Introduction

What is Glycoscience

Glycoscience is the science and technology of carbohydrates, which comprise the most abundant Biological molecules and materials on Earth, making up part of the biology of all terrestrial living organisms. Glycoscience is recognised worldwide as an area of immense important in the world economy and has the potential to solve several of the challenges faced by modern society.

CarboMet has engaged with >350 stakeholders in Europe to identify number of exciting opportunities which are of great interest to European Society and Bioindustries, in particular in the areas of Pharmaceuticals and Personalised Medicine (addressing challenges in health), Food (food security, wellbeing) and Biomaterials (resource efficiency and raw materials). Underpinning these opportunities will be a number of emerging glycoscience tools, particularly in measurements and analytics, synthesis and bioinformatics, which will open up glycosciences to a much wider scientific and industrial community and overcome barriers to entry for commercial applications. Importantly, full exploitation will only be possible, if the broader community is educated in the opportunities and application of glycoscience, through cooperation with the media and policy makers, as well as education and training for students and scientists at all levels.

Infobox: Carbohydrates are also known as sugars, saccharides and glycans; these synonyms are defined by IUPAC as compounds consisting of a large number of monosaccharide units linked glycosidically. In living systems, carbohydrates are often chemically linked to proteins, lipids or other metabolites and these are then referred to as glycoconjugates. Therefore, the terms “glycoscience” and “glycobiotechnology” are terms encompassing all activities related to the science and technology of carbohydrates respectively.

The complexity of glycans and glycoconjugates has been an ongoing challenge to fully elucidate adequately the subtleties of chemical reactivity and stereochemical structure which is responsible for complex biological function affecting the health and wellbeing of living organisms and indeed of the environment as a whole. The availability of appropriate measurement capabilities to interrogate molecular structures in detail will help advance our understanding of glycoscience. Carbohydrates clearly have unique potential to help solve in a sustainable manner some of the greatest technological challenges of our times, especially those concerning the protection of the living environment, human health and well-being and the need to slow and even reverse damaging climate change

International Sustainability Goals

In 2015, all United Nations Member states adopted a far-reaching policy document for attaining global sustainability – the 2030 agenda for sustainable development.[1] Seventeen ambitious Sustainable Development Goals ('SDGs') have been identified[2] with the target date of 2030 for attaining these goals. Since that date the public awareness of the dangers of climate change has grown enormously and the UN Climate Action Summit 2019 endorsed very specific and challenging targets of a 45% decrease in carbon dioxide emissions by 2030, with zero net emissions by 2030.[3]

At a more local level, Horizon Europe ['HEU'], the next European research and innovation framework programme, with a current putative budget of €100 billion and set to run from the beginning of 2021 to the end of 2027, is adopting a "mission-oriented approach" with a strong emphasis on sustainability aligned with the UN SDGs. The first five Mission Areas have been proposed,[4] namely:-

- Adaptation to climate change including societal transformation
- Cancer
- Climate-neutral and smart cities
- Healthy oceans, seas, coastal and inland waters
- Soil health and food

Each Mission is governed by a Mission Board, comprising "a broad mix of experts from innovation, research, policy making, civil society and practitioner organisations" and has an Assembly of high-level experts to "provide an additional pool of ideas, knowledge and expertise that will be actively called upon to contribute to the success of the 5 Missions".

UN SDGs and Innovation in Glycoscience

Significant advances in all aspects of glycoscience is required to accelerate adoption and overcome scientific and technological challenges to achieve UN SDG target by 2030. Glycoscience is central to no less than eight of the 17 SDGs.

UN SDG	Title	Role of Glycoscience
2	**Zero Hunger**	• Nutraceuticals • Prebiotics • Non-meat based diets • Carbohydrate-based fibrous foods • Soil metagenomics • Novel adjuvant materials for agriculture
3	**Good Health & Wellbeing**	• Innovative vaccine design. • Growing AMR. • Precision medicine and glycomics. • Pharmacoglycomics. • Role(s) of carbohydrates in the microbiome • Novel carbohydrate-based materials for cosmetics and prosthetics
7	**Affordable & Clean Energy**	• Waste carbohydrate-based bio-feedstock for incineration.

