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# **The Exopolysaccharide Structures and Properties Database: EPS-DB. Application to Bacterial Exopolysaccharides**

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*Abbreviations:* CPS, capsular polysaccharide; EPS, exopolysaccharide; LPS, lipopolysaccharide; LTA, lipoteichoic acid

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## **ABSTRACT**

The EPS Database (EPS-DB) is a web-based, platform-independent database of bacterial exopolysaccharides (EPSs) providing access to detailed structural, taxonomic, growth conditions, functional properties, genetic, and bibliographic information for EPSs. It is freely available on the Internet as a web service at <http://www.epsdatabase.com>. Several structural data representation schemes are used following the most commonly accepted formats. This guarantees full interoperability with other structural, experimental, and functional databases in the area of glycoscience. The scientific usage of EPS-DB throughout a user-friendly interface is presented with a subsection of the database exemplified by EPSs from lactic acid bacteria.

*Keywords:* Exopolysaccharide structure, function, genetics, database, search, sequence of residues

## **1. Introduction**

The class of bacterial polysaccharides designated as exopolysaccharides (EPSs) encompasses a wide range of carbohydrate polymers which are synthesized by bacteria of all taxa and secreted into the external environment. The occurrence of EPSs is widespread as they are produced by a great variety of microorganisms, including opportunistic human pathogens and environmental microbes. EPSs are also produced by bacteria living in sea water as well as in harsh environments like Antarctica. The overwhelming diversity of polysaccharide origin is mirrored by a myriad of structures in terms of compositions, sequences, and molecular sizes. EPSs can be classified according to their chemical composition (which also reflects the biosynthetic mechanism) as homopolysaccharides and heteropolysaccharides (1). They can be composed of repeating units of 10 or fewer monosaccharide residues and be heteropolymeric with diverse high molecular weights (10 to 2000 kDa) (2, 3). Independently of their origin,

EPSs have been classified based on their functionality as (i) constructive or structural, (ii) sorptive, (iii) surface-active, (iv) active, (v) informative, (vi) redox-active, and (vii) nutritive (4). Needless to mention that EPSs play major roles in formation and stabilization of biofilms (5). As regards their biological properties, prospects about EPSs concern uses such as antithrombotic, anticoagulant, immuno-modulators, anti-cancer, as well as bio-flocculants (6–10).

Overall, EPSs are exceedingly considered for applications in medical (e.g., vaccine), technological, and food sectors. Due to the diversity of bacterial strains producing EPSs, there are wide variations in molecular structures as well as complexity of the mechanism by which physical changes and bioactive effects are elicited. Consequently, there is a need for establishing a computational-based platform of knowledge. Databases which have been developed for polysaccharides, at large, are few. The GlyTouCan repository contains glycan structures independent of experimental information used to identify the structures (11). The Bacterial Polysaccharide Gene Database (BPGD. [sydney.edu.au/science/molecular\\_bioscience/BPGD/](http://sydney.edu.au/science/molecular_bioscience/BPGD/)) is a relational database that contains information about genes involved in the synthesis of bacterial repeat unit surface polysaccharides (12). PolysacDB is a database of microbial polysaccharide antigens and their antibodies (<http://crdd.osdd.net/raghava/polysacdb>) (13). The Carbohydrate Structure Databases (CSDBs: <http://csdb.glycoscience.ru>) store structural, bibliographic, taxonomic, and NMR spectroscopic data from bacterial, archaeal, plant, and fungal parts (14). The database is regularly updated via manual expert curation of original publications. Polysac3DB is an annotated database of three-dimensional structures of polysaccharides irrespective of their origin that contains the 3D structural information of about 160 polysaccharides (<http://www.polysac3db.cermav.cnrs.fr>) (15). The database is embedded in a portal for structural glycobiology of several interlinked databases (<http://www.glyco3d.cermav.cnrs.fr>)

(16). Of particular interest is the availability of three-dimensional models constructed using dedicated software and accompanying tools. As a complement of these existing valuable databases, we realized that a database was missing which would organize, in a comprehensive way, the scattered information about the EPS such as bacterial strain, condition of growth, composition, structure as well as functional (physicochemical and biological) properties. Such a database would provide a fast overview within the growing field of bacterial polysaccharides. Such an annotated and curated database, called EPS-DB, is described in the present article. The interface through an intuitive search structure is designed to be user-friendly, especially for biologists and technologists. The usage of the EPS-DB through a user-friendly interface is presented with a subsection of the database exemplified by EPSs from lactic acid bacteria.

