Highlights

2022

Cermav

Centre de Recherches sur les Macromolécules Végétales

A word from the director

While they have become rather commonplace, and definitely widely shared, the various environmental and climatic emergencies are an object of major societal concern, as are the advances in diagnoses and therapeutic solutions requiring a thorough understanding of the biological mechanisms at work. In a very consensual way, research and innovation are part, alongside the rationalization of resources and sobriety in consumption, of the arsenal of solutions allowing us to propose ways of improving both the quality of life in the broad sense and our common carbon footprint.

Gylcosciences, the science of carbohydrates, occupy a special place in this landscape: although omnipresent in our daily lives as the most abundant molecules produced by living organisms, including primarily terrestrial plants, algae, bacteria, insects or crustaceans, sugars are also present in the signaling of living beings, including higher animals. Alongside proteins, nucleic acids and lipids, they form a class of very complex molecules whose code is particularly difficult to decipher. In the same way, many materials, which mankind has used for thousands of years in the field of energy, food, construction but also obviously food, are made up of a controlled chain of these molecules. The mission of CERMAV is to contribute to the progress of these sciences in terms of knowledge production and innovation progresses.

Laurent Heux
Head of CERMAV

Contents

General presentation of CERMAV

Founded in 1966, the CERMAV has now 55 years of research and innovation in the field of Glycosciences. It was conceived at its foundation as an institute devoted to fundamental research on cellulose and lignin, as a complement to the Ecole d'ingénieur de papèterie and the Centre Technique du Papier. The institute has subsequently evolved towards a broader approach to the field of Glycosciences, such as the study of the diversity of polysaccharides, whether they are of plant origin, but also microbial, animal or even modified by man, their use as gels or biosourced materials, or the biological role of sugars and proteins that recognize, synthesize or degrade them Supported by teams of researchers and technicians of very high quality, CERMAV has developed over the years a variety of skills that allow it to explore multidisciplinary scientific and technological fields addressing various societal issues.

The CERMAV is thus structured in 5 teams corresponding to a thematic richness combining molecular biology, biochemistry, chemistry of oligosaccharides and glyco-conjugates, modification of polysaccharides in homogeneous, gel or heterogeneous phase, synthesis, structuring and properties of glycopolymers or glycomaterials. This research is structured in 3 axes that include the study of the structure and organization of polysaccharides, glycans for health and functional glycomaterials. This scientific diversity is supported by the highest level of characterization tools adapted to the study of these very specific molecules and materials: CERMAV is internationally recognized for its skills in structural and ultrastructural characterization of oligo- and polysaccharides. In addition to these advanced technological capabilities, the laboratory has a very good knowledge of the substrates, their production and their transformation, which makes it one of the most internationally recognized centers in the study of carbohydrates.

Resolutely turned towards the future and the progression of knowledge, the CERMAV proposes an approach combining progress in fundamental science and technological innovations. It is a major and quite unique research center in the field of Glycisciences at the national, European and international levels. Since its creation, it has been very much involved in partnership research, and more recently it has also been at the origin of development projects that have taken the form of maturation initiatives or start-up creation. It is now tackling new scientific challenges such as integrated synthetic biology for the synthesis of new molecules, green and biomimetic materials for health, databases of proteins that act or recognize sugars, etc.

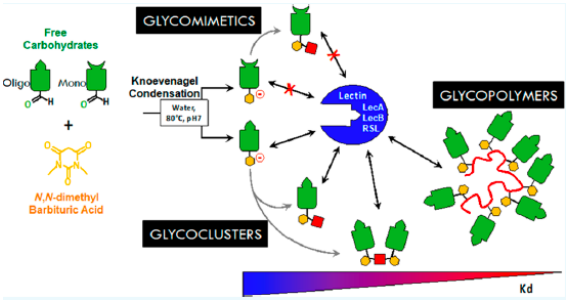
These highlights are an overview of the diversity of projects and approaches developed at CERMAV over the last few years, illustrating the vitality of the Institute in the field of Glycosciences.

Axis 1. Design of functional and intelligent materials

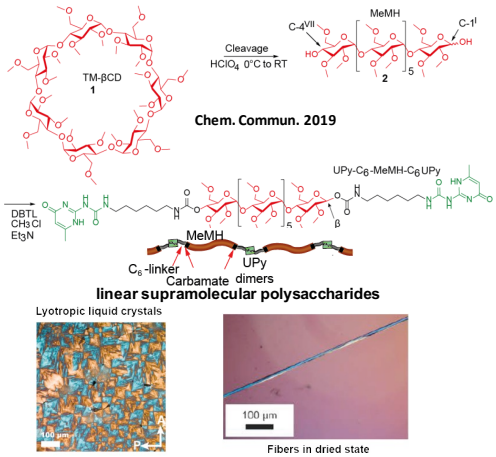
Functionalization and coupling of oligo- and polysaccharides

Glycoengineering for controlled design of carbohydrate ligands of pathogenic lectins and supramolecular polysaccharides (contact: Sami Halila)

Glycoconjugates and polysaccharides are ubiquitous in Nature. They play a critical role in a wide variety of biomechanical, biological and pathological processes acting as scaffold, signaling, recognition and adhesion molecules by interacting between them through self-assembly or with



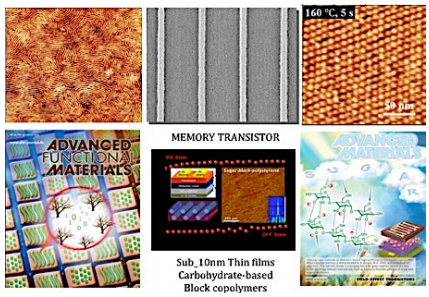
carbohydrate-binding proteins such as lectins or growth factors. Major scientific and biotechnological interests in accesing glycoconjugates or polysaccharides derive from the promise to use them, for instance, as probes for diagnostics tools or as smart biosourced materials. In our group, we recently proposed convenient synthetic approaches to glycoconjugates and α,ω-end functionalized oligosaccharide building blocks. We demonstrated that *N*,*N*'-substituted barbituric acid is a versatile and modular chemical platform for Knoevenagel condensation with unprotected carbohydrates (*Eur. J. Org. Chem.*, **2019**, *36*, 6158) leading to multifunctional *C*-glycosides. Additionaly, monovalent to polyvalent carbohydrate ligands were easily obtained and showed strong interactions with pathogenic lectins (*Bioconjugate Chem.* **2019**, *30*, 647). On the other hand, both end-functionalized maltoheptaose with UPy stickers was reached from a key step of single ring opening of per-protected β-cylodextrin. The resulting amylose-like linear supramolecular polysaccharide, featured by directed self-assembled "glycosidic" linkages, showed lyotropic liquid crystals properties with an ability to form fibers (*Chem. Commun.*, **2019**, *55*, 11739). Since this first ever built supramolecular polysaccharide exhibits reversible bonds, it should give adaptative glycomaterials with, for instance, self-healing properties.



Self-assembly of gels, nano-objects, liquid crystals and surfaces

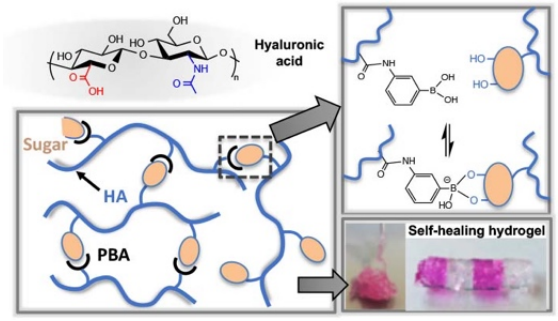
Self-assembly of glycopolymers: highly nanostructured thin films and glyconanoparticles (contact: Redouane Borsali)

Nano-organized thin films and nanoparticles that find applications in immerging nanotechnology are made today from synthetic polymers and more precisely from block copolymer systems. Most of these systems are derived from petroleum and their self-assembly is often limited to 20-30 nm resolutions (domain and size spacing) but also to short-range order. These features are highly limiting for the development of new generation of nanodevices and the main reason comes from a relatively weak interfacial incompatibility between both blocks. To overcome these bottlenecks, there is a growing interest in high-resolution patterned thin films with long-range order that derive from the promise of individually manipulating polymer chains using the bottom-up approach, via self-assembly, to create the next generation of nanostructured materials with smaller size and long-range order, improved performance and functionality compared to those provided by top-down conventional manufacturing technologies. The approach we are developing in the group is the design and the nanofabrication of novel oligosaccharide-based block copolymers with highly segregating strength to control the domain size (nanoparticles), orientation and long-range order nanostructured thin films for the next generation with high-resolution sub-10nm patterning (*Adv. Mater.* **2015**, 27, 6257; *Adv. Funct. Mater.* **2016**, 24, 4240; *Adv. Mater.* **2017**, 29, 1701645; *Adv. Funct. Mater.* **2017**, 27, 1).