[1] Transforming our world: the 2030 Agenda for Sustainable Development: sustainabledevelopment.un.org/post2015/transformingourworld
[2] https://www.un.org/sustainabledevelopment/sustainable-development-goals/
[3] UN Climate Action Summit 2019: www.un.org/en/climatechange/un-climate-summit-2019.shtml
[4] ec.europa.eu/info/horizon-europe-next-research-and-innovation-framework-programme/mission-oriented-policy-horizon-europe_en

		• Substitute materials for construction and transport having lower energy demands than currently used.
9	**Industry, Innovation & Infrastructure**	• Sustainable synthesis of carbohydrates with novel functionalities. • Manufacturing high value specialty glycan products having unique functionalities using in vitro synthetic biology.
12	**Responsible Consumption & Production**	• Biodegradable and compostable saccharides and glycans for recyclable packaging in a circular economy. • Novel textiles, packaging and next-generation display materials.
13	**Climate Action**	• Climate change and spread of disease • Climate change and renewable materials to alleviate growing demand for resources.
14	**Life Below Water**	• Novel glycans from sea weeds. • Novel non-meat based foods. • Novel glycans sourced from oceanic archaea, flora and fauna.
15	**Life on Land**	• Building healthy soil microbiomes from soil metagenomic analyses. • Systemic solutions for the sustainable use of land by balancing carbohydrate production between forestry, agricultural and re-wilded land.

Glycoscience in global supply and value chains

Responsible Consumption and Production of products and services (UN SDG12) emphasizes the need to evaluate and adapt a more sustainable and transparent supply chain, involving everyone from suppliers to final consumers.

Supply chains are essentially developed in value chain terms where innovative and transformative technologies are mapped along the roadmap measuring sustainability, quality and equitable distribution of wealth. Carbohydrates play essential roles in several industries and are directly involved in three distinct value chains:

- **Regional biomass based carbohydrates:** This is using the raw biomass feedstock such as rice, maize, wood and sugarcane to produce primary molecules such as glucose, cellulose and starch. These can be converted further to produce high-value chemical intermediates.
- **Glycomics and healthcare:** This value chain encompasses the research tools, diagnostics, biologics and vaccines in the development of new therapeutic interventions.
- **Non-regional biomass based carbohydrates:** This is the direct extraction of high-value sugar products from biomass and used immediately in consumer products.

Glycoscience community

The last decade has seen the growth of the glycoscience network bringing together a group of European experts to consider how the recent leading achievements of glycoscience and glycotechnology in Europe can be driven forward. This has previously been facilitated by the European Glycosciences Forum (EGSF) and is currently being led by CarboMet with the aim of highlighting the achievements of scientific and technological excellence in European glycoscience research. This document puts forward a number of areas where some of the most promising technologies can be translated into products in the European and global market.

Glycoscience is becoming an essential part of modern innovative biotechnology and having access to state-of-the-art knowledge and technologies in glycoscience will provide the European bio-based industries with a strong competitive advantage on a worldwide stage leading to long-term job creation and sustainability. To fully grasp the opportunities presented in this document by the glycoscience community, we recommend the formation of a European Glycoscience Group (EGG) to enact, deliver and advance the areas highlighted in the document.

Biopharmaceuticals

Vaccines for Antimicrobial Resistance

Antimicrobial resistance (AMR) is one the biggest threats to global health and food security today. The improvident use of antibiotics in clinical settings and animal husbandry has been the major cause for the emergence of AMR and is a major concern for both developed and developing countries. The number of deaths due to infections resistant to antibiotics is projected to reach to 10 million deaths annually by 2050 – more than cancer. The increased resistance and infection rate equates to healthcare and hospital costs of EUR 1.5 billion per year and will surpass EUR 1 trillion by the year 2050.[5]

Infobox: AMR is when micro-organisms such as bacteria, virus and fungi evolve resistance to antibiotics. This is a natural evolution process which normally occurs over a long time, however, the speed at which AMR is occurring is causing a major threat to the global population. As a result, drugs that were once effective in treating bacterial infection are losing efficacy. This means a simple surgical procedure can result in a life threatening bacterial infection.

