects by single particle cryo-EM.

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Group 3

EARTH & RELATED ENVIRONMENTAL SCIENCES

Dr Aurélie Boisnoir

MARINE BIOLOGY

The Caribbean Sea under close surveillance

IFREMER

Le Robert, Martinique

CIGUATERA FOOD POISONING IN THE FRENCH WEST INDIES: MORPHO-GENETIC AND CHEMICAL CHARACTERIZATIONS OF BENTHIC DINOFLAGELLATES

INTRODUCTION

Ciguatera Food Poisoning (CFP) is caused by the consumption of marine organisms that have bio-accumulated ciguatoxins (CTX) synthesized by the genera *Gambierdiscus* and *Fukuyoa* [1].

These unicellular algae are often present on macrophytes with other epiphytic dinoflagellates potentially toxin-producers, such as *Ostreopsis* and *Prorocentrum* [2].

In addition to the CTX analogs, toxins produced by *Ostreopsis* and *Prorocentrum* could contribute to the toxic cocktail of CFP and explain the variability of symptoms (gastrointestinal, neurological and neuropsychological, and cardiovascular symptoms) observed between the Pacific, Indian and the Caribbean area [3].

Despite the fact that the Caribbean Sea is the second region of the world the most affected by CFP (500 cases/100 000 inhab.) after the Indo-Pacific area (18 000 cases/100 000 inhab.) [4], only few recent studies focused on benthic dinoflagellates in the Caribbean Sea [5].
Hence, the goals of the project are to:

- evaluate the diversity and the distribution of potentially toxic dinoflagellates present in the French West Indies.
- assess their toxicity, and characterize their toxin profiles for a better risk management.

MATERIALS AND METHODS

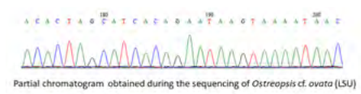
In order to study the morpho-genetic and the toxin diversity of benthic dinoflagellates according to a north-south gradient in the Caribbean area, substrates allowing the development of benthic dinoflagellates are collected at Saint Martin, Saint Barthelemy, Guadeloupe and Martinique islands.

Cells of *Gambierdiscus, Fukuyoa, Ostreopsis* and *Prorocentrum* present on macrophytes, dead corals and plastic debris are rinsed and isolated under an inverted microscope. Then, each cell is placed individually in container with nutrient medium to have mono-specific strains.

The Internal Transcribed Spacers (ITS) and Large SubUnit (LSU) regions coding for the ribosomal DNA of each strain are sequenced.
A strain of each species is selected for morphological analyzes with scanning electron microscope. Toxicity of all the selected strains is assessed with neuroblastoma cell-based assay (CBA- N2A). Then, toxins are identified and quantified with liquid chromatography tandem mass spectrometry method (LC-MS/MS).

RESULTS

The sampling settled around the French West Indies allowed to collect potentially toxic benthic dinoflagellates from four different islands. Cells of Gambierdiscus, Fukuyoa, Ostreopsis Prorocentrum and Coolia a neglected phycotoxin producer genus were found up to 20 m of depth.
The preliminary sequencing of ITS and LSU domains allowed to identify 15 species of potentially toxic benthic dinoflagellates.



Partial chromatogram obtained during the sequencing of *Ostreopsis* cf. *ovata* (LSU)

The species *Gambierdiscus belizeanus, G. carpenteri,* and *Fukuyoa yasumotoi* were found. Furthermore, *Coolia maleyensis*, *C. tropicalis,* and *C. santacroce* were found for the first time in the French West Indies and a new species of *Ostreopsis* was found in Martinique.

Some Ostreopsis species identified in Martinique island.

CONCLUSION

The acquisition of DNA sequences and toxin profiles of benthic dinoflagellates are essential to further develop reliable and rapid tests to assess the risk of toxicity in seafood before sale.

In a context a global change, more people are exposed to the CFP risk. Benthic dinoflagellates can expand their distribution area in temperate regions as in the Mediterranean Sea where CFP is emergent. They could also occur in tropical regions that were previously spared by harmful algae. In order to better manage the CFP risk, effective detection techniques must be implemented to protect human populations.

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Dr Jordane Corbeau

GEOSCIENCES

Predicting earthquakes better

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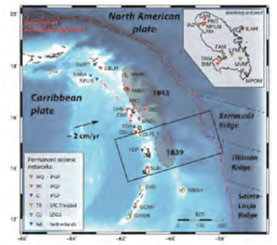
Paris, France / Saint-Pierre, Martinique

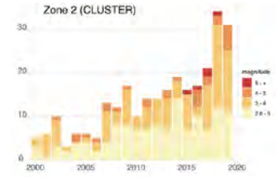
HOW OFTEN MEGA-EARTHQUAKES OCCUR IN THE LESSER ANTILLES SUBDUCTION ZONE?

INTRODUCTION



The seismic activity of the subduction zone near Martinique Island is constantly increasing since the 2007, Mw 7.4, 152 km deep earthquake [1]. Additionally, a seismic cluster occurs at about 80 km toward the NE of Martinique. In this cluster, magnitudes are increasing and Mw 5 and higher have appeared since 2015 [1].

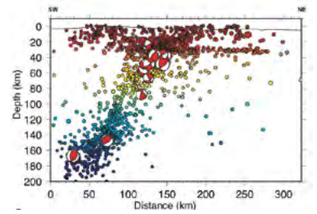
This activity takes place in the inferred rupture zone for the 1839 historical mega-earthquake [2], and questions the seismic hazard of this area.



How often mega-earthquakes occur?
What would be the recurrence time?
Are there any precursory signs?

MATERIALS AND METHODS

I use the seismicity of the Lesser Antilles subduction zone from 2000 to 2020 to study its evolution in time and space by time series calculations.
I am focusing on the earthquakes located along the slab from the outer-rise region to the intermediate depths (120 to 200 km). The final objective of this study is to identify potential precursory signs of a major subduction earthquake.

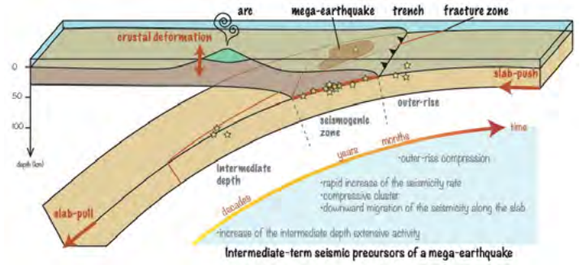


Step 1 – relocate the seismicity with a new velocity model [3] to improve and validate the hypocenters locations and depths.
Step 2 – compute focal mechanisms for stronger earthquakes [4] to estimate the stress field and identify coupled areas.
Step 3 – develop machine learning algorithms to analyze the catalog of seismicity and potentially detect new major rupture precursory signs [5].

RESULTS

Preliminary results show known seismic precursors: a downward migration of the seismicity along the slab; an increasing seismicity in the intermediate depths and in the seismogenic part of the slab (cluster) [1]. Focal mechanisms show that the stress field is compressive in the seismic cluster and extensive at intermediate depths [1].

Machine learning will help to identify potential recurrent patterns in the seismicity and other precursory signs for a major rupture.



Intermediate-term seismic precursors of a mega-earthquake

CONCLUSION

Several seismic precursors have been identified in the Lesser Antilles subduction zone, offshore Martinique. They indicate that the slab is diving at intermediate depths, while the shallower part is locked.

The seismic cluster may imply the progressive unlocking of the seismogenic part. This unusual activity questions the seismic hazards of this area that has already experimented a mega-earthquake in 1839.

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Ms Lorène Jeantet

ECOLOGY

Understanding sea turtles to better protect them

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Strasbourg, France

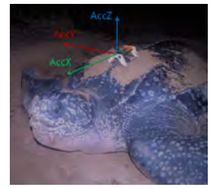
USING DEEP LEARNING TO AUTOMATICALLY IDENTIFY UNDERWATER BEHAVIORS OF MARINE TURTLES

INTRODUCTION

Marine turtles are migratory species that have roamed our oceans for 110 million years and are now threatened with extinction → **6 out of 7 species are on the Red List of Threatened Species (IUCN).**

3 of them (leatherback, olive ridley and green turtles) are nesting in French Guiana and are dramatically declining : **The number of leatherbacks' nests per season has dropped from 50 000 in the 1990s to less than 200 in 2019 [1].**

• To ensure their protection : crucial need to better know their underwater behaviors in order to identify and protect their resting/feeding areas.

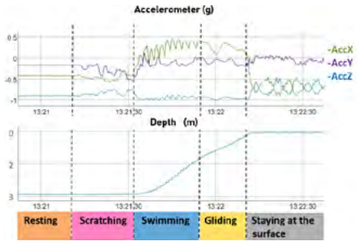


• Used tools: animal-borne tri-axial accelerometer combined with pressure captor and GPS.

Aims of the project :

1. Validation of behavioral identification from multi-sensor signals
2. Automatic identification of marine turtle behaviors using **deep learning**
3. Identification of their energetic strategies and sensitive areas

MATERIALS AND METHODS

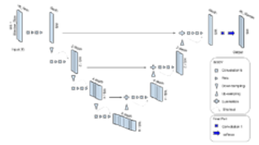


VALIDATION OF BEHAVIORAL SIGNALS

Deployment of animal-borne video-recorder combined with accelerometer, depth recorder and GPS on free-ranging immature green turtles in Martinique.

AUTOMATIC IDENTIFICATION

From labelled dataset, training of an adapted fully convolutional neural network : the **V-net** [2,3].