Injectable hyaluronic acid-based hydrogels for tissue engineering and regenerative medicine (contact: Rachel Auzély)

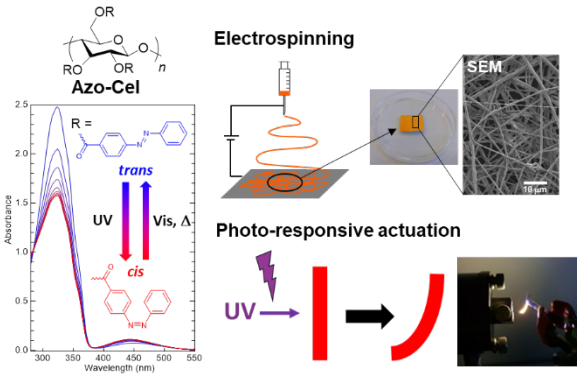
Injectable hydrogels that are capable of autonomous healing upon damage have recently drawn great attention in the fields of tissue engineering and regenerative medicine for minimally invasive delivery of cells and in the filling of irregular defects. These hydrogel networks possess adaptable linkages that can be broken and re-formed in a reversible manner without external triggers. This feature is conducive to the homogeneous entrapment of cells *ex vivo* under physiological conditions. This also allow such hydrogels to be pre-formed into syringes, extruded under application of shear (needle injection), and show rapid recovery of their mechanical properties when the applied stress is removed (i.e. self-healing). In this regard, SMP group developed a new family of injectable and self-healing HA hydrogels based on reversible boronate ester bond formation (*Soft Matter* **2020**, 16, 3628-3641; *Biomacromolecules* **2020**, 21, 230-239; *Polymer Chem*. **2020**, 11, 3800-3811). Their rapid formation by mixing the HA partner derivatives (HA modified by phenylboronic acid (PBA) groups and by sugar units), allow cell encapsulation without damaging them. Indeed, these original materials showed a high cell viability as demonstrated by 3D cell encapsulation for several days. Preliminary in vivo studies also demonstrated that it is possible to easily inject them intracerebrally in the rat. Therefore, current research is focusing on using these injectable hydrogels to facilitate delivery of human stem cells and protect them and, thereby enhance neural repair after stroke. The protection provided by these HA hydrogels can be attributed to their mechanical and compositional similarities with brain tissue.



Stimuli-sensitive systems

Electrospinning of light-harvesting polysaccharides: towards sunlight-driven smart green nanomaterials (contact: Issei Otsuka)

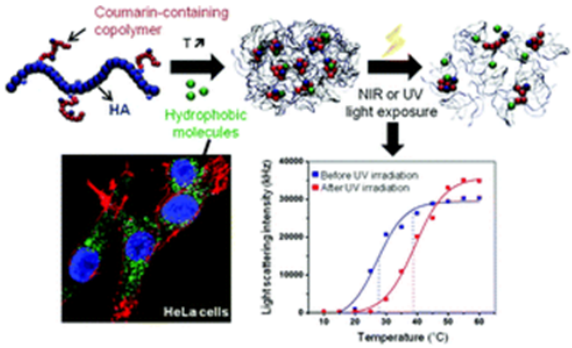
Poly-/oligosaccharides are one of the most abundant raw materials derived from biomass and renewable resources from forestry. The spotlight has been on not only their potential as alternatives for petrochemicals, but also their superior properties as biocompatible, biodegradable, and bioactive natural materials. They are also well-suited for development of stimuli-responsive polymers, which have received intense recent study since the behavior of these polymers can be controlled by simple changes of their surrounding media. Among the wide variety of stimuli-responsive polymers, photo-responsive polymers in particular have recently attracted much attention since the stimulus (light) can be precisely localized in time and space, and can also be triggered remotely from outside the system. Because of a large previous scientific gap between glycoscience and photo-science, these two research fields have not overlapped deeply yet. We prepared a photo-responsive nanofibrous textile made of an azobenzene-functionalized cellulose (Azo-Cel) via electrospinning for the first time (*Cellulose* **2019**, *26*, 6903). The novel cellulose-based textile varies its physical property (e.g. surface energy) via cis/trans isomerization of the azobenzene moiety in response to UV and visible light, leading the potential of polysaccharides to practical applications such as photo-responsive actuators for artificial muscles. This is an ongoing collaboration project with McGill University (Canada) as the PhD thesis study of H. A. Noahdani granted by France-Canada Research Fund and The French Ministry of Higher Education, Research and Innovation.



Thermoresponsive self-assembled nanoparticles for drug delivery (contacts: Anna Szarpak, Rachel Auzély)

In medicine, the doctors and the scientists search how the vehicles of nanometer size can be introduced into the human body and can play different functions such as transport of medicaments, specific organ recognition, drug release on demand, to treat specific diseases. The transport and release of enclosed medicaments is especially challenging, as it is necessary to enclose the drug and protect it from external environment during transport, avoid the release during carrying and release only when the target has been achieved. Thermoresponsive polymers which have tendency to self-assembly in water are the ideal candidates. Such polymers are soluble in water at low temperature, and undergo reversible phase transition with rising temperature, resulting in precipitation in form of the nanoparticles. In recent years, Structure and Modification of Polysacharides group (SMP) at CERMAV-CNRS developed thermoresponsive hyaluronic acid (HA) derivatives able to form nanoparticles. HA, a linear polysaccharide naturally present in vertebrate tissues and body fluids, is particularly interesting due to its non-toxicity, biodegradability and biocompatibility. In drug delivery systems, it is also used as a targeting molecule because it is recognized by cancer cells overexpressing the CD44 receptor. This polysaccharide modified with thermoresponsive ethylene glycol-based copolymers form well-defined nanostructures via temperature-induced self-assembly. It is possible to strictly control the temperature of nanoparticle formation by the design of the grafted copolymers, its size and density. Although most of thermoresponsive polymers show phase transition above ~32 °C, ideal, the self-assembled HA nanogels should be stable at room temperature required for good handling and biological application. We showed, that by suitable decoration of polysaccharides, it is possible to obtain nanogels stable at 20°C. Study of swelling–deswelling transition showed fully reversibility over multiple heating/cooling cycles (*Biomater. Sci.* **2019**, 7, 2850–2860).

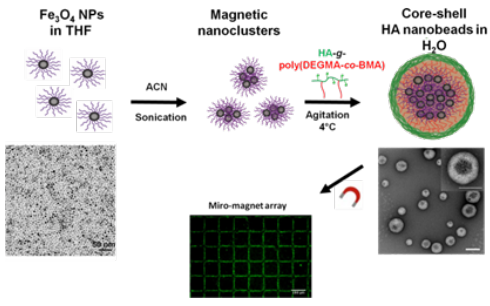
Thanks to the presence of the copolymer and the formation of hydrophobic nanodomains on HA chains, such nanoparticles can encapsulate hydrophobic molecules, like the anticancer paclitaxel. In order to release the drug on demand, a light sensitive molecule was introduced into the HA conjugate structure. Nanogels that are stable at body temperature contain hydrophobic esters of cumarin but dissassemble upon UV-irradiation due to the conversion into hydrophilic carboxylate groups (*Nanoscale* **2017**, 9, 12150–12162).



HA based nanogels prepared by such simple method can be covalently cross-linked inside the hydrophobic nanodomains Biomater. *Sci.* **2018**, 6, 1754–1763 or by covalent bridging of HA chains within hydrophilic shell (*Biomater. Sci.* **2019**, 7, 2850–2860). After injection into mice, the cross-linked nanogels were able to circulate in the bloodstream for a long period of time and accumulated in the tumor tissues.

Magnetic hyaluronic acid-based nanobeads (contact: Anna Szarpak)

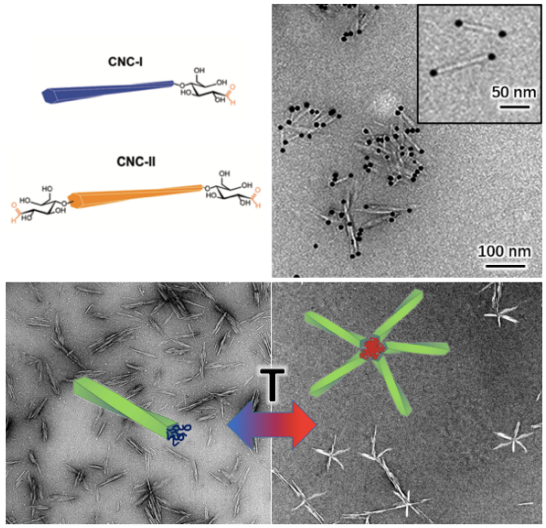
Magnetic nanoparticles (MNPs) may guide drugs to a site of interest in the body with the aid of a magnetic field, it can be used as contrast agent for magnetic resonance imaging (MRI) or can be heated upon application of an alternating magnetic field to destroy cancer cells in hyperthermia treatment. Most commonly investigated magnetic nanoparticles (MNPs) for biomedical applications are magnetite (Fe3O4), maghemite (γ-Fe2O3) and ferrites (mixed oxides of iron and other transition metals). The MNPs smaller than 30 nm exhibit superparamagnetic behavior, which means that in the absence of an external magnetic field have zero magnetization and less tendency to agglomerate. They undergo attraction only in presence of the external magnetic field. Such superparamagnetic iron oxide nanoparticles can form stable colloidal suspensions which is crucial for preparation of magnetically responsive drug transporters. However, if magnetic attraction is used for the drug guidance to the desired organ, such small individual nanocrystals have too low magnetization and cannot be attracted with a magnet. In order to improve the response upon exposure to an external magnetic field, the magnetic clusters can be performed. Clusters are aggregates of individual MNPs that still display superparamagnetic properties but profoundly enhance the magnetic moment of the overall assembly, making magnetic manipulation more effective, elevated MRI signal and better heating efficiency. The SMP group



developed the fabrication of magnetic clusters stabilized with amphiphilic derivatives of hyaluronic acid. Firstly, the superparamagnetic magnetite nanoparticles of 8 nm coated with hydrophobic oleic acid were synthesized. Secondly, by exchange of solvents at different polarities, the magnetic nanoparticles formed clusters of ~200 nm. Such hydrophobic clusters are not stable in aqueous conditions. Amphiphilic derivative of hyaluronic acid was used for the formation of hydrophilic shell. While hydrophobic chains grafted on HA interact with surface of magnetic cluster, the hydrophilic HA shell protects from uncontrolled aggregation, ensures stability and easy dispersion in aqueous conditions. The clustering of magnetite nanoparticles facilitates rapid attraction and controlled positioning by high field gradient micro-magnet arrays. In addition, clusters could be formed in the presence of a fluorescent drug model, which demonstrates the possibility of dual functionalization of our hybrid nanosystems: magnetic responsiveness and drug encapsulation.