Research priorities

It has been more than 30 years since the last class of antibiotics was discovered with many of the 'new' drugs being second and third generation antibiotics without a novel mechanism of action. Even these last resort antibiotics will be inefficient as new resistant strains emerge. The lack of antibiotics have been exacerbated with low ROI for pharmaceutical companies due to high R&D costs, low prices which are not off-set by high volume sales resulting diminishing R&D pipeline in the last 30 years.

Deep understanding of cell surface glycans on microbes: Highly targeted and effective carbohydrate-based vaccines can only be developed from a deep understanding of the molecular structure and conformation of the relevant cell surface polysaccharides on bacteria. This will also enable faster and accurate diagnosis for patients.

Large scale production of polysaccharides: Develop robust chemical and enzymatic synthesis platforms for production of specific oligosaccharide antigen for vaccine development. Modification of naturally available sugars and the development of rapid automated synthesis of target antigens will accelerate vaccine design and development.

Glyconconjugate and Adjuvant design: Carbohydrate based vaccines require a protein carrier to transfer the antigen to the body. The method to attach sugars to these carriers (also known as conjugation) are often complex and expensive. New methods should allow full control over the modification of the protein with batch to batch consistency.

New business and funding models: Cost sharing models for SMEs and incentives for large biopharmaceutical companies are required to facilitate antibiotic discovery. Require new collaborative framework between industry and academia (public private partnerships) to mitigate issues surrounding IP ownership. Open source innovation, collaborative partnership and fast track approval process will persuade public-private investments.

ETAs: Bacterial Glycan database, synthesis of standards (high purity), instrumentation and new analytical techniques. This will allow clinicians to rapidly assess and identify bacterial strains for treatment.

[5] Rappuli, R. *et al.* Nature, 2017, 552, 165-166

Glycoengineering

Sugars on the surface of cells and biomolecules play a vital role in bacterial and viral infection through cellular communication and adhesion. These sugars also play a crucial role in the stability and efficacy of biopharmaceutical drugs which make them safer and more effective. The process of decorating the surface of biomolecules is called glycosylation and is an integral process in the production of biopharmaceuticals. Current approach to modify glycans has been through either genetic engineering or process optimization. Both approaches are complex, with limited control over glycosylation and a compromise between production yield and degree of glycosylation.

Case study:

The rise of biosimilars in the next decade will bring intense competition as many of the top performing biopharmaceuticals in the last 20 years will come off patent. Glycosylation is critical in the development of biosimilars for safety and efficacy and due to the inherent difficulty in controlling glycosylation glycoengineering will play a vital role in the European biologics market.

Infobox: Biologics or biological drugs are medical products produced from living organisms in a complex and highly controlled manufacturing process. The anti-inflammatory drug Humira is one example of a biological drug and is one of the best selling drugs worldwide. A biosimilar is a biologics which is highly similar to the original biologic medicine in terms of safety, purity and efficacy.

Research Priorities

Metabolic glycoengineering: This is a method to modulate glycosylation in cells by interfering with natural biosynthetic pathways. This technique exploits the natural promiscuity of glycoenzymes to incorporate non-natural sugars and/or remove certain sugars involved in disease progression. This technology can be used for imaging tumour cells or in biomarker discovery.[6]

In vitro glycoengineering: The development of therapeutic proteins independent of fermentation processes provides much greater control on the modification of surface glycans. This requires development of a suite of sugar modifying enzymes called glycosyltransferases through enzyme discovery and engineering. The enzymes should be cheaply available and at kilogram scale in GMP grade.

Stem Cells

The trillions of cells in the human body that make up tissues like skin, blood, liver and nerves are derived from a very important class of cells called stem cells. These cells play a crucial role in the development of an organism but also in the treatment of chronic diseases such as cancer, diabetes and autoimmune diseases. Glycans play an important role in how these cells mature into tissues and organs and also in immunorejection from patients receiving stem cell treatment.[7]

Specific Challenges:

- Isolation and sequencing of cell surface polysaccharides
- Sustainable and rapid synthetic routes to oligosaccharides
- Curation of bacterial structure database to enable faster development of therapies
- Development of biocompatible micro-systems for drug delivery

[6] Yarema, K. J. *et al.* Nat. Rev. 2019, 3, 605-620
[7] Varki, A. P. *et al.* Curr. Opin. Chem. Biol. 2007, 11, 373-380

Diagnostics and Precision Medicine

Role of sugars in the human body

The cells and the proteins found in the human body are coated with sugars called glycans in a process called glycosylation. This is the most common modification cells undergo during development and changes in the sugar pattern is invariably linked to various diseases, from a rare genetically linked congenital disease of glycosylation (CDG) to prognostic indicators in cancer. Glycans also play a crucial role in cellular communication and recognition and are critical in bacterial and viral infection, autoimmune diseases and inflammation.