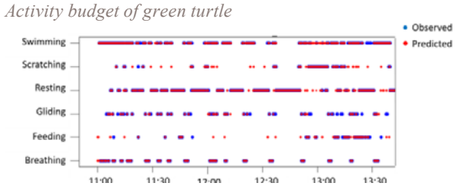
APPLICATION IN FRENCH GUIANA

Deployment of loggers over long period on adult green turtles and application of the **V-net** on the recorded data.

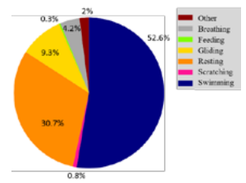
EXPECTED RESULTS

Prediction of the underwater behaviors by the **V-net** with **a global accuracy of 97%.**

Activity budget of green turtle



in Martinique



in French Guiana

The application of the **V-net** enabled us to know all the behaviors expressed by one green turtle equipped with a logger during 13 days in French Guiana. We expect to apply it on the other equipped individuals to confirm the energetic strategy of this population.

This method developed on green turtles would be applied to the other species of marine turtles in French Guiana : the **leatherback** and **olive ridley** turtles.

CONCLUSION

We developed a **deep learning** based method to automatically identify behaviors of marine turtles from animal-borne miniature multi-sensor recorders **over long period**.

The identification of their feeding/resting areas in French Guiana, would allow setting up **protected marine areas** adjustable at spatio-temporal level in order to limit their interactions with human activities.

The **V-net**, easily reproducible and light, would help the scientific community to globally better understand the ecology of these migratory species, with a necessity of multi-location conservation plans.

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Ms Valentine Meunier

MARINE BIOLOGY

Highlighting the link between plankton and coral reefs

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INTERACTIONS BETWEEN SCLERACTINIAN CORALS, MICROPLANKTON AND PLANKTONIC DIAZOTROPHS IN THE CONTEXT OF CLIMATE CHANGE

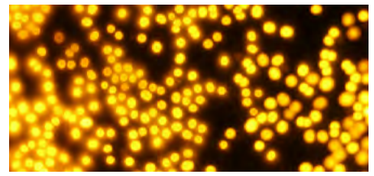
INTRODUCTION

Coral reefs are threatened by global warming which disrupts the symbiosis between corals and their photosynthetic symbionts (family Symbiodiniaceae), leading to mass coral bleaching.

While bleaching events continue to be repeated and intensified throughout the world, the reefs of New Caledonia experienced only one bleaching event in 2016.

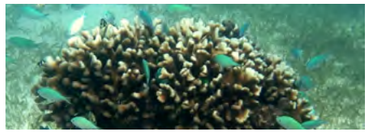
Seawater of South-West Pacific Ocean, surrounding the reefs of New Caledonia are particularly rich in planktonic diazotrophs (dinitrogen (N2)-fixing prokaryotes).

As corals being voracious predator of plankton (heterotrophy), could the ingestion of this 'special' plankton, planktonic diazotrophs, explain the resistance of New Caledonian corals to global warming?



MATERIALS AND METHODS

Coral nubbins were collected by fragmentation in the lagoon of NC. An acclimation period was performed (28 ± 0.2 °C). The temperature was then increased on half of the samples to mimic a bleaching event (31 ± 0.5°C).

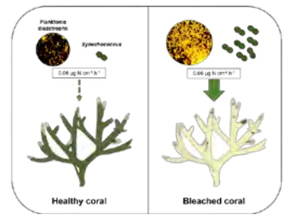


We measured for both healthy and bleached colonies *(i)* the direct feeding on planktonic diazotrophs and *(ii)* the ingestion of non-diazotrophic microplankton. Seawater with the natural planktonic assemblages and diazotrophs were labelled with ^{15}N isotope. The $\delta^{15}N$ isotopic values were measured by spectrophotometry in symbionts, coral tissues and plankton before and after incubation. N assimilation and ingestion rates were calculated to determine the use of N between the different coral compartments.

EXPECTED RESULTS

For the first time, our results show that thermally stressed corals are able to increase, not only their consumption of planktonic diazotrophs and plankton that likely benefited from N_2 fixation, but also more specifically their ingestion of a very specific taxonomic group of plankton: *Synechococcus*.
Surprisingly, bleached colonies preferentially selected *Synechococcus* cells, known to be rich in N.

For bleached coral colonies, the ingestion of diazotrophic plankton and *Synechococcuss* brings ten times more N than what healthy corals take up in the dissolved nitrogen pool when they still contain symbionts.



CONCLUSION

My results not only showed that corals are able to ingest more diazotrophic plankton when they are bleached but my latest experiments have shown that this plankton is beneficial for their resistance to temperature stress. N derived from planktonic diazotrophs within coral holobionts holds great potential to improve our understanding of nutritional interactions driving coral function and resilience in the context of climate change.

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Group 4

CHEMISTRY & PHYSICS

Dr Ada Altieri

CONDENSED MATTER PHYSICS

From infinitely small to infinitely large

ENS | PSL · cnrs · Sorbonne Université · Université de Paris

École Normale Supérieure

Paris, France

ECOSYSTEM COMPLEXITY THROUGH THE PRISM OF STATISTICAL PHYSICS

INTRODUCTION

Theoretical ecology has gathered momentum in recent years, enriched by a plethora of experimental results and the development of remarkably sophisticated techniques.

Advances in the field are particularly important to quantitatively address questions on biodiversity, adaptation and evolution of ecological/biological communities to environmental changes.

To this aim, a massively collaborative effort is being made to identify and characterize all forms of microbial life and their relation to ecological stability [1].

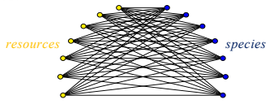
Mauritius oil spill disaster (July 2020).

METHODS

The aim of my project is to answer these questions by the aid of statistical physics. Recently, special emphasis has been devoted to ecosystems formed by a large number of species, e.g. bacteria communities, wherein interactions may lead to the emergence of **complex collective behaviors**.

Yet, understanding which kind of behaviors might arise and how to properly describe them remain widely open challenges.

A powerful theoretical framework is provided by **the Lotka-Volterra model**, which generalizes resource-competition and prey-predator systems [2] (Fig. below). It allows us to perform a rigorous analysis and to work out the phase diagrams in the limit of infinitely many randomly interacting species.

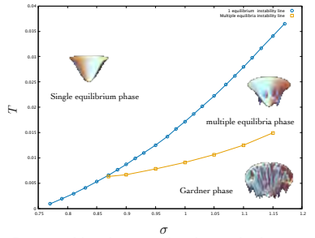


My research aims to investigate the LV model and its generalizations in the presence of finite **demographic noise** – an intrinsic source of randomness due to birth, death and unpredictable interaction events – using concepts and methods rooted in statistical physics of disordered systems, i.e. the replica and dynamical cavity methods, field theory as well as random matrix theory techniques.

CURRENT AND EXPECTED RESULTS

The existence of several phases of increasing complexity will be proven [3].

- I will show that the number of *stable equilibria* is exponential in the system size.
- In the low-demographic noise regime (low T), a **Gardner transition** to a **marginally stable** phase will be detected, where the system is expected to display diverging responses to small perturbations.



Demographic noise strength vs interaction heterogeneity.

Similarly to what observed in glasses, this new phase is characterized by a hierarchical organization of the equilibria in the configuration space following *general* principles and deeply changing our understanding of large ecosystems.

Timely questions about cooperative effects, endogenous dynamical fluctuations and possible chaotic behaviors will be also deepened.

CONCLUSION

LV equations are a key ingredient for theoretical studies in ecology, genetics, evolution, epidemiology and economy.

Main applications of this project:

1) Generalization of the model to take the so-called *Allee effect* into account [4], opening the route to a systematic analysis of bistable dynamics to habitat alteration, collective movements as well as epidemic diseases.

2) Introduction of a notion of space to reproduce meta-communities and obtain predictions on dynamical correlation lengths as a function of the dimension (e.g. cluster formation).

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Acknowledgements to the Simons Foundation on Cracking the Glass Problem.

Ms Hanna Bendjador

OPTICS

Understanding ultrasounds to transform echography

Physics for Medicine PARIS ESPCI PARIS PSL Inserm cnrs

Physics for Medicine Paris, ESPCI, INSERM, CNRS, PSL

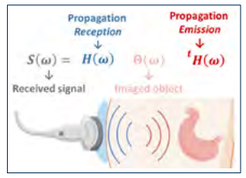
Paris, France

ADAPTIVE AND QUANTITATIVE ULTRAFAST ULTRASOUND IMAGING

INTRODUCTION

Echography relies on ultrasound transmission through biological tissues, and reception of backscattered data. The contrast image formation is an **inverse problem** between:
• The echoes received on the probe.
• The structure of the medium.

In temporal Fourier space, the signal received on the probe is a matrix product, resulting from propagation back and forth through an operator H in a medium Θ.



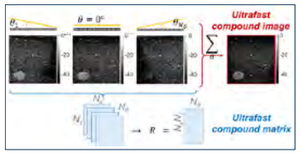
In conventional configurations, analytical models for H enable the formation of good quality images.

Though, when propagating through muscle, bone or fat layers, these models are no longer valid [1]. Aberrations strongly affect the wave front, and thus the images.

Our aim here is to **unveil propagation through aberrating media at ultrafast frame rates**, allowing also new non-invasive biomarkers.