Hybrid cellulose nanocrystals resulting from regioselective derivatization (contact: Bruno Jean)

Native cellulose nanocrystals (CNC-I) are biosourced nanorods that can be extracted from any cellulose source such as wood or cotton. These nanoparticles benefit from a strong attention from both the academic and industrial communities for the design of functional bio-based materials, targeting a wide range of applications (e.g. rheology modifiers in paints and cosmetics, packaging, biomedical area, etc.). This interest originates from their intrinsic properties (abundant and renewable origin, low density and exceptional mechanical properties, low toxicity and biocompatibility, chemical modification ability, etc.) associated with their organization in specific architectures (gels, aerogels, emulsions, etc.). Alternatively, nanocrystals of the allomorph II of cellulose (CNC-II) can be prepared. Both types of CNCs exhibit particular chemospecific characteristics that have only been scarcely exploited yet. Indeed, due to the biosynthesis process, CNC-I can be chemically derivatized at only one end of the rods, while both extremities of the CNC-II can be modified. We took advantage of this specificities to graft either gold nanoparticles or thermosensitive polymers at one end of CNC-I and on two ends of CNC-II. The labeling with gold enabled us to give insight into fundamental issues such as the interplay between CNC-I and their parent microfibril (*Carbohydrate Polymers* **2021**, 257, 117618) or to visually prove the antiparallel arrangement of cellulose chains in CNC-II. In the case of the grafting of thermosensitive polymers, the resulting hybrid particles assembled upon temperature increase into star-shaped aggregates composed of 3 to 6 nanocrystals attached by their end for CNC-I (*ACS Macro Letters* **2019**, 8, 345-351) or into supra-micron networks obtained through end-to-end associations for CNC-II (*Nanoscale* **2021**, 13, 6447-6460). These innovative assemblies were shown to exhibit tunable thermally-triggered gelation properties of interest for applications of CNCs as rheology modifiers.

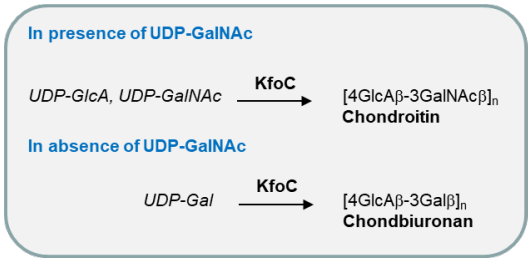


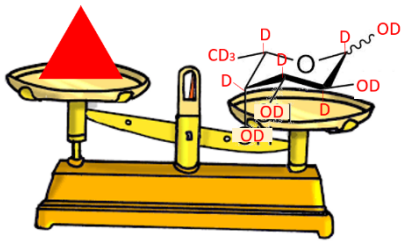
The cell factory

Contacts: Bernard Priem, Eric Samain, Anne Imberty

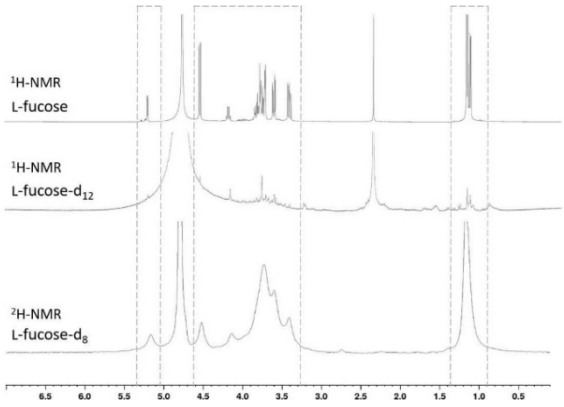
The cell factory process developed at CERMAV is the most attractive route for the *in vivo* synthesis of oligo- and polysaccharides of biological interest in large quantities. This technique involves a single step of high-density culture of a *E. coli* strain that has been genetically modified to contain all necessary metabolic pathways, including genes coding for glycosyltransferases but also those of nucleotide-sugar biosynthesis.

Glycosaminoglycans (GAGs) are among molecules of interest whose synthesis such as hyaluronic acid, heparosan, and chondroitin, can be achieved in genetically modified *E. coli*. Controlling the whole metabolic pathway of GAGs in a recombinant strain offers the possibility of tuning the level of expression of individual proteins belonging to multi-enzymatic complexes, in order to modify yield and structural features of the final product. In recent work, we have shown that when KfoC, the chondroitin synthase of *E. coli K4*, was overexpressed without UDP-GlcNAc 4-epimerase which provides UDP-GalNAc, one of the nucleotide-sugar of the synthesis, a new polysaccharide containing galactose instead of *N*-acetylgalactosamine and called "chondbiuronan" accumulated into the cells.





The cell factory can be also used for production of labeled sugar, such as perdeuterated L-fucose. A *E. coli* strain was modified with a 2'-fucosyltransferase gene from *Helicobacter pylori* and fucosidase gene from *Bifidobacterium bifidum*. In collaboration with the Institut Laue Langevin, with the use of a deuterium oxide-based growth medium and a deuterated carbon source, perdeuterated fucose was produced with a final yield of 0.2 g L^{-1}. The perdeuterated fucose produced in this way will have numerous applications in structural biology where techniques such as NMR, solution neutron scattering and neutron crystallography are widely used. In the case of neutron macromolecular crystallography, the availability of perdeuterated fucose can be exploited in identifying the details of its interaction with protein receptors and notably the hydrogen bonding network around the carbohydrate binding site.



Galactolipid synthases: key players in the biogenesis of photosynthetic membranes

Contact: Christelle Breton

Photosynthesis is the process by which atmospheric CO_2 enters the biosphere, producing glucose that is the source of all organic molecules that make up living organisms. Light energy is captured by photosystems inserted into photosynthetic membranes, which have a unique lipid composition comprising almost 80% galactolipids. Our recent advances suggest membrane biogenesis by extremely rapid lipid phase transition through the concerted action of galactolipid synthases.

A unique feature of chloroplastic membranes is their high content of the galactolipids monogalactosyldiacylglycerol (MGDG) and digalactosyldiacylglycerol (DGDG), which constitute up to 80% of their lipid content. Other lipids mostly consist of the anionic sulfoquinovosyl diacylglycerol (SQDG) and phosphatidylglycerol (PG). The galactolipids are essential for the biogenesis of plastids and the photosynthetic machinery. MGDG, which accounts for ~50% of total lipids, is a non-bilayer forming lipid due to its cone-like shape, whereas DGDG and other lipid components are bilayer-forming lipids. The fine-tuning of MGDG/DGDG ratio, could be a key factor in the biogenesis of chloroplast membranes.

In Arabidopsis, the bulk of galactolipids is synthesized in the chloroplast envelope membrane through the concerted action of two galactosyltransferases, MGD1 and DGD1, which use UDP-galactose as donor (Fig. 1). MGD1 is a monotopic membrane protein located in the inner envelope membrane of chloroplast. Major advance was recently obtained in the structural characterization of MGD1 (Fig. 2). A striking feature is the presence of a long and flexible region in the N-domain. This region seems to contribute to the anchoring MGD1 in the membrane and is essential to capture the DAG acceptor. The C-domain is mostly involved in donor-sugar binding. MGD1 needs anionic lipids such as PG to be active, and a mechanism involving a PG-His catalytic dyad has been proposed (Nitenberg et al., *Glycobiology* **2020**, 30, 396-406). Interestingly, the SQDG can fulfil the same role as PG. It remains to be determined which anionic lipid (SQDG or PG) will be the preferred MGD1 activator in planta. The role of phosphatidic acid (PA) in MGD1 activity is more puzzling. PA is barely detectable in chloroplast membranes but it acts as an allosteric activator of MGD1. Intriguingly, MGDG exerts a positive effect on MGD1, facilitating its binding to the membrane, whereas DGDG has a negative effect and tends to exclude the enzyme, thus illustrating the importance of the MGDG/DGDG ratio. These data suggest that MGD1 localizes to specific microdomains. To support this assumption, MD simulations showed that MGD1 induces a reorganization of lipids by attracting DAG molecules to create an optimal platform for binding (Fig. 3) (Makshakova et al., *Sci. Rep.* **2020**, 10:13514). A central question remains on how MGD1 recognizes and interacts with DAG. We are also addressing two other key questions, namely what is the molecular mechanism of PA-mediated MGD1 regulation, and the importance of galactose for the properties of chloroplast membranes.

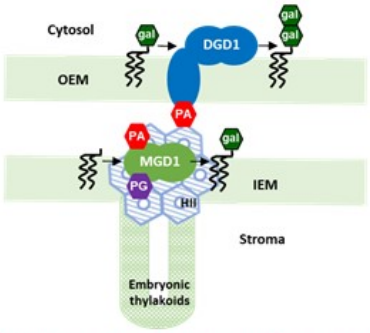


Figure 1. Biosynthesis of galactolipids in the chloroplast envelope membranes in Arabidopsis. The main pathway is mediated by MGD1 and DGD1 which provide the bulk of MGDG and DGDG in normal growth conditions.