Glycosylation is a highly complex operation controlled by genes and utilising >200 enzymes. The process is also affected by environmental factors and is therefore susceptible to mutations. These changes in the glycan structures can be used to identify certain diseases or provide information regarding the progression of certain diseases.

Case study: Influenza

Viruses cannot reproduce on their own and require the complex machinery in cells to proliferate. They typically infect humans and animals by attaching to sugars found on the surface of the cell.[8] Specifically, the influenza virus recognizes a sugar called sialic acid which begins the process of infection. While individual sialic acid sugars play an important role in recognition, the larger glycan structure is important in affinity and how strongly the virus binds to the surface. The diversity of glycans make developing vaccines challenging which require fast and efficient production of a wide range of sugar structures for testing.

Glycomics a new frontier in drug discovery

With an average cost of drug discovery reaching over €2 billion with a timeline of 10-15 years, there is an urgent need for innovation to transform the way new drug targets are identified. The next generation of precision medicine will use glycomics data to identify patient sub-population for therapeutic intervention.

Infobox: What is Glycomics?

Glycans, which are sequences of sugars attached to proteins and lipid are the most structurally diverse biomolecule in the human body. They play a vital role in cell communication, viral and bacterial infection, cancer metastasis and cell growth. The Human Glycome Project (HGP)[9] and GlySign[10] are two European projects with the aim of translating glycan biomarker research into clinical practice.

Glycans on the cell surface provide tremendous amount of data on the development and progression of diseases. Researchers can exploit this vast information in the discovery of new drugs bringing immense value to the biopharmaceutical and diagnostics industry.

[8] Liu, Y et. al. 2009, J. Virol. 2009, 84, 12069-12074.
[9] The Human Glycome Project: https://human-glycome.org/
[10] Glycosylation Signatures for Precision Medicine: https://www.glysign.eu/

Case study: Cancer vaccine

Cancer cells exhibit different glycosylation patterns from normal healthy cells. These glycans on the surface also known as tumour-associated carbohydrate antigens (TACA) are an important target for the development of cancer vaccine. The differences in the structure can be used in diagnostics and also to develop cancer vaccine by isolating the TACA found only on cancer cell.

The complexity of the glycome has made it difficult to analyse and accurately quantify the subtle changes found in different diseases. This diversity also offers an incredible source of new data and access to novel therapeutic biomarkers which would otherwise be difficult to determine through genomic analysis. Glycans with specific sequences play an important role in cell recognition and immunity. For example, alterations in the glycan structure on the surface of immunoglobulin (IgG; an antibody used by the immune system to neutralize pathogen) has been observed in several autoimmune diseases including rheumatoid arthritis.[11]It can also be used as a predictive indicator, for example, IgG variants with altered glycans on the surface can be used as a predictive marker for the onset of disease.[12]

Research Priorities

Mapping of the human glycome: Significant investments are required to fully map the human glycome. This requires a concerted effort between public-private institutes and a partnership between several key research infrastructures in Europe.

Clinician engagement: Academics need to work with clinicians to develop robust value proposition of research. Scientists must consider market opportunity, cost-effectiveness and affordability of the therapeutic intervention.

Glycan targeting drugs: Cell surface sugars are critical in cellular communication and adhesion, for example, viral infections are mediated by surface glycans. Designing drugs to selectively bind to sugar moieties on pathogens is one approach to halt infection. In addition, many viruses exploit certain sugars on cells as a gateway to infection, designing these sugar mimics also known as glycomimetic drugs is one approach to trick the pathogen and disrupting the process of viral replication.