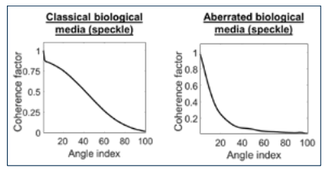
MATERIALS AND METHODS

To ensure ultrafast frame rates [2], our formalism was adapted for plane wave imaging.
We designed a matrix containing the images for each transmitted angle: **the Ultrafast Compound Matrix R.**



The angular covariance, $(\_\hat{}t)R\hat{}*\ R$, tells us the degree of similarity between plane wave images.

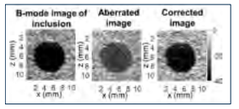
Thanks to the Van Cittert Zernike theorem [3,4], we know it is a triangle function of the angle lag. In aberrated media, it decreases dramatically.



Thus, **maximizing the angular covariance** is a key towards aberration correction in plane wave imaging. Mathematically, we demonstrated that the Singular Value Decomposition (SVD) provides, in its first singular vector, the solution to this optimization problem. Interestingly, SVD separates the angular variation (with respect to the transmit angle), and the spatial variation (the image itself).

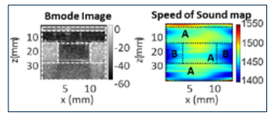
RESULTS

We proposed a novel and simple approach to perform aberration correction in the context of ultrafast ultrasound imaging [5]. For the first time in real-time, we both retrieve:
• The **corrected imag**e: the first spatial singular vector.
• The **aberration phase and amplitude** in the plane wave basis: the first angular singular vector.



On gelatin phantoms, we showed experimental evidence of our method's efficiency. We fully recovered the degradation effect of aberration on the image quality.

Also, the phase aberration law was fitted to propagation models, and derived [6] to build the first real-time local sound speed maps.



CONCLUSION

Finally, we developed a theoretical and mathematical formalism providing the first real-time approach for sound speed quantification, and adaptive image formation in complex media.

We offer a unique physical understanding of the mathematical SVD operation.
These results pave the way to unprecedented ultrafast ultrasound applications such as transcranial neuroimaging or motion correction in cardiovascular imaging with an accessible, non-invasive and reliable technique.

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Ms Léa Bonnefoy

ASTRONOMY

Dreams of planetology

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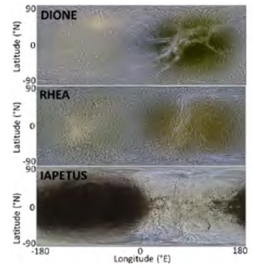
THERMAL MICRO-WAVE EMISSION FROM SATURN'S ICY MOONS

INTRODUCTION

Iapetus, Rhea, and Dione, Saturn's three largest satellites after Titan, are in synchronous rotation, featuring leading and trailing hemispheres.

Their surfaces, mainly composed of water ice, are modified by particles circulating around Saturn, such as meteorites, ring particles, and charged particles.
On Iapetus especially, dust from the Phoebe ring darkens the leading hemisphere.

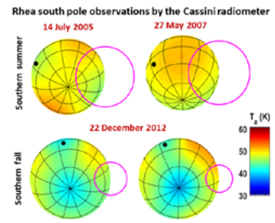


Part of this history is contained in the satellites' icy regolith, and can be accessed from their thermal microwave emission. Using observations from the Cassini 2cm Radar/radiometer and Earth-based radiotelescopes, the goal of this project is to characterize the composition and structure of the subsurfaces of Saturn's icy satellites, especially Rhea, Dione, and Iapetus. Variations in these properties inform on the processes which shape these icy surfaces.

MATERIALS AND METHODS

1. Analysis of Cassini radiometry by comparison with simulated data

- The radiometer measures antenna temperatures T_a, which depends on thermal and structural properties down to meter depths.
- Simulated T_a are computed from a combination of thermal, radiative transfer, and emissivity models [1].
- Simulations are fitted to observations to derive thermal and structural properties.



Observations of the same area at different seasons constrain the thermal properties.

2. Building the microwave spectrum of Iapetus from radiotelescope data

- Pre-existing data (Cassini, SMA, GBT)
- New millimetric observations: NIKA2 camera on the IRAM 30-meter telescope
- New centimetric observations: VLA

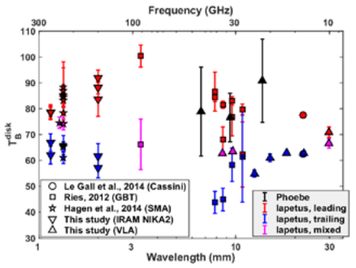
RESULTS

Rhea and Dione
- The Cassini radiometer probes down to 6-13 m below Rhea's surface
- Both Rhea and Dione are radar-bright, indicating subsurface scattering
- Dielectric constant is very low (<1.5)
- Thermal inertia is higher at 2 cm (50-300 MKS) than IR wavelengths (4-30)

→ High-purity water ice, with compaction increasing with depth, with imbedded scattering voids or inhomogeneities

Iapetus
- Leading hemisphere (LH) is warmer
  → Thickness of dark material is tens of cm
- Low trailing (TH) ~3-10 mm values of TB
  → Scattering by mm-sized particles? [2]
- Decreasing LH TB at cm wavelength
  → Probing the icy substrate below
- High LH 1-3 mm slope
  → sub-mm particle scattering?

Changing composition/structure with depth?
- Phoebe close to LH temperatures
  → Consistent with dark material from Phoebe [3]



CONCLUSION

Analysis of Cassini radiometry observations of Rhea and Dione using a thermal model is consistent with a scattering, porous, high-purity water ice composition down to meter depths.

Current emissivity-backscatter models [5] are unable to explain both the radiometry and radar data, pointing to the presence of exotic scattering structures [6,7].

On Iapetus, scattering also plays an important role on the icy trailing hemisphere. On the leading side, both structural (porosity, grain size) and compositional changes with depth are found.

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Dr Monu Kaushik

PHYSICAL CHEMISTRY

From the study of nanomaterials to sustainable industrial development

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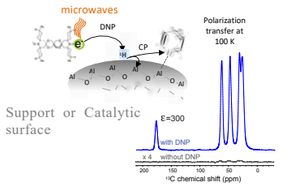
ATOMIC-LEVEL STUDY OF CATALYTIC SURFACES USING DNP ENHANCED NMR SPECTROSCOPY

INTRODUCTION

Characterization of surface sites is extremely difficult experimental task due to their scarcity and reactivity.

NMR spectroscopy even though capable to revealing atomic-level structure, suffers from inherent lack of sensitivity. A signal enhancing method Dynamic Nuclear Polarization Surface Enhanced NMR spectroscopy (DNP SENS) is therefore the method of choice for atomic-scale information.



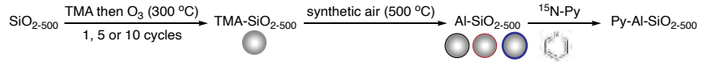
^{1}H-X Cross–Polarization (CP) technique ensures additional signal enhancement from abundant and highly polarized protons.

Silica-alumina materials are an important class of industrial supports and catalysts whose surface acidity is crucial to their catalytic performance.

In this study, we present a DNP SENS as the method to study such surfaces. Materials are prepared by Atomic Layer Deposition (ALD) of alumina on dehydroxylated silica microparticles.

The thickness of alumina layer is varied to control the nature of acidity of their surface.

MATERIALS AND METHODS



Materials denoted Al1-, Al5-, and Al10-SiO_{2-500} were prepared by 1, 5, or 10 ALD cycles of trimethylaluminum (TMA) onto dehydroxylated silica. To avoid rehydroxylation of the support, ozone was used during ALD as an oxidant in place of more frequently used steam, followed by calcination.

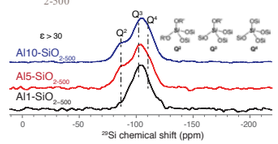
The calcined materials were exposed to ^{15}N-pyridine vapor, and thus obtained materials are dubbed Py-Al1-, Py-Al5-, and Py-Al10- respectively.
^{27}Al, ^{29}Si, and ^{15}N DNP NMR spectra are recorded at 9.4 T using the best performing biradical TEKPol as the polarization source.

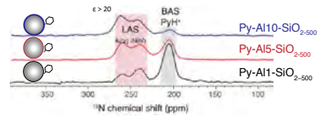
Surface acidity of these materials is probed by monitoring the interaction of pyridine with the support material using DNP SENS. Fourier Transform Infra Red (FTIR) provides supporting information about types of bonds present in these materials.

Eventually, surface acidity of a catalytic material i.e., Al5- grafted with Ni, is compared with the support material containing the amount of alumina.

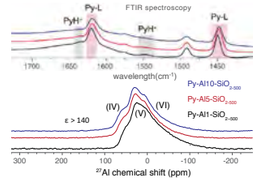
IMPORTANTS RESULTS

The feasibility of ^{1}H-^{29}Si CP confirms that protons are present in alumina coating. Growth of alumina layer by replacing –OSi bonds is evidenced by appearance of Q2 sites in Al5- and Al10-SiO_{2-500}.





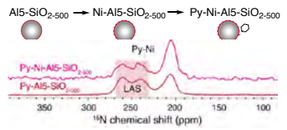
^{15}N DNP NMR spectra demonstrates that Py-Al1- contains most Brønsted Acid Sites (BAS) due to close proximity with silica core, that are replaced by Lewis Acid Sites (LAS) as the thickness of alumina layer increases.



^{27}Al spectra can not provide surface information due to chemical shift anisotropy and quadrupolar broadening.

CONCLUSION

DNP NMR Signal from paramagnetic Ni containing sample is less sensitive due to enhanced relaxation, however, it reveals that Ni grafting increases Brønsted acidity of the surface.