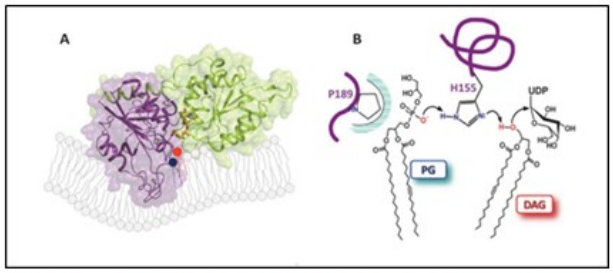


Figure 2. Proposed model for MGD1 membrane binding and reaction mechanism. (A) MGD1 partly embedded in the bilayer through its large and flexible region in the N-domain, which seems essential to the capture of DAG (red) and PG (blue) molecules. (B) Schematic representation of MGD1 active site showing the PG-His catalytic dyad capable of deprotonating OH group of DAG acceptor.

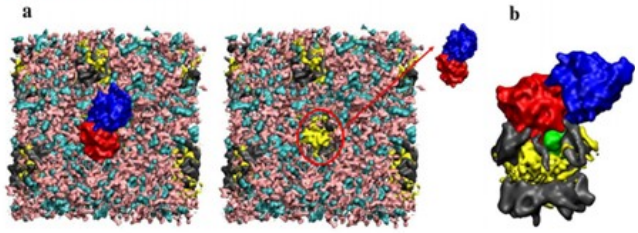


Figure 3. A snapshot of MGDG(cyan)/DGDG(pink)/PG(grey)/DAG(yellow) biomimetic bilayer and MGD1 (N-domain in red, C-domain in blue, LOOP in green) showing the accumulation of DAG in the vicinity of MGD1. (a) View from the top. (b) Frontal view of PG/DAG cluster with bound MGD1.

Chitinoligosaccharides and plant health

Contacts: Sébastien Fort, Sylvain Cottaz, Stéphanie Pradeau, Sylvie Armand

Chitinoligosaccharides are important signal molecules in plants. They can trigger immune responses and help plants defend themselves against pathogens or allow the establishment of symbioses with beneficial soil microorganisms for a better uptake of water and mineral nutrients. How do these molecules trigger such varied biological responses? Understanding of plant perceive chitinoligosaccharides will help develop a more sustainable agriculture.

Chitinoligosaccharides (COs) have been known for some thirty years to have beneficial activities in plants however, their mode of action is still misunderstood. Long chain COs, those with a degree of polymerization higher than five, are pathogen-associated molecular pattern which trigger plant innate immune system. Short-chain COs induce oscillations of the calcium concentration in the plant cell nucleus, which is a hallmark of early arbuscular mycorrhizal and root-nodule symbiosis signaling. Mutualistic relationships between a host plant and nitrogen-fixing bacteria or arbuscular mycorrhizal fungi enhance the supply of essential nutrients such as nitrogen, potassium or water to the host. Until the 2000's, lipochitinoligosachcarides (LCOs) were the only signal molecules known able to trigger those symbioses. Later on, short-chain COs were also shown to activate symbiosis signaling and very recent studies concluded that long-chain COs have this ability as well. How plants discriminate COs from LCOs and therefore pathogen from beneficial microorganisms still raises many questions today that remain to be elucidated. In this context, the CERMAV CBO team develops chemo-enzymatic methods to produce chitinaceous probes in order to decipher the complex biological functions of COs and related molecules. In the last years, important achievement was made in the synthesis of LCOs. *Sinorhizobium meliloti* chitin deacetylase NodB was produced in high yield in *E. coli* as a thioredoxin fusion protein (Fig. 1). The recombinant enzyme was expressed in soluble and catalytically active form and used as an efficient biocatalyst for *N*-deacetylation of chitin tetra- and pentaose allowing the synthesis of LCOs on gram scale (*Carbohydr. Res.* **2017**, 442, 25-30). Another important outcome is the discovery of a new generation of affinity-probes to study carbohydrate-protein interactions. Triazinyl-glycosides derived from COs were shown for the first time to allow covalent labelling of CO-binding proteins without any photoactivation requirement (Fig. 2). This remarkable property of triazine was efficiently applied to other classes of sugars and their binding proteins (*Bioconjug. Chem.* **2019**, 30, 2332−2339). At least, long-chain COs produced in the group contributed to unravel for the first time how plant discriminate COs from LCOs. Unknown motifs in the LysM1 domain of COs and LCOs receptors were identified as determinants for immunity and symbiosis (Fig. 3). Only very few, but important, residues separate an immune from a symbiotic receptor and it is now possible to reprogram LysM receptors by changing these residues (*Science* **2020**, 369, 663–670). The long-term goal is to transfer the unique nitrogen-fixing ability that legume plants have into cereal plants to limit the need for polluting commercial nitrogen fertilizers and to benefit and empower the poorest people on Earth.

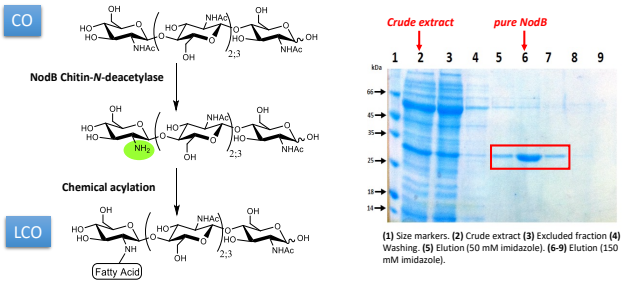


Figure 1. *In vitro* chemo-enzymatic synthesis of LCOs using NodB chitin-*N*-deacetylase

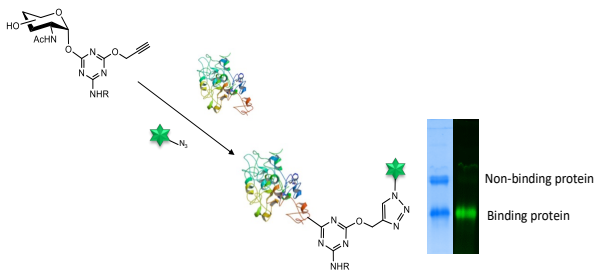


Figure 2. Specific carbohydrate-binding protein labeling with triazinyl-glycosides

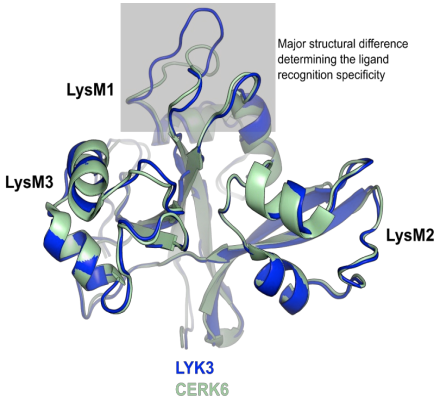


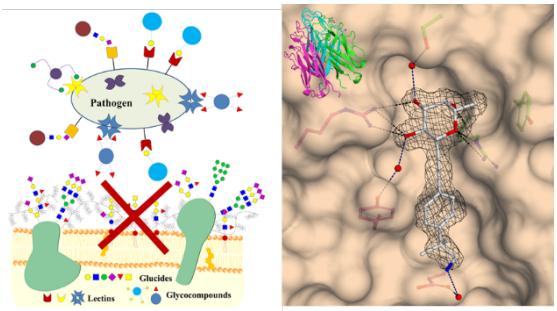
Figure 3. Superposition of the crystal structures of the Nod Factor receptor LYK3 (blue) and the chitin receptor CERK6 (green). Credit: M. Blaise

Lectins for deciphering the glycocode

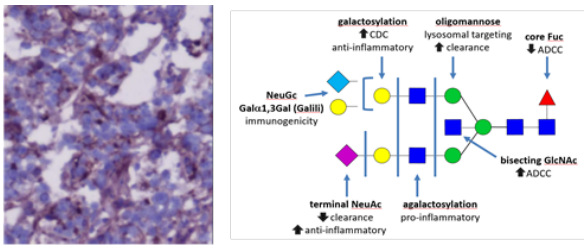
Contacts: Anne Imberty, Annabelle Varrot

Lectins are carbohydrate binding proteins able to specifically recognize glycans, in particular the glycoconjugates covering any cell surface. They are protein receptors essentials in many cellular processes: tissue cohesion, immunity or cell signalling but also, in pathological processes such as infections. Lectins are the ubiquitous translators of sugar-encoded information or glycocode and hence, have great potential for biotechnological and biomedical applications.

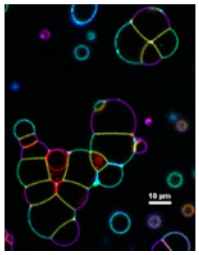
Lectins play an essential role in host-pathogen interactions, either as a first-line defense molecule against foreign organisms or by promoting microbial adhesion, a crucial step in the initiation of infection. They use multivalency to enhance affinity and selectivity for their interactions to attain biologically relevant strength. We have identified and characterized biochemically and structurally at least eigth lectins from bacterial and fungal opportunistic pathogens responsible of life-theatening and hospital-acquired infections (HAI). Those are actively targeted for the development of glycodrugs for anti-adhesive therapy as new anti-infective drugs. Some compounds have revealed good potential and also present anti-biofilm properties. Information on multivalency obtained either by oligomerisation and/or tandem repeats are essential for design of highly specific and selective glycodrugs.



The glycome is hallmark of cell identity and fate but also a signature of health and disease. Lectins can discriminate particular glycan patterns in their environment, depending on their accessibility and density characteristics. They are therefore sought-after biomolecular tools for analysis of glycosylation whose alterations are often associated with diseases such as cancers where they can aid in the diagnosis and prognosis as they can differentiate healthy cells from cancerous cells. They can be used also for controlling the glycosylation of biotherapeutic products. 30 lectins of diverse origins are available in recombinant form in the GBMS group with a large panel of specificity and fold.