## **2. Database Format and Content**

### *2.1 Data Sources and Format*

EPS-DB is a web-based, platform-independent database of bacterial EPS repeating unit structures. It is freely available on the Internet as a web service at <http://www.epsdatabase.com>. Original data are manually extracted from the publications indexed in the Web of Sciences (<https://apps.webofknowledge.com>) and NCBI PubMed (<http://www.ncbi.nlm.nih.gov/pubmed>) with a carbohydrate-related term and taxon name in the keywords, title, or abstract. After manual extraction from the original article, all information is curated prior to their incorporation within the repository. Among the large number bacterial polysaccharides of known structure, only extracellular polysaccharides composed of repeating units such as excreted EPSs, capsular polysaccharides (CPSs), cell wall polysaccharides, teichoic acids, and pellicles, but not lipopolysaccharides (LPSs) and lipoteichoic acids (LTAs), nor statistical homopolysaccharides, were selected to be included in the database. The structural data were collected by extensive literature search describing

structure characterization of a total of 105 bacterial EPSs. However, The EPS-DB is dynamic and continuously expanding in number of entries based EPS structure and/or function deposition from the users of the database. The EPSs were incorporated into the EPS-DB with the ability to tune the appearance in a user-friendly manner.

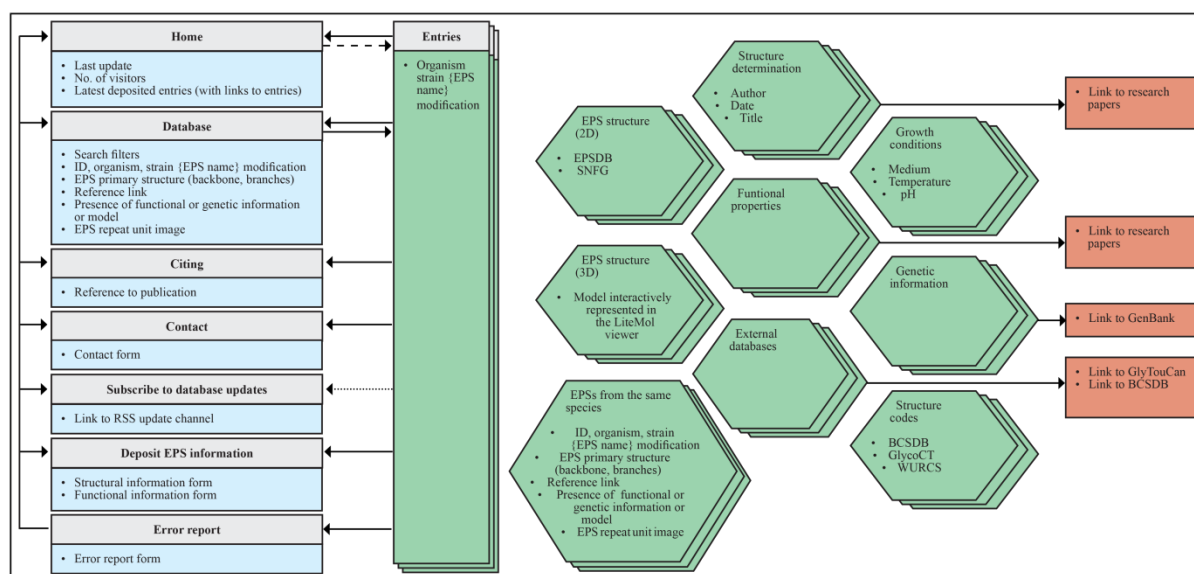
The variety in nomenclature, topology, and structural representations of EPSs requires several formats making sense to both the chemical and the biological communities along with meaningful graphical representations. These difficulties are accompanied by a major hurdle which remains namely the encoding of polysaccharide structures to facilitate computational processing. With this aim in mind, the following set-up was selected. The EPS repeating sequence is presented as graphical representations using the IUPAC extended format (EPS-DB) (17) and the SNFG format (18). Both formats account for the pyranose/furanose nature and the chirality (D or L) of the constituting monosaccharides, as well as for the anomeric configuration (alpha or beta). The IUPAC extended format is fairly human readable as standardized by the IUPAC and IUBMB Joint commission on biochemical nomenclature. As for the representation of monosaccharides, the Symbol Nomenclature For Glycans (SNFG) was selected, since it results from a concerted international agreement; it is compatible with graphical glycan and polysaccharides such as “Essential” cartoon representation (18, 19).