^{15}N DNP is a unique method to successfully discern presence and strength of Lewis and Brønsted acid sites on the surface of support and catalytic materials.

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Lesage et. al., JACS 2010, 132, 44, 15459–15461 ; Brunauer et. al., JACS 1938, 60 (2), 309-319 ; Coperet et. al., Chem Rev 2016, 116 (2), 323-421 ; O'Neill et. al., ACS Catal 2015, 5 (3), 1804-1825 ; Moroz et. al., J. Phys. Chem. C 2018, 122, 20, 10871–10882

Ms Sarah Lamaison

ELECTROCHEMISTRY

Recycling CO_2 to overcome dependence on fossil resources

Collège de France
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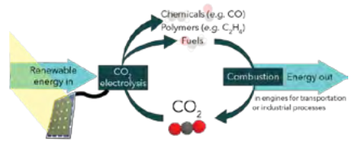
Paris, France / Stanford, USA

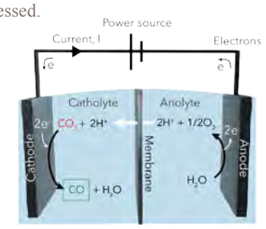
ENGINEERING HIGH-PERFORMANCE ELECTROCATALYTIC DEVICES FOR THE CONVERSION OF CO_2 TO CHEMICAL FUELS

INTRODUCTION

To abate atmospheric levels of greenhouse gases, research efforts have sought routes to recycle emitted CO_2. This can be achieved through electro-reduction of CO_2 to generate value-added fuels and chemicals such as CO,



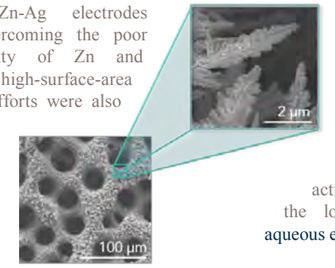
a precursor to chemical feedstocks currently derived from fossil sources. In such a process, an electricity source is used to power the oxidation of water at the anode and the reduction of CO_2 into CO at the cathode. For this process to be economically viable, both high energy efficiency and CO_2 conversion rates must be achieved. Electrocatalysts with high activity and selectivity for CO (measured by the partial current density of CO, j_{CO}) and their implementation as cathodic materials in devices with enhanced CO_2 mass transport to the catalytic surface will be key to reach such performance. In the work presented herein, both catalyst and cell engineering were addressed.



MATERIALS AND METHODS

Among the proposed cathodic electrocatalysts, record activities are reported for Au and Ag, due to both their high intrinsic catalytic performance and amenability to nanostructuration, contrary to Zn.
Yet, scarcity and price of such metals hamper industrial developments. Here, we employed alloying strategies, through co-electrodeposition with low quantity of Ag, to promote Zn-based catalysts nanostructuration.

Hierarchically porous Zn-Ag electrodes were thus generated, overcoming the poor nanostructuration capability of Zn and providing inexpensive high-surface-area CO_2 reduction catalysts. Efforts were also devoted to implement such catalyst in devices designed to enhance CO_2 mass transport. First, a high-pressure reactor was built to run the reaction in a 10-bar CO_2 atmosphe-re,



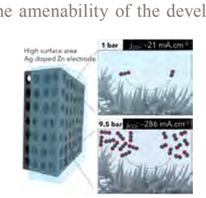
increasing the dissolved CO_2 available for reaction. A second design referred to as a (GDE) was also investigated. By uncoupling the CO_2 gas flow from the electrolyte flow, such design suppresses activity limitations due to the low solubility of CO_2 in aqueous electrolyte

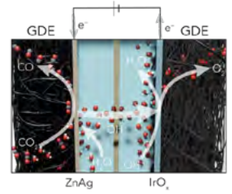
RESULTS

electrolyte, otherwise capped at jCO less negative than -30 mA.cm^{-2}.

Use of so-prepared Zn-Ag catalysts in a 10 bar-CO_2 reactor reached j_{CO} as high as -287 mA.cm^{-2}, representing a ~10 fold increase compared to the performance obtained in 1 bar of CO_2. The unique structuration of the Ag-alloyed Zn catalysts was further exploited through GDE.

This further improved CO_2-to-CO performance with j_{CO} as high as -614 mA.cm^{-2}. Such results prove the amenability of the developed Zn-Ag catalysts to sustain remarkable activity provided sufficient CO_2 supply to the catalytic sites.





CONCLUSION

For CO_2 electroreduction to reach industrial applications, electrocatalytic current densities more negative than -300 mA.cm^{-2} must be achieved, requiring a catalytic surface able to accommodate high CO_2 conversion rates. Such a target was achieved in the present work. This was made possible upon engineering inexpensive high-surface-area Ag-alloyed Zn catalysts further implemented in Gas-diffusion electrodes leading to record CO_2 conversion rates.

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Dr Lucie Leboulleux

ASTRONOMY

Observing distant worlds… to better understand our own

LESIA
Observatoire de Paris

Meudon / Paris, France

HOW TO IMAGE OTHER WORLDS?

INTRODUCTION

1992 discovery of the 1st exoplanets

2020 >4000 confirmed exoplanets

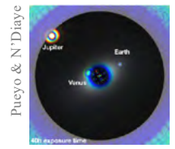
Do exoplanets host life?

To detect life markers, the spectroscopy and so **direct imaging** of exo-Earths are needed.

→ The design and tolerancing of exo-Earth imaging instruments have to respond to two main constraints:

- **Contrast**: for 1 photon coming from an Earth-like planet, 1010 photons come from the star (vis/near-IR light)
  → a coronagraph can be used to hide the star, like a solar eclipse.

Observation of a solar system twin with a 12m telescope and a coronagraph (simulation)



- **Angular separation**: planet and star are very close to each other (typically 0.1'')
  → larger telescopes enable to reach small separations. However, they have to be **segmented.**

Hubble (space, 1990) 2.4m, no seg. | LUVOIR (space, 2039) 15m, 120 seg. | ELT (Chile, 2026) 39m, 798 seg.

THEORETICAL WORK

Development of analytical models:

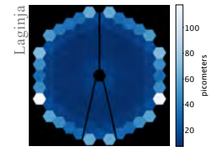
Telescope design and tolerancing are traditionally done with **numerous numerical simulations**.

→ Replacing these simulations with analytical models relieves the computational burden and enables to explore a larger space of parameters.

Example of parameters to explore: **local instabilities** due to the segmentation of the mirror.

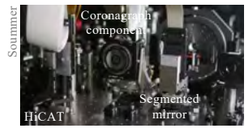
PASTIS[1, 2]:
Analytical model for contrast prediction of segmented telescopes: it provides constraints for segment alignment and polishing.

Example of tolerance map for LUVOIR (target contrast: 1010), obtained with PASTIS



EXPERIMENTAL WORK

Design or concept validation on optical testbeds[3]
Application of a technique to detect segment misalignment on **HiCAT**, a testbed mimicking a segmented telescope imaging exoplanets.



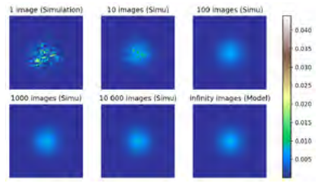
RESULTS

Development of a new analytical model of long exposure images for ground-based giant telescopes[4]:

Ground-based images are subject to **dynamic atmospheric turbulence**, and have to be integrated over long exposure times.

Number of images needed to express one 10 minute exposure image	
Simulations	My model
~1000 to 10 000	1

→ Infinite exposure images: existing models (see fig. above)
→ Finite exposure images: coming soon4!



CONCLUSION

Analytical models offer a significant gain of time when designing instruments, enabling to explore more parameters and to optimize the final architecture.

Before use, designs and concepts have to be experimentally validated in laboratories.

→ crucial in the search for Earth-like planets, which imposes drastic constraints.

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Acknowledgement: IRIS OCAV – PSL – Program Investissements d'Avenir – ANR-10-IDEX-000102 PSL

Ms Johanne Ling

ORGANIC CHEMISTRY

How sustainable chemistry can accelerate the discovery of therapeutic active ingredients

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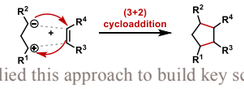
DEVELOPMENT OF INNOVATIVE CATALYTIC CYCLOADDITION-BASED PROCESSES AS GREENER SYNTHETIC TOOLS

INTRODUCTION

Considering the current ecological and economic requirements, organic chemists are paying close attention to the development of greener processes to access molecules of interest. On the other hand, the demand for bioactive substances is still growing and imposes substantial environment impacts.
This context highlights the need for innovative sustainable synthetic tools. Thus, **catalysis** offers a valuable solution by the reagent activation, allowing to valuate simple and abundant raw materials, reduce energy costs and provide new reactivities.

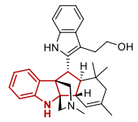
Here we report the development of original methodologies using an organometallic catalyst, based on (3+2) **cycloaddition** reactions. This strategy relies on the use of 1,3 dipolar reagents and gives access to high molecular complexity in a single step, without generating by-product.



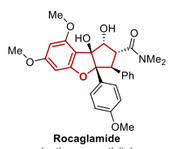
We applied this approach to build key scaffolds prevalent in natural or bioactive molecules, such as cyclopenta[b]indoline in Spermacoceine or cyclopenta[b]benzofuran in Rocaglamide.