New lectins are of interest in biotechnology. Two strategies are developed for bringing these new tools to the community. Lectins can be searched by data mining approaches in the ever-growing numbers of newly sequenced genomes of various organisms. A web portal (Unilectin) has been designed for gathering all known structures of lectins and for identifying in translated genomes. At the present time 570 000 putative lectins have beren identified. The other approach used synthetic biology for engineering novel lectins, either by introduction non-natural amino acids in their binding site or by modifying their architecture. Janus lectins with two faces bining to different glycans were built by linking domains from different species. They have been used for supramolecular assembly of sugar/ protein sandwiches and for gluing together different tipes of giant vesicles, creating pseudo tissues.



Axis 3. Polysaccharide structure and cell wall architecture

Morphological and structural diversity of amylose inclusion complexes

Contact: Jean-Luc Putaux

Amylose, the linear constituent of native starch amylose has the remarkable property to form so-called "V-amylose" crystalline complexes with a large variety of small organic molecules (alcohols, flavors, lipids, etc.). Compounds that are poorly soluble in water can thus be encapsulated in a starchy matrix and released later in specific conditions and media, with potential applications in the food and pharmaceutical industries.

Starch is the main form of carbohydrate used by plants to store carbon and energy. Together with cellulose, this natural homopolymer of glucose is one of the most abundant biological substances in the biosphere. It is the main source of calories for humans as well as an important raw material for non-food applications (adhesives, paper, bioplastics, etc.). Starch is biosynthesized in the form of 1-100 µm semicrystalline granules, insoluble in cold water, composed of a mixture of two macromolecules: the mostly linear amylose (20 wt%) and the branched amylopectin. While it is considered to be amorphous in native starch granules, when crystallized *in vitro*, amylose can form so-called "V-amylose" crystalline complexes with many types of small organic molecules. Depending on the guest molecule size and conformation, amylose forms single helices made of 6, 7 or 8 glucosyl units per turn, organized into different unit cells. The complexing molecules can be entrapped inside the helices, in-between, or both (Fig. 1).

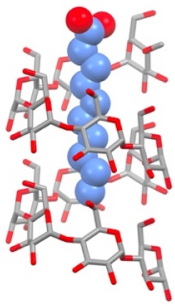


Figure 1. Molecular model describing the encapsulation of a linear fatty acid inside the hydrophobic cavity of a 6-fold amylose single helix.

So far, it has not been possible to grow V-amylose single crystals large enough to be analyzed by X-ray crystallography. Our strategy has thus been to prepare lamellar crystals from dilute aqueous amylose solutions and characterize their morphology and structure by combining experimental data from transmission electron microscopy (TEM), solid-state NMR, X-ray and electron diffraction with conformational and packing energy analyses.

We have tested the ability of 120 compounds to induce the crystallization of amylose. The resulting structures could be classified into 10 families, 5 of which were described for the first time. Surprisingly, in some cases, like with linear saturated fatty acids (Fig. 2) or diols, a given ligand could induce different crystal structures, suggesting that the polymorphism of V-amylose is a more general property than what was previously reported (*Int. J. Biol. Macromol.* **2018**, 119, 555–564; *Polymer* **2021**, 213, 123302).

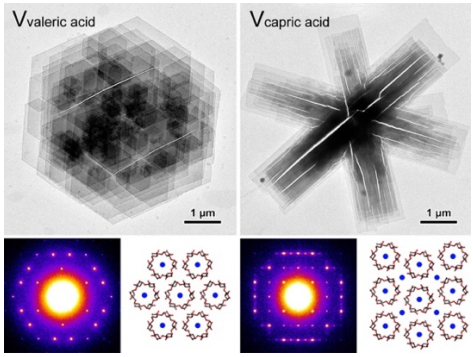


Figure 2. Examples of V-amylose single crystals prepared with linear fatty acids. A TEM image, an electron diffraction pattern and a molecular model seen along the helical axis are shown for each complex. Both structures are based on 6-fold amylose single helices. The position of intra- or interhelical guest molecules is indicated by blue spots.

In particular, crystalline complexes prepared with ibuprofen, a well-known anti-inflammatory drug, were used as a model to evaluate the potential of V-amylose as a delivery system of bioactive molecules (Fig. 3). Distinct fractions of ibuprofen, likely corresponding to the different locations of the guest in the crystal (*Carbohydr. Polym.* **2021**, 261, 117885), were selectively released by varying the pH of the dissolution medium. Since the release was maximized at high pH, these inclusion complexes are potentially interesting for intestinal targeting and would thus improve the therapeutic effect of ibuprofen while avoiding stomach damage.

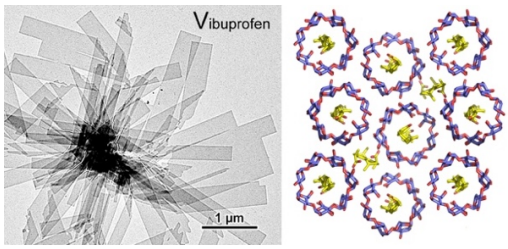


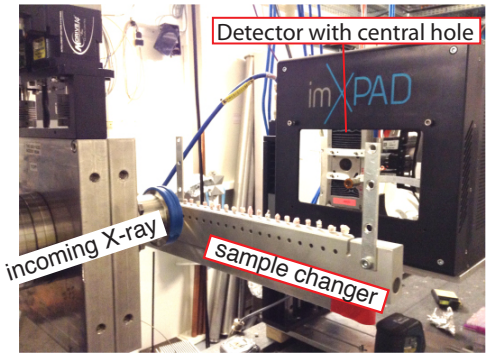
Figure 3. TEM image of single crystals of V-amylose complexed with ibuprofen and tentative molecular model. The guest ibuprofens (in yellow) are located inside and between 7-fold amylose single helices. Hydrogen atoms are not shown.

Variability of wood cell wall nanostructure

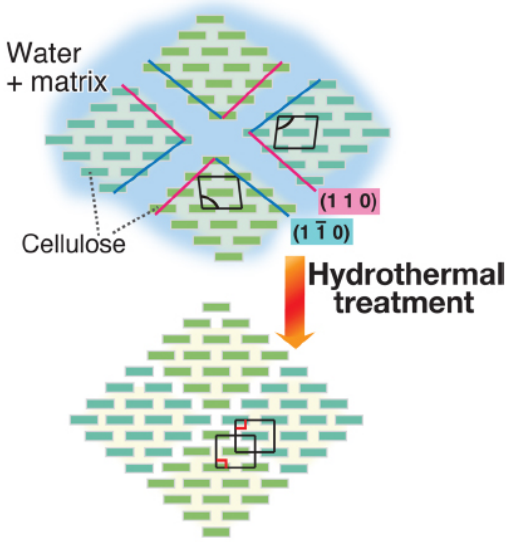
Contact: Yoshiharu Nishiyama

The X-ray scattering signal form wood is highly conserved among various species. The wood cell wall is in general composed of 2-3 nanometers-thick crystalline cellulose separated by hemicellulose and lignin. We revisited a wide spectrum of wood specimen from xylarium of Kyoto university, among which three species, persimmon, Chinese hackberry and castor aralia gave remarkably sharper diffraction compared to dominant type, indicating larger microfibril sizes.

There is a general consensus today that cellulose in higher plants are produced by enzyme complex in form 6 membered rosette, each of them containing three catalytic units. Thus 18 chains would be polymerized simultaneously to from crystalline microfibrils. However, due to the small size and dense packing in side the cell wall, and the small contrast between wood substances, the direct observation of microfibril arrangement in side wood is a huge challenge. X-ray scattering allows us to probe the internal structure due to the crystalline diffraction and small angle scattering fieatures. Although crystalline, the diffraction arising from cellulose is blurred in the direction lateral direction, due to the small lateral size. This broadening can be directly related to the crystal size. Also, the relatively high volume fraction of cellulose microfibrils in wood cell wall of 30-40% leads to high correlation between microfibrils that as function of their lateral size, and indicates us the number density of microfibrils.



Kyoto University is maintaining a xylarium containing 15 thousand samples from 3617 species. Among them, we selected 20 species spanning wide range in the angiosperme phylogeny group, and collected X-ray scattering at the French beamline D2AM at the ESRF. The new pixel detector with central hole "WOS" combined with a small camera seeing through the hole, allows us the simultaneous recording of large Q-range in one shot, giving the information on the crystal size, orientation and their lateral arrangement. Most of the samples from the collection gave almost identical scattering, but samples from persimmon (*Diospyros kaki*), Chinese hackberry *(Celtis sinensis)* and castor aralia (*Kapolanax septemlobus*) gave much sharper peak corresponding to roughly double the size of standard wood cellulose. The correlation peaks in the small angle also shifted to lower Q (larger correlation distances). Those outliers were sporadically situated in the phylogenic tree and were cannot be related to evolution.



Heating wood in water at 200 ˚C drastically change the nanostructure leading to much sharper diffraction peaks. This is due to the co-crystallization between neighbouring microfibrils that were probably separated by hemicellulose in the native state. The estimated lateral size is doubled by this treatment, meaning that in average four crystals would be fused into one. With most species, the unit cell becomes pseudo-orthorhombic which can be explained by co-crystallization of microfibrils that are statistically in opposite orientations. The ones with larger starting microfibril size also showed sharpening of the peak, but the tendency to transform to orthorhombic structure was smaller.