With regards to the encoding of polysaccharide structures, the choice was made to use BCSDDB, GlycoCT, and WURCS codes. The BCSDDB format has a linear coding difficult for humans to read, but it is most appropriate to describe the topological moieties, e.g. backbone and branches, occurring in EPSs (14). The GlycoCT code uses a graph notation and follows strict rules to represent monosaccharides; it uses a library to represent substituents (20). The WURCS 2.0 code can uniquely present any sequence, including those containing rare monosaccharides and ambiguous linkages, but is not human readable (21). All are universal

codes describing the sequence of complex carbohydrates and carbohydrate polymers; they can be used between several glycan databases and operate using the Semantic Web Technologies.

## 2.2. Structure and Usage of The EPS DataBase

A complete description of EPS-DB architecture is given in Figure 1. The database table is designed with an interactive front end with HTML web pages and embedded PHP and Java scripts, providing the user with several tools for modifying the interface as needed.



**Figure 1** Graphical representation of The EPS Database architecture. Rectangles represent websites. Hexagons represent paragraphs in the database entries. Blue represents main taps accessible from all sites in the database. The blue “Error report” in the bottom left is accessible from every entry sites. Green represents entries content. Red represents external websites. Full arrow indicates direct access to between sites. The dashed arrow indicates direct access from the homepage to the newest submitted entries. The dotted arrow indicates that access to the RSS feed from the entries are possible via the browser, and not through a direct link in the website.

Figure 2 provides an overview of the descriptors associated with the EPS collection.

The number of visible entries is controlled by a built-in pagination property that also provides two different numbers of entries in the repository ①. The first set of numbers represents the total number of entries per page out of the total number of entries matching the search-filter

**The EPS Database**  
The Bacterial Exopolysaccharide Structures and Properties Database

HOME DATABASE CITING CONTACT DEPOSIT EPS INFORMATION SUBSCRIBE TO DATABASE UPDATES

Page: 1 1 - 10 / 105 (105)