Borreria verticillata

Agalia elliptifolia



Spermacoceine
(antimicrobial activity)



Rocaglamide
(anticancer activity)

MATERIALS AND METHODS

As usual in methodology development studies, we proceeded as such:

1. Preliminary results
New classes of molecules tested as potential cycloaddition partners, based on the reported reactivity of dipolar compounds.

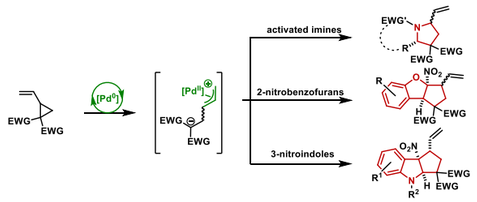
2. Optimization studies
Starting from promising hits, investigation of the influence of reaction parameters to enhance the performances of the transformation.

3. Evaluation of the scope
Examinating the optimized reaction system compatibility with similar compounds.

4. Mechanistic studies
Rationalization of the reaction according to the literature and our results, providing a mechanistic proposal.
Conventionally, molecules are characterized by mass spectroscopy (MS), nuclear magnetic resonance spectroscopy (NMR) and melting point measurements.

RESULTS

First, we successfully employed vinylcyclopropanes bearing electron-withdrawing groups (EWG) to generate 1,3 dipoles under palladium catalysis and to promote (3+2) cycloadditions with original partners.



In a single step, we managed to synthetize a wide range of highly functionalized pyrrolidine, cyclopenta*[b]*benzofuran and cyclopenta*[b]*indoline derivatives, with high yields and selectivity.
Starting from another type of dipolar precursors, propargylic nucleophiles, we achieved the development of a new straightforward method to afford differently substituted cyclopenta*[b]*indolines, in the presence of a base and a copper catalyst.

CONCLUSION

These innovative synthetic tools provide complex molecular structures by the catalytic activation of readily available raw material with a metal catalyst. These sustainable processes give an efficientaccess to a wide variety of compounds with valuable cores. We managed to reach high performances while reducing financial and environmental costs.
Another research axis of green chemistrywe investigated combines electrochemistrywith reactions engaging more than two partners (multicomponent reactions).
Ultimately, these methodologies could be used to accelerate the discovery of new molecules of interest in pharmaceutical industry, for instance.

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Dr Simona Lombardo

ASTRONOMY

From stargazing to the telescope of the future

Laboratoire d'Astrophysique de Marseille

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THE CALAR ALTO SCHMIDT-LEMAITRE TELESCOPE: AN INNOVATIVE CONCEPT FOR WIDE FIELD ASTRONOMY

INTRODUCTION

The new challenges in astronomy often require to build telescopes able to observe large parts of the sky at once. Most times the solutions offered focus the light on a curved surface (like the eye), rather than a plane. Therefore, by matching the shape of the sensor to the ideal one for the system, we can optimize its performances. This technology, however, is still very new and not quite widespread1,2.

Fig.1: Galaxies NGC 474. Credit: CFHT/Coelum.

When applied to astronomy, curved sensors can make a difference in the detection of a category of astrophysical objects and features that are characterized by extremely low surface brightness (>29 mag/arcsec2), and that, contrary to stars, are extended over quite large spatial dimension on sky (from a few arcmin to degree scales). From their properties we can learn more on how galaxies formed and evolved (Fig. 1).

AN INNOVATIVE SOLUTION

The Calar Alto Schmidt-Lemaitre Telescope (CASTLE) is a compact telescope[3,4,5] (the primary mirror is only ~40 cm) that allows to obtain an image of a large part of the sky (the field of view is 2.36ºx1.56º). Its characteristics makes it competitive even compared to larger telescope because its designed is highly optimized thanks to the introduction of a curved sensor. I will test the detector unit (provided by CURVE-ONE start-up at LAM/CNRS, Fig. 3) by the end of 2020.

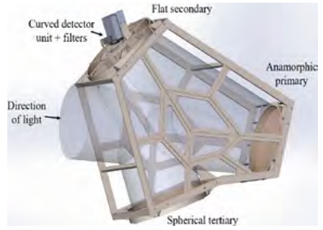


Fig. 2: Opto-mechanical design of CASTLE[5]

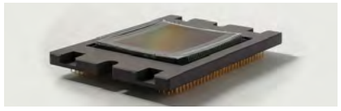
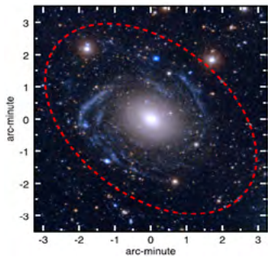


Fig. 3: Curved detectors prototypes from CURVE-ONE. Credit: CURVE SAS.

The telescope will be integrated and installed at the observatory of Calar Alto (Spain) by the end of 2021.

EXPECTED RESULTS



By the beginning of 2022 the observational campaign of CASTLE will start and it will be able to detect faint objects of 29.5 mag/arcsec^2 (V band) at 5σ limit, in 15 h integration time[5] (ex. Fig. 4).

I will use CASTLE also to search and detect a category of extremely interesting objects called transients, to which the gravitational wave optical counterparts belong[6] (Fig. 5).

Left Fig. 4: Example of galaxy observable with

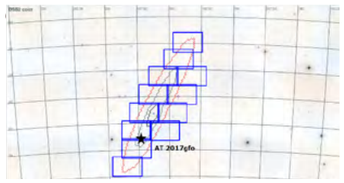


Fig. 5: Error box and position of kilonova AT2017gfo. The blue rectangles correspond to the field of view of CASTLE. CASTLE would need 12 pointings to detect it,

CONCLUSION

The project will generate a wealth of science data that will increase our understanding on galaxy formation and evolution.

Additionally, I want to make this telescope easily accessible remotely to become a tool for education and outreach. This will provide unique opportunities to students of different educational levels (from high school to PhD) to be involved in STEM subjects and train on real

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Ms Marine Moussu

MAGNETIC RESONANCES

Why the scientific approach is an essential tool for shaping critical thinking

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Marseille, France

ELECTROMAGNETIC MODELLING OF MRI DIELECTRIC COILS

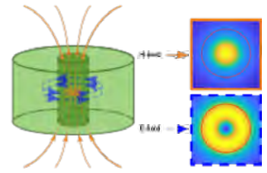
INTRODUCTION

Magnetic Resonance Imaging (MRI) exploits the magnetic resonance of particular atom nucleus, like protons, when immersed in a static magnetic field, to provide images of organs in the human body or of biological samples. It requires using one or several radiofrequency (RF) coils to induce the excitation magnetic field in the sample and receive the protons response.

The image quality is quantified by the acquisition Signal-to-Noise Ratio (SNR). It relies on the acquisition time (limited for clinical applications), the static field strength B_0 (fixed by the MRI device) and the RF coil efficiency. Enhancing its ability to induce and detect a signal (magnetic field) from the sample with a limited level of noise is therefore a solution to improve the SNR. This project focuses on an alternative coil design that exploits the resonances of high permittivity dielectric cylinders. The final goal is to develop a ceramic coil dedicated to wrist imaging at 3 T, to help diagnosing arthrosis and monitoring therapeutic treatments. Indeed, this requires high SNR levels to distinguish the thin layers of affected cartilaginous tissues.

MATERIALS AND METHODS

The ceramic coil is designed as a ring, with the sample placed in its hole. Several of its resonant modes have a magnetic field distribution fitting the excitation field requirements. Among them, the $TE_{01\delta}$ mode has been selected. We developed a theoretical model describing this mode in terms of field distribution, power losses in the ring and the held sample, and reachable SNR [1].

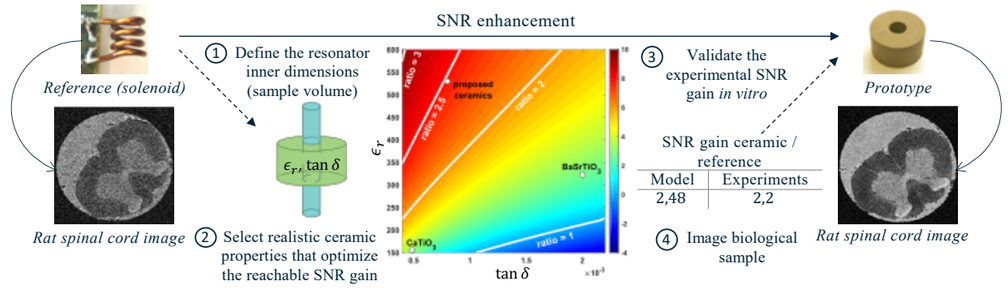


"Cylindrical resona" $TE_{01\delta}$ mode: field lines schematics (left) and transverse 2D profiles (right)

With this code, the performance of the coil is computed as a function of its geometrical and electromagnetic properties. It also allows to compare the theoretical SNR provided by the dielectric probe to conventional metallic coils for which such tools already exist [2]. Our model is therefore dedicated to designing optimized dielectric probes exploiting the $TE_{01\delta}$ mode for a given B0 and with respect to a reference antenna.

RESULTS

Methodology for designing a microscopy probe at 17,2 T with optimized properties to overcome the reference coil performance [3]:



CONCLUSION

The proposed theoretical tools were validated in microscopy. The prototype benefited from recent advancements in high permittivity and loss ferroelectric materials. Next part of the project will be the development, with the same methodology, of a ceramic coil for wrist imaging at 3 T.