In the next step, studying the material properties including the outliers would allow us to establish the nano-structure and property relationship, for the better use of such biomass materials

Twist geometry of cellulose crystals probed by electron diffraction

Contact: Yu Ogawa

One of the most fascinating aspects of cellulose nanoparticles, or nanocelluloses, is their intrinsic chirality, which gives rise to various useful properties such as chiral photonic property and chiral induction ability. The chirality of cellulose is present at various length scales, from its monomer, optically active glucosyl residue, to the suspensions of nanocelluloses that are susceptible to spontaneously self-organize into chiral nematic structures. At the nanometric scale, the chirality is observed as unidirectional right-handed twists along the fiber axes of nanocelluloses. Such twists are of great importance since they are considered to govern the chiral-related properties of nanocellulose materials. Despite this, the ultrastructural details of the twists of nanocelluloses have not been elucidated. Microscopy observations have shown that the nanocelluloses dried on flat substrate have discontinuous twists where sharp twists occur regularly spaced with apparent flat regions, while computational simulations predict continuous twists along the fiber axis (Fig. 1). These contradicting observations lead to a debate on the exact twist geometry of nanocelluloses.

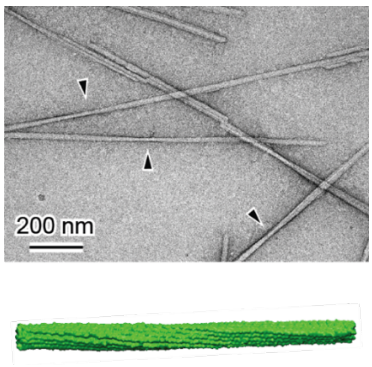


Figure 1. Fibrillar twists of nanocelluloses. Top: TEM image of tunicate cellulose nanocrystals. Arrows indicate apparent twist regions. Bottom: simulated morphology of cellulose crystal based on force field-based molecular dynamics.

To address this question, one requires devising a methodology that allows quantitative description of local geometry of the cellulose crystal at the single nano-object level. For this purpose, a combination of cryogenic transmission electron microscopy and electron microdiffraction (µED) was used to follow the exact geometry of the twist of nanocelluloses. The µED analysis can provide crystallographic information on individual nano-sized crystalline domains, thus leading to their local crystallographic orientation from two-dimensional diffraction patterns. By recording sequential µED patterns along the axis of cellulose nanocrystals, the structural details of the twist of cellulose nanocrystals (CNCs), such as twist angle and pitch could be described (Fig. 2).

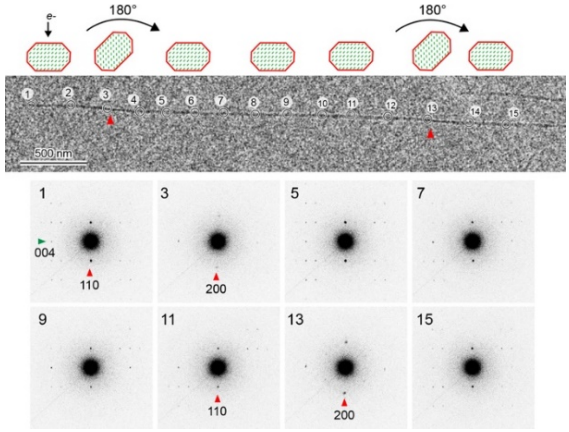


Figure 2. Example of µED analysis of tunicate cellulose nanocrystal dried on a flat carbon film. The orientations of cross-sections of cellulose crystal along the fiber axis (top panel) can be determined using the sequential µED patterns (bottom panel).

CNCs under dry and frozen conditions were compared, which allowed quantitatively characterizing their twist geometry and the effect of their drying on a supporting substrate (Fig. 3) (*Nanoscale* **2019**, 11, 21767-21774). The µED analysis under cryogenic condition revealed the continuous twisting of CNCs in the aqueous suspension state. This intrinsic regular twist was drastically modified to discontinuous sharp twists when the CNCs were dried on flat surface. This observation indicates that the previously observed discontinuous twists are the consequence of the drying artifacts. The developed sequential µED method was further applied to CNCs from different sources Carbohydr. Polym. 2021 251, 117102 2 and also to other twisted carbohydrate crystals (*Angew. Chem. Int. Ed.* **2022**, 132, 22766-22772).

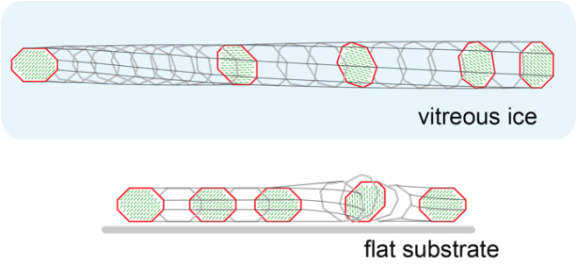


Figure 3. Twist geometry of tunicate cellulose nanocrystals in frozen (top) and dry (bottom) conditions.

Axis 4. e-Cermav

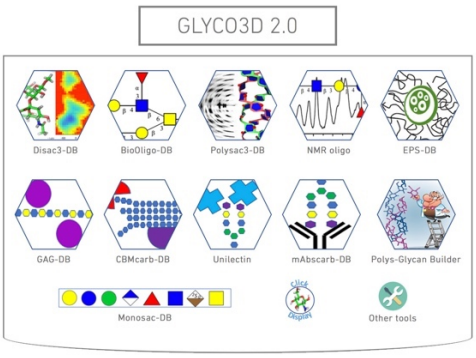
A portal for structural glycosciences

Contacts: Alain Rivet, Jean-Luc Putaux, Serge Pérez

The e-CERMAV axis is dedicated to the development of the CERMAV digital resources. Its objectives are to organize access to scientific information of the laboratory and add value to the large volume of collected data. The accumulation of information and the development of enabling technologies allow the coverage, in the form of databases, of some of the structural and functional features in structural glycosciences.

Glyco3D is a portal of several interlinked databases covering the 3-D features of mono-, di-, oligo-, polysaccharides, lectins, monoclonal antibodies, glycosaminoglycans binding proteins, and carbohydrate binding domains. A common nomenclature has been adopted for the structural encoding of the carbohydrates.

http://glyco3d.cermav.cnrs.fr/



BiOligo contains a collection of annotated NMR data of 180 entries and the 3D structural information of 250 entries of bioactive oligosaccharides which have been subjected to conformational sampling to determine their conformational preferences.
https://glyco3d.cermav.cnrs.fr/

PolySac3DB contains the structural information of about 150 polysaccharide entries that have been established using various structure determination techniques. Attention was given to the recording of the available diffraction patterns as the original experimental data from which the structures were established (120 diffractograms have been collected).
https://glyco3d.cermav.cnrs.fr/

EPS Database. This database provides access to detailed structural, taxonomic and bibliographic information on bacterial exopolysaccharides (EPS), their repeating unit structure and the producing organism, growth conditions for expression and structure determination and functional property.
http://www.epsdatabase.com/

GAG-DB is a curated database that classifies the 3D features of the six mammalian GAGs (chondroitin sulfate, dermatan sulfate, heparin, heparan sulfate, hyaluronan, and keratan sulfate) and their complexes with proteins. GAG-DB provides detailed information on GAGs, their bound protein ligands, and features their interactions to several open access applications.
https://gagdb.glycopedia.eu/

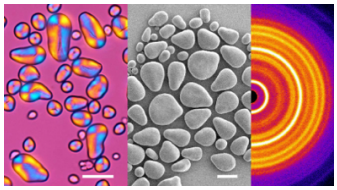
CBM-CARB DB. Carbohydrate Binding Modules are defined as discrete auxiliary protein modules with a non-catalytic carbohydrate binding function. Based on 400 X-ray structures, the database organizes and displays the interactions between carbohydrates and their binding modules.
https://cbm-carb db.glycopedia.eu/

UniLectin3D is a database of carbohydrate-binding proteins with curated information on 3D structures and interacting ligands (2278 3D X-ray structures (1456 with interacting ligands, 549 distinct lectin sequences, 239 distinct glycans).
https://www.unilectin.eu/unilectin3D

These databases are developed and maintained either internally, or within the framework of national and international collaborations.

Amidothèque. This database collates information on the morphology, structure and composition of native starch granules from a wide range of botanical sources. Each starch entry describes the shape, size, allomorphic type and composition of the granules, including bibliographic references and relevant links. A selection of pictures, polarized light optical micrographs, scanning electron microscopy images and X-ray diffraction patterns is available for most specimens. The "advanced search" tool allows comparing groups of different starch granules according to selected criteria.

https://amidotheque.cermav.cnrs.fr/



CERMAV and its environment

CERMAV is affiliated with Université Grenoble Alpes (UGA) and the staff is strongly involved in the academic life in Grenoble.

CERMAV is a member of Institut de Chimie Moléculaire de Grenoble (ICMG) and participates to some of the technical platforms by hosting electron microscopy and NMR equipments.

Glyco@Alps

The Glyco@Alps Cross-Disciplinary program of UGA, funded since 2017, aimed at exploring the fascinating structural diversity and complexity of sugars, including those found in the Alpine biodiversity, and focusing on their exploitation for biopharmaceuticals, medical diagnostics, personalized medicine, materials, environmental sustainability and innovative bio-industries. The CDP has been very successful in developing an interdisciplinary local network of about 100 academic permanent researchers and 80 young scientists (PhD and post-doc) on topics ranging from chemistry and biology to material sciences, process and economy.