EPS-DB ID	Organism	Strain (EPS) modification	Backbone	Branches	Author	Date	Function	Genetic	Model	Structure
1	<a href="#">Lactobacillus sake</a>	0-1	{ 4}b <sub>0</sub> GlcP(1-4)α <sub>0</sub> GlcP(1-3)β <sub>0</sub> Rhap2Ac <sub>2,6</sub> (1-) <sub>n</sub>	[ b <sub>0</sub> GlcP(1-6) ] [ <sub>0</sub> Glc(1- <i>n</i> )α <sub>0</sub> Rhap(1-3) ]	<a href="#">Robijn et al.</a>	1995	-	-	-	
2	<a href="#">Lactobacillus helveticus</a>	2091	{ 6}b <sub>0</sub> GalP(1-4)α <sub>0</sub> GalP(1-3)β <sub>0</sub> GalP(1-4)β <sub>0</sub> GlcP(1-6)β <sub>0</sub> GlcP(1-) <sub>n</sub>	[ b <sub>0</sub> GalP(1-6) ]	<a href="#">Stauf et al.</a>	1996	-	-	-	
3	<a href="#">Lactococcus lactis ssp. cremoris</a>	SBT 0495 (villian)	{ 4}b <sub>0</sub> GlcP(1-4)β <sub>0</sub> GalP(1-4)β <sub>0</sub> GlcP(1-) <sub>n</sub>	[ α <sub>0</sub> Rhap(1-2) ] [ α <sub>0</sub> GalP(1- <i>n</i> ) ]	<a href="#">Nakajima et al.</a>	1992	+	-	-	
4	<a href="#">Lactobacillus delbrueckii ssp. bulgaricus</a>	291	{ 4}b <sub>0</sub> GlcP(1-4)α <sub>0</sub> GlcP(1-4)β <sub>0</sub> GalP(1-) <sub>n</sub>	[ b <sub>0</sub> GalP(1-4)β <sub>0</sub> GlcP(1-6) ]	<a href="#">Faber et al.</a>	2001	+	-	-	
5	<a href="#">Lactobacillus paracasei</a>	34-1	{ 3}b <sub>0</sub> GalPNAc(1-4)β <sub>0</sub> GalP(1-6)β <sub>0</sub> GalP(1-6)β <sub>0</sub> GalP(1-) <sub>n</sub>	[ <sub>0</sub> Glc(1- <i>n</i> ) ]	<a href="#">Robijn et al.</a>	1996	-	-	-	
6	<a href="#">Streptococcus thermophilus</a>	CNCMI 733	{ 3}b <sub>0</sub> GalP(1-3)β <sub>0</sub> GlcP(1-3)α <sub>0</sub> GalPNAc(1-) <sub>n</sub>	[ α <sub>0</sub> GalP(1-6) ]	<a href="#">Doco et al.</a>	1990	-	-	-	
7	<a href="#">Lactobacillus helveticus</a>	766	{ 3}b <sub>0</sub> GlcP(1-4)β <sub>0</sub> GlcP(1-6)α <sub>0</sub> GlcP(1-6)β <sub>0</sub> GalP(1-6)α <sub>0</sub> GlcP(1-) <sub>n</sub>	[ b <sub>0</sub> GalP(1-3) ]	<a href="#">Robijn et al.</a>	1995	-	-	-	
8	<a href="#">Streptococcus thermophilus</a>	OR 901	{ 2}α <sub>0</sub> GalP(1-3)α <sub>0</sub> GalP(1-3)α <sub>0</sub> GalP(1-3)α <sub>0</sub> Rhap(1-2)α <sub>0</sub> Rhap(1-) <sub>n</sub>	[ b <sub>0</sub> GalP(1-6)β <sub>0</sub> GalP(1-4) ]	<a href="#">Bubb et al.</a>	1997	-	-	-	
9	<a href="#">Lactobacillus rhamnosus</a>	RW-9595M	{ 3}α <sub>0</sub> Rhap(1-3)β <sub>0</sub> GlcP(1-3)α <sub>0</sub> Rhap(1-3)α <sub>0</sub> Rhap(1-3)α <sub>0</sub> Rhap(1-2)α <sub>0</sub> GlcP(1-) <sub>n</sub>	[ α <sub>0</sub> GalP4,6RP(1-2) ]	<a href="#">Van Calsteren et al.</a>	2002	+	+	-	
10	<a href="#">Lactobacillus rhamnosus</a>	R	{ 3}α <sub>0</sub> Rhap(1-3)β <sub>0</sub> GlcP(1-3)α <sub>0</sub> Rhap(1-3)α <sub>0</sub> Rhap(1-3)α <sub>0</sub> Rhap(1-2)α <sub>0</sub> GlcP(1-) <sub>n</sub>	[ α <sub>0</sub> GalP4,6RP(1-2) ]	<a href="#">Van Calsteren et al.</a>	2002	-	+	-	

The EPS Database

Figure 2 Database displaying the 10 first entries. Blue text under Organism and Author indicates embedded links to the matching entry and publication, respectively.

criteria. The number within parentheses represents the total number of entries in the repository. All entries are classified as EPS-DB ID, Organism, Strain, Backbone, Branches, Author, Date, Function, Genetic, Model, and Structure (2). The *Organism* class includes at least genus followed by species and subspecies, pathovar, or serotype when appropriate. When an EPS has been given a name, for example when a strain produced multiple EPSs, it is given within curly brackets in the *Strain* class; in addition, when the structure is not that of a native EPS, the nature of the modification is indicated. For structures in *Backbone* and *Branches* classes, a shortened form is used to represent monosaccharides (a/b for alpha/beta anomeric configuration, D/L for absolute configuration, monosaccharide abbreviation according to IUPAC, substituent abbreviation following its linkage position) and glycosidic linkages (anomeric position-linkage position). The *Function* and *Genetic* classes indicate that an entry provides links to references on functional (physicochemical or biological) properties and GenBank, respectively. Similarly, the *Model* class indicates whether a 3D model of the



polysaccharide is available. The *Structure* class shows an expandable mini version of the two-dimensional EPS-DB representation of the EPS structure.