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[3] Moussu et al., 2019, 10.1002/adma.201900912

This project has received funding from the European Union's Horizon 2020 research and innovation program under grant agreement No 736937.
More information on mcube-project.eu/

Ms Gaëlle Rondepierre

PHYSICAL CHEMISTRY

Meeting the major challenges of water management, a vital resource that is becoming increasingly scarce

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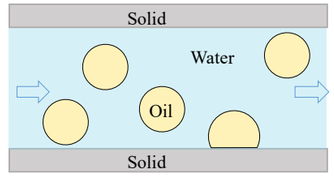
STUDY OF THE WETTING OF OIL ON A SOLID IN WATER FOR IMPROVEMENT OF WATER TREATMENT MEMBRANES

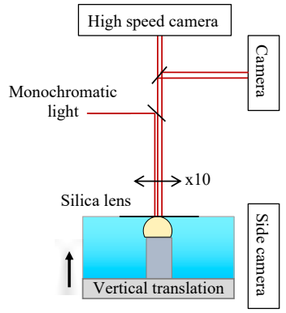
INTRODUCTION

The problem of industrial water treatment is a critical environmental concern. A process commonly used is filtration with ceramic membranes.
One of the main drawbacks of this technique is that wastewater contains oil that can stick to the surface of the membrane and damage it. This phenomenon is called fouling.



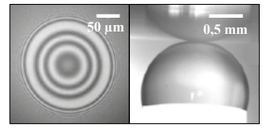
It is then necessary to understand and control the interactions between oil and solid in water to prevent fouling or restore the membrane properly.
In this context, my work aims to study these interactions in the presence of surfactants. These molecules modify the affinity of the surface to oil and the dynamics of oil spreading on it.

MATERIALS AND METHODS



The experiments are conducted with an interferometry set-up, enabling to control the approach of an oil drop towards a solid surface in water.
The oil drop is created in a tank filled with a surfactant solution. A silica lens is held at the water surface and set to a 10x microscope objective.

When the drop is squeezed towards the surface, a water film remains trapped between oil and silica, deforming the oil/water interface. Its thickness is around a few hundreds of nanometers and can be monitored in real time.



In some cases, the film can be destabilized, leading to the wetting of oil on the silica, recorded via an high-speed camera.

Finally, millimeter size views of the oil droplet are imaged with a side camera, enabling to explore a wide range of space scales.

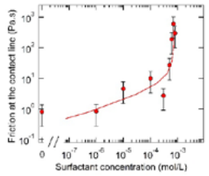
RESULTS

2 main phenomena are observed :

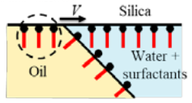
The presence of surfactants increases highly the stability of the water film up to several hours.

This is explained by the presence of micelles layers, creating steric and electrostatic interactions.
The expulsion of the successive layers was evidenced through a step-by-step drainage.

The film can be destabilized through nucleation leading to wetting. In this case, the triple contact line dynamics is controlled by a friction term.



We measure its variation with the concentration of surfactants and evidence an increase of 3 orders of magnitude at high concentrations. We relate this increase to the adsorption of surfactants on the silica surface. More precisely, part of these surfactants stay trapped under the oil while it advances.



CONCLUSION

The presence of surfactants does not prevent the wetting of oil on the solid surface but it delays it in 2 ways:

1. The confined micelles increase the lifetime of the water film between the drop and the surface
2. The adsorbed surfactants dissipate energy through friction at the contact line, decreasing its velocity

These results open new perspectives to understand adhesion of oil on solid surfaces and will be completed by a study with a new set-up in a flow situation

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Ms Cynthia Sinyeue

ORGANIC CHEMISTRY

Treating diseases with wood

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PHARMACOLOGICAL AND ECOLOGICAL VALORIZATION OF CO-PRODUCTS FROM TROPICAL FOREST INDUSTRY

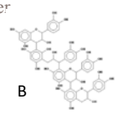
INTRODUCTION

Nowadays, plant extracts are widely used in pharmaceutical and cosmetic industries with bio-sourcing concepts.

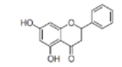
In New Caledonia, the main harvested timber is *Pinus caribaea*. Its exploitation generates a large amount of co-products such as sawdust, knots and barks (A) which are undervalued. How could we use them? Can they play a role in health or in protecting environment?

My research aims to valorize molecules and polymers from co-products with a strategy respectful to the environment.

1. Polymers (90% of the total mass of wood) are studied as biosorbent of trace metals to decontaminate fresh water



2. Extractables (10% of total wood) are studied for their composition and their bioactivities.



C

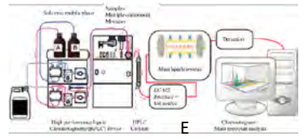
3. Synthesis of derivatives of major compounds (C) followed by biological tests are carried out in order to find the structure requirements to improve anti-inflammatory properties.

MATERIALS AND METHODS

1. Polymers (B) are sequentially extracted from wood, then characterized by chemical analysis (SEM, FTIR, GC-MS). Biosorption tests are carried out in crude biomass and improve by surface modifications (D).

D

2. Co-products are extracted using organic solvents. Compositions of the extracts are determined by HPLC-UV-MS (E). In parallel, biological activities are evaluated through antioxidant and antibiotic tests.



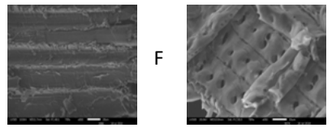
E

3. Twenty flavonoids derivatives are synthesized (C) in a two-step route by thermical and photochemical methods. Molecular structures are characterized by ^{1}H and ^{13}C NMR.

Anti-inflammatory activity is evaluated using an in vitro model of RAW264.7 macrophages induced with bacterial LPS (E.coli 0111) and based on the quantification of NO using Griess assay.

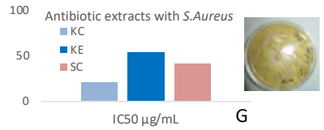
EXPECTED RESULTS

1. IR analysis confirm modifications of functional groups of polymers. The microscopic analysis shows the increase of pore diameter in modified biomass which allows better surface adsorption (F).



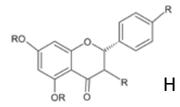
F

2. Analysis of the extracts shows a characteristic composition of the genus Pinus. Biological tests revealed promising antibiotic (G) and antioxidant activities of polar extracts which concentrate molecules like polyphenols.



G

3. Structures of all derivatives molecules are confirmed by NMR experiments. The evaluation of anti-inflammatory activity (H) leads us to conduct a structure-activity-relationship (SAR).



H

CONCLUSION

1. Co-products can adsorb metal ions and could be an effective and ecological biosorbant.

2. This work reports the first analysis of *P. caribaea* molecular composition.

3. SAR highlights the functional groups essential to anti-inflammatory activities. Thus, natural flavonoids could be use as platform molecules for future development of new pharmaceutical compounds.

As a source of biodegradable, less toxic and bioactive compounds, pine co-product represents a valuable biomass with a promising economic potential.

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Group 5

ENGINEERING SCIENCES, MATHEMATICS & INFORMATICS

Ms Lesly-Ann Daniel

COMPUTER SCIENCES

Automatically uncovering computer security breaches

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Nice, France

AUTOMATED PROGRAM ANALYSIS: FROM SAFETY TO HYPERSAFETY

INTRODUCTION

Software take an increasing place in our society and are used in many critical systems:
- encrypt our communications
- manipulate health data
- secure banking transactions, etc.

It is crucial to ensure not only that these software are bug-free (safety), but also that they preserve the confidentiality of secret data they manipulate (security).

Safety vs. Security.
- **Safety**: no bugs (e.g. crash due to a division by 0) along *one execution* of the program.
- **Security**: a program does not leak secret (e.g. crypto keys) to an attacker.
  Relates *pairs of executions* (2-hypersafety).

Problem.
We have automated bug-finding tools for safety, but we lack automated bug-finding tools for 2-hypersafety.

Goal.
Adapt automated bug-finding tools for safety to security (2-hypersafety).

We focus on a crucial 2-hypersafety property to protect against timing attacks: constant-time.

BINARY ANALYSIS AGAINST TIMING ATTACKS

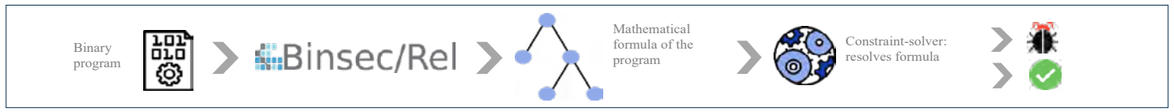
Timing attacks exploit the execution time of a program to leak secret data.

```
bool password_check(guess, pass, length) {
  for (int i = 0; i < length; i++) {
    if (guess[i] != pass[i]) return false;
  }
  return true;
}
```

Constant-time programming ensures that execution time is independent from secrets. Implemented in cryptographic libraries like OpenSSL, BearSSL, Libsodium, etc.

Challenges of constant-time analysis:
- 2-hypersafety → requires to reason about pairs of executions efficiently
- Not necessarily preserved by compilers → requires binary analysis

Our contributions [1]:
- Binary-level RelSE, a new relational symbolic execution technique for constant-time analysis at binary level
- Based on dedicated optimizations (speedup of 2 orders of magnitude)
- Implementation in the Binsec/Rel tool: found 2 new bugs introduced by the compiler & new security proofs at binary-level for 296 crypto binaries



WHEN PROCESSORS SPECULATE AGAINST US

In 2018, Spectre attacks [2] exploit optimizations based on *speculative execution* in processors to open new possibilities for timing attacks, even in constant-time programs.

New challenge: Efficiently model the speculative behavior of the processor to protect software against Spectre attacks.