Case study: 'Oseltamivir mechanism of action'

Diagnostics

Glycans play an important role in maintaining a balance health in humans. The process of glycosylation is highly sensitive and changes in this process can give rise to different sugar patterns on cells. These changes can be used to provide important information on disease diagnosis and development.

In vitro diagnostics: Fast and reliable diagnostics is the driving force behind the development of precision medicine. Carbohydrate based sensors are still in its infancy and require substantial investment to translate basic research to clinical services.

Research Priorities

While carbohydrate based biomarkers provide significant data on disease development, a major challenge is the separation and identification of glycans from patient samples.

[11] Maverakis, E. et. al., J. Autoimmune, 2015, 0, 1-13.
[12] Nimmerjahn, F. et al., Nat. Rev. Rheumatol. 2017, 13, 621-630.

Design of new diagnostics devices: The analysis of free glycans has commonly been a long and tedious process. An alternative strategy is the development of an electrochemical characterization technique. This requires development of highly specific systems which can recognise and bind to glycans of interest eliciting and electrical response.

Integrating Glycomics in drug discovery: Changes in glycan structure is one of the first indication in the development of cancer, autoimmune disease and other pathological processes. These changes profoundly affect disease development and progression through cellular communication facilitated by cell surface glycans. These aberrant changes are often caused by deregulation of enzymes involved in the glycosylation process. Combining glycomic and genomic analysis will provide a powerful tool to identify novel drug targets for precision medicine.

Specific Challenges:

- Improved manufacturing capability to obtain high-purity glycan standards for diagnostics.
- Development and integration of pharmacoglycomics along with pharmacogenomics in clinical evaluation.
- The use of clinical glycomics and blood groups as risk factors in disease diagnostics.

Food, Nutrition and the Gut Microbiome

The promotion and maintenance of a healthy relationship with our gut microbiota is increasingly understood to be important for human health and well-being. The 100 trillion symbiotic microorganisms that reside in the human gut fulfils several vital biological functions and these imbalances in the microbial populations are associated with a number of inflammation and infections, such as gut disorders (e.g. Irritable Bowel Syndrome, and the Irritable Bowel Diseases, Ulcerative Colitis and Crohn's disease) and non-communicable diseases (e.g. diabetes, cardiovascular diseases and cancers). In Europe, an estimated 2.5 - 3 million people are affected by Irritable Bowel Disease (IBD) with a direct healthcare cost of more than EUR 4 billion per year.[13]

Carbohydrate in food and nutrition

Carbohydrates play a number of crucial roles in maintaining microbial communities. For example, dietary fibre has a major influence on overall gut health and carbohydrates are the main modulators of the gut microbiota structure and function.[14] Carbohydrates are also found in the human gut lining and are the first point of contact between the microbiota and the host. Alteration of the carbohydrates in the lining give rise to several disease profile and are associated to gut, autoimmune and inflammatory bowel disease. The promotion and maintenance of a healthy relationship with our gut microbiota is increasingly understood to be important for human health and well-being. Recent studies suggest intestinal microbiota even affects distant organs and is involved in skin homoestasis.[15]

Infobox: Carbohydrate play two crucial function in the gut. Food derived polysaccharides provide essential nutrients to the good bacteria in the gut. These bacteria consume the sugars to produce chemicals that are beneficial in human health and well-being. Sugars also line the gut lining and mediates the interaction between the microbiota and the host body. Changes in the sugar structure in the lining can lead to infections and disease.

Case study: Around the end of the 19th century observations indicated that breast-fed infants had higher survival rates than those who were bottle-fed in cases of infection and other diseases. It was later discovered these were a class of compounds called human milk oligosaccharides (HMO). 2'-Fucosyllactose (2'-FL), an oligosaccharide (made up of the 3 sugar units fucose, glucose, and, galactose) is the most abundant HMO in breast milk. While these prebiotics pass through the infants gut undigested, the 'good' bacteria in the intestine consume it to promote immunity, digestion and cognitive health benefits.