Every classification has a built-in functionality which allows numeric or alphabetic sorting without requirement to refresh the page (3). The column sorting can be done individually or simultaneously by holding down the shift key and selecting multiple column headers. Additionally, the *Organism* class provides a direct link to a subsite with detailed information on taxonomy, bibliography, EPS repeating unit structure, and other EPS structures related by organism. The *Author* class refers to the publication describing the EPS structure characterization and provides a direct link to the original research article.

Figure 3 provides an overview of the descriptors associated with each EPS entry.

The subsite interface contains information and links to the publication describing the EPS structure characterization and information on growth medium, pH, and temperature used during EPS production (4). Additionally, each entry provides a direct link to Functional (physicochemical and biological) properties (5), Genetic information (6), and two External databases (7), GlyTouCan and BCSDB. Three structure codes are embedded when possible in the entry: BCSDB, GlycoCT, and WURCS codes (8). The EPS repeating unit sequence is presented in two different graphical formats; EPS-DB (IUPAC extended form) (9) and SNFG (10). Both the EPS-DB and the SNFG images are downloadable in .png and high-resolution .pdf and .eps vector format.

For each EPS a primary carbohydrate structure can be translated into the coordinate set of the corresponding tertiary structure, in one or several of its low energy conformations, using a previously described computer application (11) (22). The 3D structure can be viewed over the website via the LiteMol application (23). Downloading the atomic coordinates for further use is another option with the possibility of using the molecular visualization program tailored to

# The EPS Database

The Bacterial Exopolysaccharide Structures and Properties Database **13**

HOME DATABASE CITING CONTACT DEPOSIT EPS STRUCTURE ERROR REPORT

## Streptococcus macedonicus Sc136 (NCC 2419)

### Structure determination **4**

**Author** Vincent *et al.*  
**Date** 2000, August  
**Title** Structure and properties of the exopolysaccharide produced by *Streptococcus macedonicus* Sc136

### Growth conditions

**Medium** 10% reconstituted skim milk with addition of a mixture of amino acids in quantities corresponding to those found in 1% Proteose Peptone No. 3  
**Temperature** 30°C  
**pH** 5.5, maintained with 2 M NaOH

### Functional properties

**Reference** Conformational analysis in aqueous solution and estimation of the persistence length of exopolysaccharides produced by *Lactobacillus helveticus* Lh59 and *Streptococcus macedonicus* Sc136 **5**