Our contributions (under submission):
- HauntedRelSE: new optimizations for constant-time analysis under speculation
- Implementation & experiments on crypto
- New attacks & countermeasures

CONCLUSION

We work on closing the gap in **automated bug-finding techniques** between safety and **hypersafety**.

Applications to **security analysis** of **cryptographic programs** against timing attacks.

We developed a tool, **Binsec/Rel**, for **constant-time** analysis at **binary-level** and extended it to encompass new classes of **Spectre** attacks.

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Ms Mercedes Haeich

PURE MATHEMATICS

Connecting universes thanks to mathematics

UNIVERSITÉ DE RENNES 1 — IRMAR

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STUDYING DIFFERENTIAL EQUATIONS THROUGH DIFFERENTIAL ALGEBRA AND ALGEBRAIC GEOMETRY

INTRODUCTION

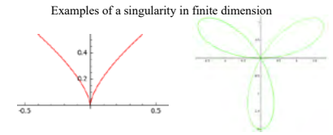
Differential equations occur naturally in a wide range of fields, from physics to biology including finance.

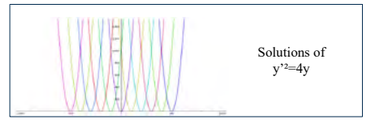
Each solution of these equations cannot always be described effectively. Another way to understand them is to study the whole set of solutions.

More precisely, the set of the solutions of a system of differential equations can be endowed with a geometrical structure : a scheme structure.

In the case of differential equations, the geometrical object obtained is of infinite dimension.
However, it is possible to identify certain specific points - which are solutions of the system of differential equations - as singularities.

Examples of a singularity in finite dimension





Algebraic geometry provides tools to study singularities in finite dimension, for example the formal neighbourhood of a point. The goal is to use these tools to study the singular solutions of differential equations.

MATERIALS AND METHODS

The study of differential equations with a algebraic point of view has opened a new sub-discipline called differential algebra. It has been introduced by J. F. Ritt in the 50's and developed by his student E. Kolchin.

From left to right :
J.F. Ritt, E. Kolchin

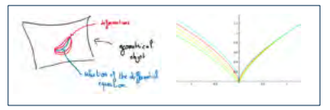
The differential equations that can be considered in differential algebra, are algebraic ones, that means they have a polynomial form.

As in classical algebra, the solutions of the differential equations are encoded by the differential ideal generated by the system of differential equations -that is a set stable under the natural operations that can be done on differential equations. For example if an element is in a differential ideal, then its derivative is also in it.

A better way to understand the equations is to find their prime factor decomposition.
The algebraic method to do that is to write the differential ideal generated by the differential equations as an intersection of prime differential ideals.
The low power theorem from J.F. Ritt gives a way to identify some of the prime differential ideals -called essential components- involved in the decomposition of an differential ideal generated by only one equation.

EXPECTED RESULTS

Let stick to the case where only one differential equation is considered. The set of solutions of this differential equation can be seen as a geometrical object, At a point of this object -which corresponds to a solution of the differential equation-, the goal is to understand the existence of singularities by looking at the deformations of the point. Or, more precisely, at the dimension of some kind of tangent space called the embedding dimension.



At a point that is not singular -a condition described by the fact that a certain equation does not vanish-, the embedding dimension only depend of the order of the differential equation and is finite.

However, at a singular point the embedding dimension may decrease.

Some examples and special cases suggest a link between the existence of essential components and the decreasing dimension of the tangent space at some singular points, even if the nature of this link is still unknown.

CONCLUSION

The geometrical object defined by the solutions of a system of differential equations is, in general, of infinite dimension.
In the frame of algebraic geometry, geometrical objects can be entirely described by rings.
The rings that encode infinite dimensional objects are in a family called non-Noetherian rings.
Studying the set of solutions of differential equations may deepen the knowledge about geometry in infinite dimension and non-Noetherian ring, where most of the known theorems do not apply.

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ROBOTICS & AUTOMATIC CONTROL

Developing prostheses to restore the taste for music or sport

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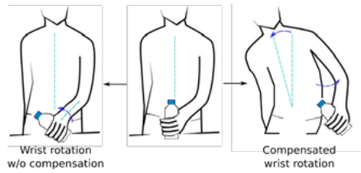
A CLOSED-LOOP AND INTUITIVE CONTROL FOR UPPER-LIMB PROSTHESES BASED ON BODY COMPENSATIONS

INTRODUCTION

With the latest advances of mechatronics, the motion possibilities of upper-limb prostheses have increased a lot. Yet, they are not fully exploited by users because the control remains highly challenging.

The muscular fatigue and the mental burden induced by current control approaches often lead prostheses users to employ their device as a rigid tool and move their end-effector with compensatory movements [1].

Body compensations are indeed efficient to achieve many tasks, but they are to be avoided since they cause musculoskeletal disorders.



We propose to take advantage of this natural reaction to control the device: the hand's position and orientation will be achieved by the human subject while prosthesis motions will correct the human posture.

Upper-arm amputee wearing a prosthesis

MATERIALS AND METHODS

Contrary to what is usually considered, the function of the prosthesis is not to perform a specific task in joint- or end-effector space but to control and optimize its user's posture, while the latter is in charge of the task.

The prosthesis is served to its user's body compensations in order to reduce them. This assumes a human-robot coupling, in which the user reacts to the prosthesis motions.

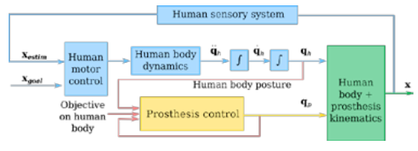


Diagram of the proposed control scheme: the prosthesis detects body compensation and moves to cancel them.

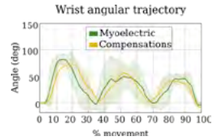
We have tested this concept on various experimental set-up, to control either wrist pronosupination [2] or elbow flexion/extension [3] of an upper-arm prosthesis.

Able-bodied wearing an emulated prosthesis as well as amputated people wearing their own device participated to this validation. They have no information on how the controller works, to assess the natural character of the concept.

RESULTS

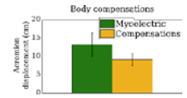
The proposed control scheme was compared to both natural motions (with able-bodied participants) and motions performed with the conventional control of the amputated participants (myoelectric).

Emulated prosthesis for able-bodied participants



Results are similar for wrist and elbow control: the task is well performed and prosthetic joint motions based on body compensations reduction are similar to natural or conventional control.

It was checked that using body compensations as prosthesis controller input does not enhance them.
Amputated participants also reported that compensations-based control was easier and less tiring to use than their proper one.



CONCLUSION

Using upper-limb prosthesis to correct the user's posture, while letting him/her in charge of positioning and orientating the hand, allows a natural control of the device. Without any specific knowledge and with very few training, subjects managed to perform different tasks.

Validated on individual joints, the proposed concept can be adapted to simultaneously control several joints. It opens new possibilities for an intuitive upper-limb prosthesis control.

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Ms Cécile Patte

MECHANICAL ENGINEERING

From puzzles to scientific challenges

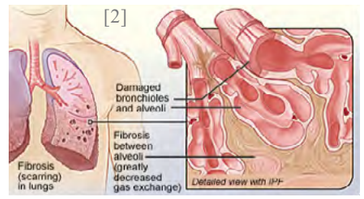
INRIA & École Polytechnique

Palaiseau, France

PATIENT-SPECIFIC PULMONARY MECHANICS: MODELING, ESTIMATION AND APPLICATION TO PULMONARY FIBROSIS

INTRODUCTION

Lungs are vital organs where gas exchanges take place. During breathing, they undergo large deformations to make air flows in and maximize the alveolar surface area available for gas diffusion.
However, some pulmonary diseases impact lung compliance, like Idiopathic Pulmonary Fibrosis (IPF) which makes lung stiffer and reduces lungs function [1].

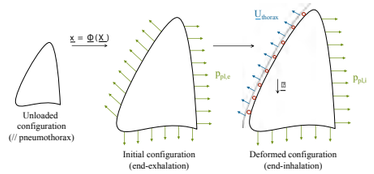


The present work aims to:
- better understand pulmonary mechanics
- address clinical diagnosis and prognosis challenges using numerical modeling.

Thus, a patient-specific poromechanical model at organ spatial scale and breathing time scale is developed using clinical data.

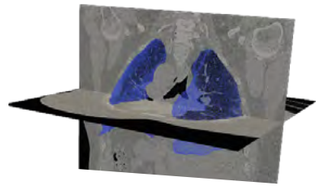
MATERIALS AND METHODS

1- Pulmonary poromechanical model
- constitutive law from experimental data able to reproduce lung volume response to a pressure change



- physiological boundary conditions
- definition of both effective and absolute compliance using porosity
- estimation of unloaded configuration

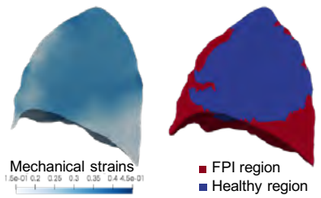
2- Model personalization using data
- 3D CT scans at two timesteps
- Patient-specific lung geometry generated with image segmentation [3]
- Lung displacement field computed with image registration [4]



- Inverse problem to estimate regional mechanical parameters: minimization of the difference between model and data

RESULTS

So far, the personalized model has been applied on one healthy control and one IPF patient.
- Improvement of accuracy of the model to the data when considering two random regions in lungs. Even better results when regions match with the disease segmentation.
- Better model accuracy with absolute than effective compliance → validation of poromechanics choice.