Diet and the intake of certain food plays a vital role in maintaining a healthy balance. The advent of several chronic diseases in the last century can be attributed to a change in diet. Western diets today are typically high-fat, high sugar compared to the relatively low fat, high polysaccharide diets of the past, resulting in the typically modern lower diversity of microbial composition in the gut. This loss of diversity or unbalance, also referred to as 'dysbiosis', has been associated with a number of diseases affecting westernized or "developed" countries. These include neurological diseases (e.g. autism, Parkinson's, Alzheimer's), metabolic diseases (mainly diabetes and obesity), gut diseases (e.g. Irritable Bowel Syndrome, Inflammatory Bowel Diseases (Ulcerative Colitis and Crohn's disease), Coeliac disease, liver disease, colon cancer), food allergies or cardiovascular diseases.

[13] Lakatos *et. al*., J. Crohn's and Colitis, 2013, 7, 322-337
[14] Juge, N. *et. al.*, Biochem. J., 2017, 474, 1823-1836.
[15] Ghannoumi, M. A. *et al*., Front. Microbiol. 2018, 9, 1459

Research Priorities

A comprehensive understanding of the role of carbohydrates in the gut is essential to elucidate the interactions between the human host and gut microbiota in order to exploit these relationships for the benefit of human health. The ageing population and the growing prevalence of non-communicable disease is continuously adding strain to the healthcare system and it is vital to develop new strategies to improve health outcomes and to reduce healthcare costs.

Elucidating the relationship between microbiota and the human gut: The European glycoscience community is leading the development of new analytical tools and knowledge to understand the mechanisms behind the interactions between our gut, the microbiota and diet. It is essential to integrate and develop glycobiology, glycosynthesis and glycometrics approaches to provide mechanistic insights to determine: 1) How gut microbiota influence human health 2) Identification and validation of novel biomarkers 3) Development of novel microbiome targeted strategies.

Carbohydrate production: The carbohydrates involved in microbiota-host interactions need to be available as validated, high quality pure standards, both for allowing high-throughput analysis and for providing materials as probes for functional studies. While significant advances in carbohydrate synthesis and analysis have been made to produce a range of bespoke carbohydrates, there is an urgent need to be able to produce these on scale, economically and efficiently.

- **Isolation of naturally occurring carbohydrates:** Fermentative production from microbes/naturally producing microorganism or in genetically modified strains. Require technologies in biomanufacturing with accurate monitoring and purification systems.
- **Chemical synthesis:** Require development of new and routine synthetic methodologies for rapid access to sugar building blocks.
- **Enzymatic synthesis:** A sustainable approach compared to traditional synthetic approaches. However, a major limitation is the availability of carbohydrate-active enzymes with the required properties and chemical activities. Therefore there is an urgent need to build an arsenal of more glycoenzymes showing an expanded repertoire of chemistries.

New metrology and analytics: Core to the success of developing new targeted therapies for the microbiome is the development of new standards for measurements and analysis including ISO standards. The subtle differences in surface carbohydrates of bacteria will make classification and identification of ‘good’ and ‘bad’ bacteria easier. ISO standards will aid the safe development and production of bespoke carbohydrates for human intervention; through to the safe design of clinical trials and targeted drug design and delivery.

Nutraceutical and food supplement: Carbohydrates with high glycaemic-index has often been associated with long-term health risks. The awareness of consumers on the role of carbohydrates in the diet has ensured research and development on new products with significant health benefits.

Case study: There is a general perception among consumers to preferentially choose healthy and sustainable food sources. Seaweed polysaccharide has recently emerged as a potential source of functional foods and have been shown to have anticoagulant, anti-inflammatory and anti-oxidant properties.[16] Polysaccharide such as Agar, Alginate, Carrageenan and Fucoidan are found in a variety of food products including desserts, milk and pastries.

[16] Mishra, A. et al. Compr. Rev. Food Sci. Food Saf. 2019, 18, 817-831

Specific Challenges:

- New techniques to synthesise and/or isolate novel polysaccharide as nutraceuticals.
- Large scale development of human milk oligosaccharides (HMO) and sugar alternatives as functional food ingredients.
- Elucidating relationship between intestinal microbiota and antibiotic resistance.