### Genetic information **6**

**GenBank accession number** Not registered  
**BPGD** Not registered

### External database IDs **7**

**GlyTouCan** G89490UM  
**BCSDB** 5295

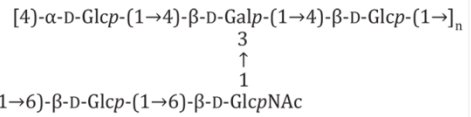
### Structure codes **8**

Select format ▾

-4)aDGlc(1-4)[bDGalf(1-6)bDGlc(1-6)[Ac(1-2)]aDGlcN(1-3)bDGalp(1-4)bDGlc(1-

## EPS structure **9**

### EPS-DB format

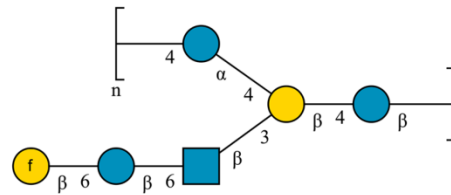


Download image as .eps

Download image as .pdf

Download image as .png

### SNFG format **10**

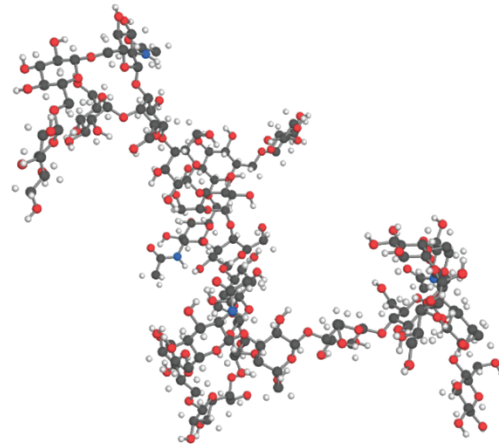


Download image as .eps

Download image as .pdf

Download image as .png

### LiteMol Viewer **11**



Download pdb file

**12**

## EPSs from the same species

EPS-DB ID	Organism	Strain (EPS) modification	Backbone	Branches	Author	Date	Function	Genetic	Model	Structure
101	<i>Streptococcus macedonicus</i>	Sc136 (NCC 2419)	{ 4}jaoGlc(1-4)[boGalp(1-4)boGlc(1-)] <sub>n</sub>	[ boGal(1-6)boGlc(1-6)boGlcNAc(1-3) ]	Vincent <i>et al.</i>	2000	+	-	+	
EPS-DB ID	Organism	Strain (EPS) modification	Backbone	Branches	Author	Date	Function	Genetic	Model	Structure

The EPS Database

Figure 3 Example of an EPS entry page.

deal with the range of 3D structures of complex polysaccharides (16). Finally, the EPS entries of the same species are illustrated in an automatically generated table similar to the main Database (12). Each entry is provided with an *Error Report* tap to enable the user to report potential error or additions to the EPS-DB (13).

### *2.3 Data Updating Tools and Administration*

At the present time, the set of information associated to each EPS from published articles is added manually. This allows for proper curation and annotation, at the expense of a time lag between the date of deposition and the date of formal insertion into the database.

## **3. Application to Exopolysaccharides (EPSs) from Lactic Acid Bacteria**

Lactic acid bacteria synthesize a wide variety of EPSs. These are either synthesized extracellularly from sucrose by glucan-sucrases or intracellularly by glycosyltransferases from sugar nucleotide precursors to form repeat units, which are then assembled and exported to the extracellular space and typically present in fermented milk products (24–27). Noteworthy, the EPS-DB only comprises extracellular polysaccharides composed of repeating units: excreted EPSs, CPSs, cell wall polysaccharides, teichoic acids, pellicles, but not LPSs and LTAs. In addition to textural properties in fermented dairy products, EPSs may confer beneficial health effects in humans including antitumor effect (6), immunomodulation (7, 8), antioxidant properties (28), anti-atherosclerotic activity (29), antimutagenicity (9), and biosorption of lead (10). It has been established that the intrinsic properties of EPSs (e.g. composition, branching, charge, mass) are crucial for protein interaction (30, 31) and their complexations with bacterial cells are of great importance in (i) rheological properties of fermented dairy products; (ii) pro- and prebiotics interactions; and (iii) biofilm formation (5, 32–34). These inter-macromolecular associations are highly specific and driven by hydrogen

bond, electrostatic, and ionic forces (5, 35). This emphasizes the importance of EPS structural knowledge for adequate description and understanding of the properties of such complexes.

#### **4. Conclusion**

Within the global efforts devoted to expanding and organizing knowledge on the biological and biotechnological context of complex glycans and carbohydrate polymers, it was the aim of the present work to set-up the framework of a database focused on the structural and functional features of EPSs. To ensure interoperability with other existing glyco-databases, particular attention was given to the selection of formats, in terms of structural depiction, graphical representation, and informatics coding. The registration of the structures within an international glycan structure repository widens the scope of search and applications and operations using the Semantic Web Technologies.

EPS-DB goes beyond a simple structural description of EPSs, as curated information about the EPS strain, condition of growth, composition, as well as functional properties are contextualized. This is in view of the immense scientific and technological interests that microbial polysaccharides offer either as carriers of unique functional properties or as a source of new material, new chemicals, new vaccines, or synthons for biotechnological synthesis. The subset of EPSs from lactic acid bacteria (85 structures on a total of 105 in the database) illustrates the use of EPS-DB and provides a typical example of what may be achieved in the fundamental understanding of properties resulting from their interactions with proteins in regulating sensory characteristics of dairy food products (30).

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