- Effective compliance smaller in the fibrosis region than in the healthy region → coherent with the current knowledge of IPF.
- Same trend for absolute compliance → diseased solid tissue stiffer than healthy solid tissue.
- Impact of IPF on mechanical stress distribution → study of the hypothesis of a mechanical vicious circle in place for IPF (fibrosis → high stress → fibrosis) [5].

CONCLUSION

The present model allows to quantify mechanical aspects of IPF with estimation of regional compliance.

After validation on more patients, it can be used for IPF diagnosis, as an objective and quantitative tool.

With longitudinal data, it could be used for prognosis or to test drugs impact.

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Acknowledgements: **Dominique Chapelle** and **Martin Genet**, my two thesis supervisors – **Jean-Francois Bernaudin, Pierre-Yves Brillet, Hilario Nunes** and **Thomas Gille**, clinicians from Avicenne APHP Hospital, who brought the subject and the data – **Catalin Fetita**, for images segmentation.

Ms Marie-Morgane Paumard

COMPUTER SCIENCES

How artificial intelligence can support archeology

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JIGSAW PUZZLE SOLVING METHODS WITH DEEP LEARNING FOR HERITAGE

INTRODUCTION

Reassembly of archaeological artifacts is a challenging and time-consuming task that is automatable with computer vision. The standard approaches are contours-based and semantics-based.
As fragment erosion may lead to weak contour-based reassemblies, we propose to use a neural network that infers semantics and performs reassembly. We use square fragments to prevent it from learning with their contours.

Using deep learning for jigsaw puzzle-solving is new: most authors settle for solving the standard 3×3 fragments puzzle task and do not address the major issues of heritage reassembly, namely missing and extra fragment.

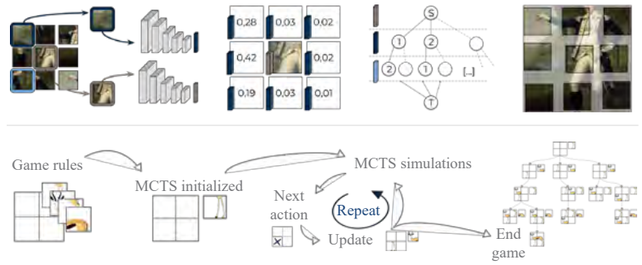
Our Deepzzle method improved the reassembly quality for both the standard and the heritage tasks, yet the computed reassemblies are based on semantic cues obtained from a single fragment rather than the whole dataset.

We introduce Alphazzle to overcome that limitation and increase the jigsaw puzzle size seen by the neural network. As expected, it delivers more consistent reassemblies.

METHODS

Deepzzle [1,2] proceeds by comparing all the fragments to a significant one, ordering them by probable relative positions, and thus minimizing the joint probability for composing a reassembly.

Alphazzle [3] builds on AlphaZero. It uses a single-player MCTS that places recursively one fragment after another. The decision policy is devised by two neural networks, P and V.

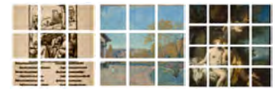


RESULTS

We outperform state-of-the-art results by 15% on the standard task with Deepzzle; Alphazzle even performs 10% better on our heritage dataset.

We also significantly reduced the complexity of the standard puzzle-solving algorithms, allowing us to increase the number of considered fragments to 15 for Deepzzle and 25 for Alphazzle.

Besides missing and extra fragments, we solved with Deepzzle puzzles whose fragments have been digitized under various conditions, which proves its efficiency and robustness.



With Alphazzle, we demonstrate that the game reward does not have to be known and can be estimated by V. Plus, this estimation is more precise than the action predicted by P.

CONCLUSION

Puzzle-solving is a very specific problem, and its impact can be seen on many applications, including among other things: forensic science, genome, biology, cryptography, medicine, and archaeology.

In our work, we proposed two original methods that advanced state of the art, as well as new tasks for heritage.
The next step is to apply our algorithms to heritage digitized data, such as 3D-scans and photogrammetry.

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Dr Liat Peterfreund

INFORMATION SCIENCE

Mathematics and data to transform everyday life

ENS Département Informatique | PSL | cnrs | Inria | FSMP Fondation Sciences Mathématiques de Paris

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FOUNDATIONS OF GRAPH QUERY LANGUAGES

INTRODUCTION

Property graph databases use graph structures to represent and query data and arise in a plethora of domains such as social networks, retail, banking, and more.

Retail

Social Networks

In the **academic community**, the study of graph databases is very active (see surveys [1, 2]).

In **industry** graph databases have gained popularity in the last decade with companies such as Amazon, Oracle, and SAP producing their own graph database products, in addition to many independent companies offering graph databases for many aspects of data analytics.

MOTIVATION

Various graph query languages look like different **dialects** of the same language:

- Cypher by Neo4j
- PGQL by Oracle
- GSQL by TigerGraph
- GCore by LDBC (Linked Database Benchmark Consortium - consists of partners from academia and industry)

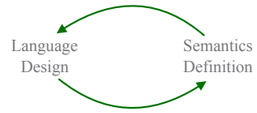
```
Cypher 9
FROM languageGraph
MATCH (a:Engineer)-[:LIKES]->(l:Language)
WHERE (l)-[:SUPPORTS]->(:Feature {name: "Pattern Matching"})
RETURN a.name, l.name

PGQL 1.1
SELECT a.name, l.name FROM languageGraph
MATCH (a:Engineer)-[:LIKES]->(l:Language)
WHERE EXISTS {
  SELECT *
  MATCH (l)-[:SUPPORTS]->(:Feature {name: "Pattern Matching"})
}

G-Core
SELECT a.name, l.name
MATCH (a:Engineer)-[:LIKES]->(l:Language) ON languageGraph
WHERE EXISTS {
  CONSTRUCT ()
  MATCH (l)-[:SUPPORTS]->(:Feature {name: "Pattern Matching"})
  ON languageGraph
}
```

In the world of relational databases, there is much **uniformity**: almost all commercial products use **SQL**. In graph databases, there is no such uniformity yet. This led to a joint decision of Neo4j and Oracle, under the auspices of ISO and W3C to create **GQL** a new standard for graph languages that will play the same role for graph databases as SQL for relational databases.

METHODS

Formal Semantics of GQL

Defining properly and accurately the semantics enables to reason formally about the language — to verify correctness of programs, to analyze their complexity, to check correctness of optimizations, and more.

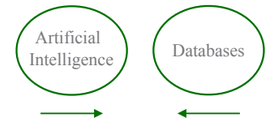


Incomplete Information

The flexibility of property graph databases makes them more prone to incompleteness which arises various challenges.

Fraud Detection (Banking)

Bridging the Gap



In the past, these two were considered as different and separated fields of research. Nevertheless, recently the gap is narrowing as they can benefit from each other: using knowledge to infer answers, doing machine learning in databases, handling incompleteness, and more.

CONCLUSION

Providing a formal semantics of a language is crucial for understanding it, using it properly, and avoiding confusion.

Not only it is an involved task, but also it emerges various intriguing research directions and challenges.

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COMPUTER SCIENCES

Combining sophistication and security of information systems

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ADVANCED CRYPTOGRAPHY FROM LINEARLY HOMOMORPHIC ENCRYPTION

INTRODUCTION

Cryptographic protocols protect information systems against malicious abuse, while ensuring a controlled flow of information.

Advanced cryptographic systems deal with the complex tasks raised by our current use of information systems (e.g. computations involving inputs from multiple parties, or the delegation of computations from constrained devices to powerful servers).

Naturally, the stronger the adversary one wishes to protect against, and the more complex the task at hand, the heavier (in terms of computation time and bandwidth consumption) the resulting protocol tends to be.

Honest but curious adversary Follows protocol. Gets information by observing the system.

Malicious adversary Deviates from protocol (unexpected inputs, induce system crash…) to cause information leakage.

My research aims at devising advanced cryptographic protocols — securing large scale information systems against increasingly powerful adversaries — while incurring minimal overhead.

TOOLS AND METHODS

Castagnos and Laguillaumie in [1] introduce the CL framework, which can be implemented from class groups of orders of imaginary quadratic fields.
In this framework they create a linearly homomorphic encryption scheme with an uncommon feature:

One can choose the size of the message space.
→ Efficiency gains by fitting message space according to application.

Linearly Homomorphic Encryption

We enrich their framework by:
- formalising hardness assumptions.
- building projective hash functions (PHF) [2] with homomorphic properties from these assumptions.

PHFs abstract away the essential properties of the framework.
→ Genericity in subsequent work.
Homomorphic properties provide malleability.
→ Combine PHFs to build advanced cryptographic systems.

EXPECTED RESULTS

These PHFs allow to build a variety of advanced cryptographic primitives [3,4,5], among which secure multiparty computation (MPC) protocols requiring remarkably little bandwidth consumption.

MPC: Computing protocol that allows ≥ 2 parties to jointly compute a function while keeping data supplied by each party private.

They have allowed for the construction of multi-party digital signatures [4,5], where the function to be computed in MPC is a digital signature.

Distributing digital signatures significantly reduces the risk of key theft — allowing a malicious party to sign on behalf of the original key owner — as key shares are spread over multiple devices and so are hard to steal. Applications include securing crypto-currency wallets and custody solutions.
We expect to extend these results to more general MPC protocols.

CONCLUSION

Tools built from the CL framework allow:
Construction of a range of advanced cryptographic primitives
Control over space in which sensitive information is encoded
→ Improved efficiency

This project aims at:
Finding applications most suited to using the CL framework
Devising **lightweight** cryptographic protocols
→ Can be deployed in large scale information systems.

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