CERMAV has been instrumental in the creation of Glyco@Alps and Dr. Imberty coordinated the network for 2017 to 2021. CERMAV researchers were also strongly involved in the scientific animation of the network, particularly with organization of a summer school on structural glycosciences and a winter school on nanocellulose. Glyco@Alps also succeeded in attracting and training the next generation of glycoscientists, with a pluridisciplinary approach and a broad view to environmental and innovation issues. CERMAV hosted the doctoral research work of six doctoral students, with a co-direction between CERMAV and high ranked laboratories in Europe (Cambridge, Hannover, Geneva, etc.) or with other laboratories in Grenoble.

Labex Arcane

The Laboratoire d'Excellence (LabEx) ARCANE – Bio-driven chemistry – was created through the "Investissements d'Avenir" programme of the French government in 2012. It is now part of the Chemistry, Biology and Health Graduate School of Université Grenoble Alpes. CERMAV and six other research institutes are united to develop research themes in bio-targeted and bio-inspired chemistry in order to address two crucial challenges: shaping the future of chemistry without fossil fuels and integrating knowledge from molecular biology when designing more efficient bio-targeted molecular systems.

CERMAV researchers have been involved in the management of ARCANE since its creation, with participation to the scientific council. Funding from Arcane has been very incentive for setting-up scientific collaborations between CERMAV and other chemistry laboratories of the Grenoble area, with the funding of six doctoral students and two post-doctoral researchers.

Institut Carnot Polynat

PolyNat is part of the European drive to build a sustainable bio-economy, which aims to strengthen the links between economy, society and environment. The search for alternatives to fossil resources and the need to fight against climate change encourage the development of new materials and a more environmentally friendly chemistry. Carnot PolyNat aims to make the most of biomass for the eco-design of bio-based materials and devices, with hitherto unmatched properties, and developed from renewable and sustainable resources. Researchers from CERMAV, and from five other academic laboratories and two technical centers, rely on physicochemistry, materials science and biotechnologies to design materials by directed self-assembly nanostructured and biosourced devices with high added value. PolyNat is also an international influence through the industry forum it organises every year in the field of bio-based materials.

International

CERMAV and the HORIZON 2020 European program

CERMAV is identified as the largest glycosciences research center in Europe and researchers participate in several European projects within the HORIZON 2020 framework. CelluWiz is a project of the Bio Based Industries Joint Undertaking with overall objective to develop all-cellulose solution to replace plastic packaging materials.

CERMAV is also involved in two Marie Skłodowska-Curie Actions networks for training researchers to doctorate level. PhD4GlycoDrug is a joint-doctorate program (EJD) that targets the development of glycocompounds through modern drug design and specific glycochemistry. Four PhD students registered with co-tutelle at Université Grenoble Alpes are carrying out their research at CERMAV, developping novel glycocompounds as antiadhesives against opportunisitic bacteria and fungi. The SynBIOCarb project brings together chemists, structural biologists, biophysicists, cell biologists and protein engineers for pioneering the development of "synthetic glycobiology". The first international conference in this field has been co-organized by CERMAV and University of Leeds.

CERMAV is also an active participant in the COST European program through the Actions INNOGLY (Innovation with Glycans: new frontiers from synthesis to new biological targets) and Glyconanoprobes (Functional Glyconanomaterials for the Development of Diagnostics and Targeted Therapeutic Probes).

CERMAV is actively involved in CARBOMET, a Coordination & Support Action of Horizon 2020 FET-OPEN. A workshop on glycomaterials was organized at CERMAV in 2019, and the conclusions were included in

the white paper “Sustainable Materials” for EEC deciders. A roadmap that aims at identifying key opportunities and applications has now been finalized. "Glyco 2030: A Roadmap for Glycoscience in Europe" is a document for the promotion of glycosciences for the media and policymakers available from carbomet.eu.

A strong international network of bilateral collaborations

Research in Glycosciences is very international and this is reflected in the ratio of CERMAV publication that are in collaboration with foreigh universities and research group (60 % for 2020). Long-standing collaborations are established with colleagues all over the world and funded through various international schemes. The Fonds de Recherche France Canada supports a collaborative research project on electrospinning of light harvesting polysaccharides between Dr. Issei Otsuka and Prof. Christopher J. Barrett from McGill University. Dr R. Borsali has a long term-collaboration with Hokkaido University (group of Prof. Toshifumi Satoh, expert on the synthesis of glycopolymer systems) financially supported by CNRS and/or the French and Japanese Ministry of Science. In 2020, Dr R. Borsali got a visiting professor position at Hokkaido University, and could deliver his lectures with the use of remote tools. A French-German ANR project involves CERMAV and two prestigious german research institutes, the Max Planck Research Institute, and the Helmholtz Center for Infection Resarch for discovery of small drugs that would mimick carbohydrates involved in lung bacterial infections. The Campus Rhodanien funds scientific exchanges around the glycobioinformatics activity (databases, software, etc.) developed between the Swiss Bioinformatics institute, Université Lyon 1 and CERMAV. CERMAV was also involved in a collaborative project with Chalmers University in Göteborg funded by Sweden’s Innovation Agency Vinnova about the use of scattering techniques to investigate chemically-modified polysaccharides.

An international research project with NTU

Dr. Redouane Borsali has successfully applied for a CNRS International Research Project (IRP) with Prof. Chen Wen-Chang of the Advanced Research Center for Green Materials Science and Technology at National Taiwan University (NTU). The project is entitled "New Ultra-nanostructured and Stretchable Biomaterials for Bioelectronic Device Design ". This project will benefit from the building of the “Green Material Institute” at NTU Taipei, and will be a a hub for biobased materials, with collaborations between academics and industrial groups from France and Taiwan, but also from Japan. This will be an opportunity for CERMAV researchers to continue their work in nanobioelectronics, on the devices of the future, for example, transistor memories, OLEDs [organic light-emitting diodes], photovoltaics, etc.

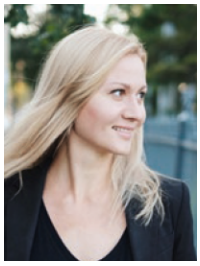
International training through summer and winter schools

CERMAV researchers participated in the organization of the first Winter School on Nanocellulose, which took place at the stunning location of Joseph Fourier Alpine Station at Col du Lautaret, from 11 to 13 December 2019. Young researchers from China, Finland, Sweden and France met the European specialists of the Nanocellulose field, including several speakers from CERMAV. The training was much appreciated and all participants keep vivid memories of the quality of the talks… and of the snow storm!

CERMAV organizes every two years the Structural Glycoscience Summer School with a much-appreciated visit of ESRF beamlines. The 2020 edition took place fully online due to the Covid-19 pandemic. The Virtual Structural Glycoscience Summer School took place on June 17th and 18th, 2020, with conferences, but also virtual practicals on modeling in glycosciences that were much appreciated. The event gathered 46 participants from all over Europe.

Visiting scientists in 2019-2020

Collaborations also took place through the visit of foreign researchers, even though the international exchanges were slowed down in 2020. During the last two years, through funding by the French embassy in Moscow, we had the pleasure to welcome two researchers from the Russian Academy of Sciences: Dr. Daria Pochina (Institute of Macromolecular Compounds, St. Petersburgh) and Dr. Olga Makhshakova (Kazan Institute of Biochemistry and Biophysics), for projects on electrospinning of polysaccharides, and modeling of glycoconjugates in membranes, respecitively. Dr. Sebastián Cerminati obtained a visiting grant from Glyco@Alps (Institute of Biotecnological and Chemical Processes Rosario, Argentina) to develop the fermentation of novel polysaccharide-producing micro-organisms. In 2019, Dr. Takuya Isono from Hokkaido University joined CERMAV as a postdoc fellow for a few months and, in 2020, he won a JSPS award for young scientists.



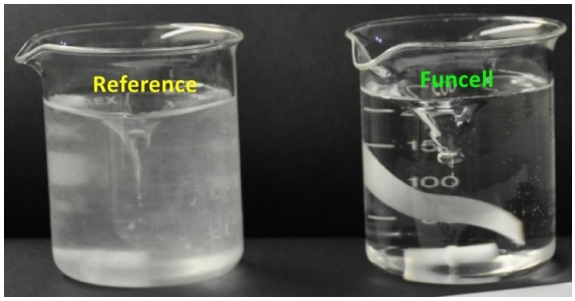
Technology transfer and start-ups

Actors

With about fifteen patents in the last evaluation period, and several licences in various fields like nutraceutics, pharmaceutics, phytosanitary products and biomaterials for health, CERMAV has a long-lasting experience in valorization. Accompanied by the local CNRS service and CNRS Innovation, the private subsidiary of CNRS devoted to technology transfer is fostering research in the pre-maturation stage. CERMAV has also closed links with the SATT Linksium, which is a state-owned company devoted to the acceleration of technology transfer from laboratories to market, with an expertise focusing on the risky steps of startups departure and upstream phases of the development of technological innovation projects. Linksium provides a wide portfolio of technologies which pushes back scientific boundaries. Since 2018, Linksium has assisted three pre-incubation deep-tech innovations from CERMAV, representative of the diversity of our subjects in the fields of biosourced materials and biomaterials, and in biotechnology and health.

FunCell

The quest of FunCell (FUNctionalization of CELLulosics) for sustainable and biosourced materials together with the progressive ban of single-use plastics is a huge societal concern. It is both a challenge and an opportunity for the paper industry which needs to reinvent its traditional market. Since papers and boards have usually poor mechanical properties, especially in wet conditions, papermakers use additives mainly oil-based and toxic, with limited results.