Sustainable Materials

The advent of the European bioeconomy first presented in 2012 set out plans to transform the chemical industry in Europe to a more sustainable economy. One of the key underlying principles of the new bioeconomy framework was the utilization of waste resources, in particular food and agricultural waste. On average the EU produces 956 million tonnes of agricultural biomass per annum and a large constituent of this is carbohydrate. The development of bio-inspired sustainable materials from carbohydrates has steadily gained interest from the chemical industry as a strategy to produce new materials with unique properties from waste resources. Natural polysaccharides such as cellulose, hemicellulose, starch, chitin, pectins, and xyloglucan all have properties that make them useful for a variety of applications and their exploitation is crucial to reduce the dependence on fossil fuels and towards the development of the circular economy.

Carbohydrate based Biomaterials

Nature has provided an unlimited resource of carbohydrate-based materials and whilst the complexity and diversity of carbohydrates is challenging, this very diversity provides an opportunity to access new chemical and sequence space by tailoring the polysaccharide structure and functional properties for various applications. The inter-relationship between structure and function is perfectly highlighted when comparing cellulose and starch. Both are made of glucose residues but they play different roles in nature. Cellulose provides structural support to plants, whereas starch is primarily used as an energy source. This relationship is a prerequisite to developing a new generation of sustainable biomaterials that can address global challenges in packaging, healthcare, agriculture and consumer care products.

Infobox: Materials used in biodegradable films and in next-generation displays[17] is composed of cellulose nanofibers derived from wood and forestry residues.[18]In addition carbohydrate polymers are being used in bio-inks to house viable cells in regenerative medicine.[19]

Current attempts to establish a comprehensive R&D framework for the development of new biomaterials has been hindered by a lack of funding opportunities for SMEs to support early development (TRL 1 and 2) and the technology that is required to enable accurate measurements and analysis of the materials. To fully exploit the potential of carbohydrate polymers, knowledge sharing from other disciplines such as maths, computer science, physics and engineering is vital with the overall aim to create, transform and enhance existing materials to confer better performance for specific applications. New analytical tools and advances in the physical and biological science will be needed to investigate the relationship between the structure of materials at the atomic and molecular scale and its varying influence on the macroscopic properties. We envisage a future where digitization

[17] LTG ULM GMBH, Bistable ChLCD displays press release: https:// www.bmgmis.de/en/products/bistable-chlcd-displays
[18] Futamura cellulose films division: http://www.futamuragroup.com/divisions/ cellulose-films/products/cellophane
[19] Xu, F. *et. al*. Trend Biotechnol. 2016, 34, 746-756

is integrated into the R&D workflow and manufacturing processes themselves, with machine-based learning approaches being used to guide the design of new materials.

Research Priorities

Packaging, Films and Next-Generation Displays: Agricultural waste has been seen as a major source of valuable feedstocks for carbohydrate based materials. Several research programs and industrial investment has been dedicated to biomass valorization for speciality chemical production. While there have been tremendous achievements and developments in this area over the years, the field still requires further exploration to develop materials with substantially better properties than fossil-based polymers.

Specific Challenges:

- Discovery and evolution of enzymes to modify existing carbohydrate polymers.
- Improve dimensional stability of biodegradable films by developing new materials resistant to humidity.
- Large scale sustainable production and application of cellulose nanocrystals.

Prosthetics and Regenerative Medicine: Tissue engineering and regenerative medicine is a rapidly evolving area in healthcare with a projected global market outlook of $16.82 billion by 2023.[20] As a multi-disciplinary field, it also brings with it a set of challenges across both academia and industry. With a high demand for biomimetic scaffold materials, additional investments are required to keep up with developments in this field. Carbohydrate polymers also lack the processing abilities of synthetic polymers and this has largely hindered their application in biomedical science. For example, 3D printing technology can be used in a clinical setting to provide bio-compatible and biodegradable scaffolds for cells providing immense value in regenerative medicine.

Specific Challenges:

- Improved processing capabilities of carbohydrate based polymers to obtain desirable microstructure, properties and shape of final product.
- Smart biomaterials that can undergo structural and functional changes upon external simulation. These materials can be used in 4D bioprinting of artificial tissues and organs.

[20] "Tissue Engineering - Global Market Outlook 2017-2023", Research and Markets, 2017: https:// www.researchandmarkets.com/reports/4449999/tissue-engineering-global-market-outlook-2017