The FunCell project arose from more than 20 years of fundamental and applied research at CERMAV on cellulosic materials. Initiated by various PhD works, Institut Carnot PolyNat projects with CTP and FCBA, and a maturation/ incubation project with the SATT Linksium from 2017 to 2020, the project led to the creation of the FunCell company in September 2020 which won – with great success – the same year, the grand prize of the 22th national innovation contest ("i-Lab") from BPI France.

Today, the company proposes the BioWet solution: biobased and non-toxic additives which multiply mechanical performances of papers and boards by 2 when dry, and up to 20 in the wet state. In parallel, FunCell and CERMAV keep on collaborating to develop innovative additives and biosourced materials

Dr. Julien Leguy was awarded in 2019 the prize of the 1st i-PhD innovation competition of BPI France, for the FunCell project

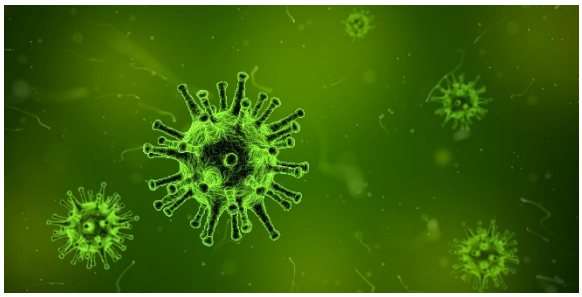
AIS Biotech

In France, flu is a major public health issue as it affects 2 to 6 million people and causes more than 10,000 deaths per year. Two antivirals currently on the market show notable limitations due to resistances, and the seasonal vaccine is not very effective.

The GlycoFlu project is based on 20 years of research on microbial engineering and oligosaccharide production. Our technology consists in providing innovative sugars (called glycans) which are specifically recognized by various strains of influenza virus. Such binding will act as a lure, thus preventing the virus interaction with respiratory cells and limiting the infection.

We have already demonstrated the in vitro efficacy of our molecules and we are currently performing preclinical trials in collaboration with the International Center for Infectiology Research Inserm U1111 CNRS UMR5308 based in Lyon, France. The project is granted by the SATT Linksium, with the objective to create the startup AIS-Biotech in 2022.

Dr. Emeline Richard-Millot was the winner of Grand Prize of the 1st i-PhD innovation competition of BPI France, for the GlycoFlu project – 2019. The i-PhD competition, as part of the National Deeptech Plan, aims at rewarding young researchers with entrepreneurial projects mobilizing disruptive technologies.



Hall of fame

Dr. Redouane Borsali, CNRS Director of Research and Group Leader of the "Self-Assembly of Glycopolymers" team and Director of Institut Carnot PolyNat was awarded

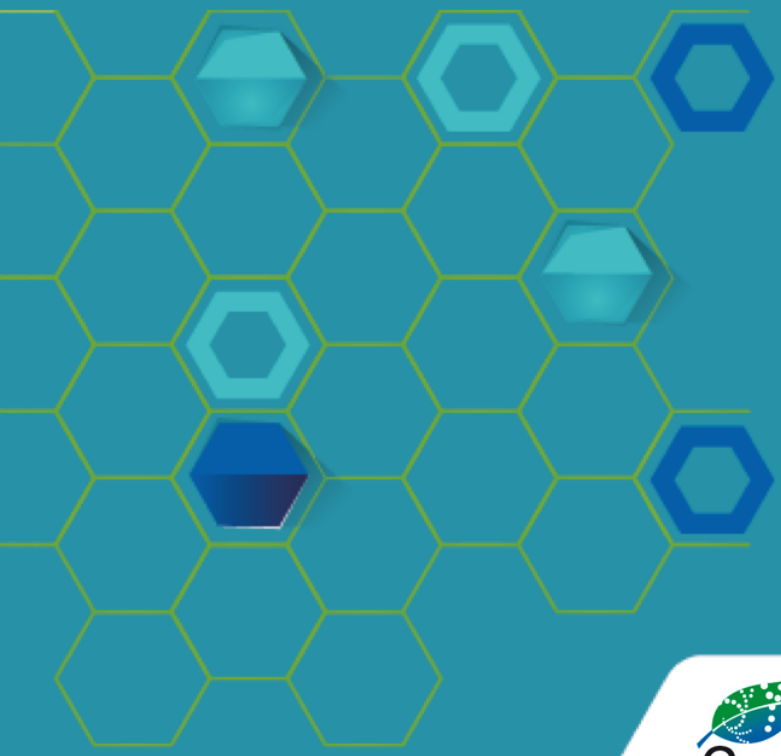
- in 2020: the prestigious International Award of the Japan Society of Polymer for his major contribution of "Self-Assembly of carbohydrate-based block copolymer systems: Nanoparticles, thin films, smart surfaces and devices";
- in 2018: the Scientific Grand Prize France-Taiwan– Awards Academy of Science, Paris, France, for his major contribution to transistor devices using carbohydrate block copolymers;
- in 2017: "Stars of Europe" ("Etoiles de l'Europe"), the Award in Research and Innovation given by the Ministry of Education and Research for the coordination of the European Greenanofilms Project. The prize has been awarded for groundbreaking contributions in the conception and development of new classes of carbohydrate-based block copolymers and their self-assembly in thin films at sub-10 nm scale for microelectronics applications as well as the design of new glyconanoparticles for various applications (cosmetics, biomedical, etc.). The award ceremony took place in Paris.

Dr. Anne Imberty, CNRS Director of Research, Cermav Director from 2015 to 2020 and researcher in the" Structural and Molecular Glycobiology" team, was awarded in 2020 the International Hispano-French "Miguel Catalán - Paul Sabatier" prize. This is a biennial award, created as a collaboration between the French Chemical Society and the Spanish Royal Society of Chemistry and awarded in France to a Spanish chemist every even-numbered year and in Spain to a French chemist every odd-numbered year. The prize has been awarded for groundbreaking contribution to structural glycobiochemistry and advancement of our understanding of the interaction between proteins and carbohydrates with applications in the design of anti-infectious compounds.

Dr. Yoshiharu Nishiyama received in 2021 the prestigious Anselme Payen Award from the Cellulose Division of the American Chemical Society for his studies on many aspects of cellulosics, mainly in the solid state. His main lines of research can be defined as the following: the use of scattering (X-rays, electrons and neutrons) and spectroscopy (NMR, infrared) methods to get insights on the structure of cellulosics and other crystalline polysaccharides (amylose, chitin, chitosan, etc.), the study of the properties of cellulose suspensions, and the modeling of the physical properties of cellulose

Dr. Sami Halila is the winner of the 2022 international competition "The Cosmetic Victories". for his Carbogel project: "a Simple and Eco-Friendly Carbohydrate-Based Gelling Agent for Oily Phase". The project focuses on the supramolecular gelling of organic liquids, such as oils, solvents or fatty esters, by monosaccharide derivatives that self-assemble into a 3D network. The gel can serve as a stimuli-sensitive matrix for the controlled delivery of cosmetic agents. Carbogel contributes to "green" and sustainable cosmetics by limiting our environmental and social impact.

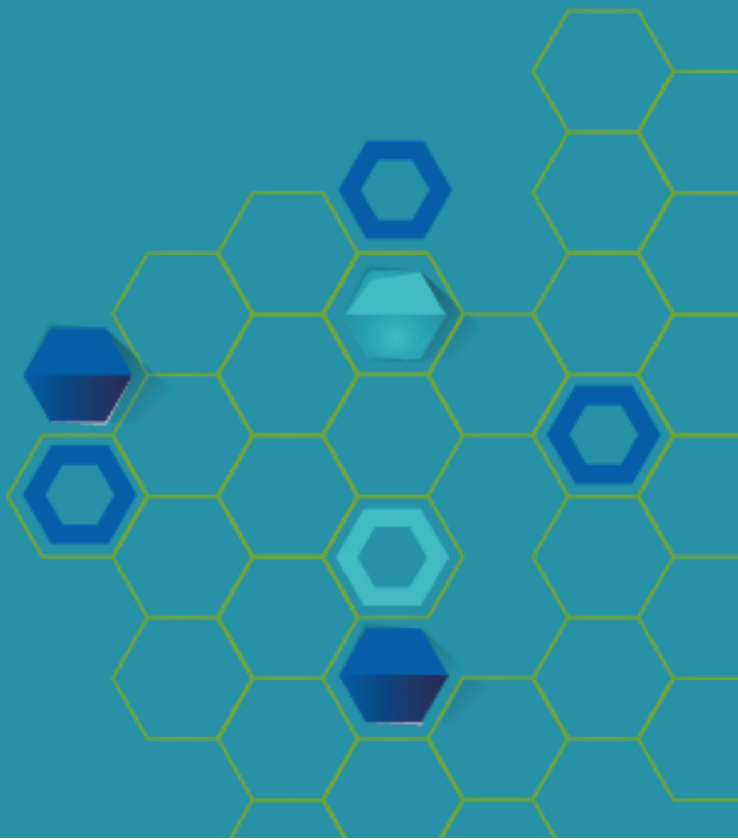
Maxime Leprince a PhD student of CERMAV, was a finalist for Ma Thèse en 180 secondes (« MT180 ») competition in 2020. MT180 allows doctoral students to present their research topic, in French and in simple terms, to a lay and diverse audience. Each student must give a clear, concise and nonetheless convincing presentation of their research project in three minutes, with the support of a single slide. Maxime Leprince thesis is entitled « Development of conductive and absorbable inks and hydrogels for stimulus and monitoring of biological tissues».



Cermav

CS40700
38041 Grenoble cedex 9
France

cermav.cnrs.fr



cnrs
dépasser les frontières