Databases and ontologies

**GlyGen data model and processing workflow**

Robel Kahsay1,* Jeet Vora1 Rahi Navelkar1, Reza Mousavi1, Brian C. Fochtman1, Xavier Holmes1, Nagarajan Pattabiraman1, Rene Ranzinger2, Rupali Mahadik2, Tatiana Williamson2, Sujeet Kulkarni2, Gaurav Agarwal2, Maria Martin3, Preethi Vasudev3, Leyla Garcia4, Nathan Edwards5, Wenjin Zhang5, Darren A. Natale5, Karen Ross5, Kiyoko F. Aoki-Kinoshita6, Matthew P. Campbell7, William S. York2 and Raja Mazumder1

1Department of Biochemistry & Molecular Medicine, The George Washington School of Medicine and Health Sciences, Washington, DC 20052, USA, 2Complex Carbohydrate Research Center, The University of Georgia, Athens, GA 30602, USA, 3European Bioinformatics Institute, Hinxton CB10 1SD, UK, 4ZB MED Information Centre for Life Sciences, Cologne 50931, Germany, 5Department of Biochemistry and Molecular & Cellular Biology, Georgetown University, Washington, DC 20007, USA, 6Faculty of Science and Engineering, Soka University, Tokyo 192-8577, Japan and 7Institute for Glycomics Griffith University, Southport QLD 4222, Australia

*To whom correspondence should be addressed.

Associate Editor: Peter Robinson

Received on January 29, 2020; revised on March 31, 2020; editorial decision on April 3, 2020; accepted on April 16, 2020

**Abstract**

**Summary:** Glycoinformatics plays a major role in glycobiology research, and the development of a comprehensive glycoinformatics knowledgebase is critical. This application note describes the GlyGen data model, processing workflow and the data access interfaces featuring programmatic use case example queries based on specific biological questions. The GlyGen project is a data integration, harmonization and dissemination project for carbohydrate and glycoconjugate-related data retrieved from multiple international data sources including UniProtKB, GlyTouCan, UniCarbKB and other key resources.

**Availability and implementation:** GlyGen web portal is freely available to access at https://glygen.org. The data portal, web services, SPARQL endpoint and GitHub repository are also freely available at https://data.glygen.org, https://api.glygen.org, https://sparql.glygen.org and https://github.com/glygener, respectively. All code is released under license GNU General Public License version 3 (GNU GPLv3) and is available on GitHub https://github.com/glygener. The datasets are made available under Creative Commons Attribution 4.0 International (CC BY 4.0) license.

**Contact:** rykahsay@gwu.edu

**Supplementary information:** Supplementary data are available at Bioinformatics online.

1 Introduction

This application note introduces the GlyGen data-processing workflow used to build the backend for the GlyGen (York et al., 2019) knowledgebase. This includes detailed information on the molecular, biophysical and functional properties of glycans, genes and proteins organized in pathways and ontologies as well as a rapidly growing body of biological big data related to mutation and expression. All data integrated in the GlyGen project are publicly available in standard formats supported by NCBI (Sayers et al., 2019) and EMBL-EBI (Cook et al., 2018) to promote standardization and sharing of data within the broader glycomics community. GlyGen is a five-star linked open data compliant knowledgebase and a registered member of FAIRsharing.org fulfilling BioDBcore requirements (https://fairsharing.org/biodbcore-001375/).

2 Data integration workflow

The framework used to integrate GlyGen data starts by collecting glycan, protein and glycoprotein datasets from major data resources and data generators. The collected heterogeneous datasets are processed following the workflow shown in Figure 1.

2.1 Data sources

In GlyGen, GlyTouCan (Tiemeyer et al., 2017) and PubChem (Kim et al., 2016) provide glycan-related data, whereas protein-related data are collected from resources, such as UniProtKB (UniProt Consortium, 2019), NCBI Reference Sequence (RefSeq) (O’Leary et al., 2016), BioMuta (Dingerdissen et al., 2018), BioXpress (Dingerdissen et al., 2018), Mouse Genome Institute
protein and glycoprotein datasets is given in the Supplementary Texts S1–S3, the GlyGen data page and dataset sample view page are shown in the Supplementary Figure S1a and b.

2.3 Biocompute Objects for GlyGen datasets
The dataset BCOs are created in conformance to the current BCO specifications (1.3.0) (https://github.com/biocompute-objects/BCO Specification/tree/master/schemas). A dataset BCO is created with the data integration process perspective to enable capturing all the metadata related to the processing steps performed in the workflow. The dataset BCOs constructed this way can be used as a ‘readme’ for the dataset that provides precise details on how the dataset is integrated. The use of the BCO standard facilitates granular tracking of metadata especially the provenance that helps in providing appropriate attribution and license information that dictates the usage of the dataset, workflow exchange between the researchers and the reproducibility of the dataset. These dataset BCOs are recorded and represented in machine-readable JavaScript Object Notation (JSON) format and can be viewed and downloaded from the GlyGen data page (https://data.glygen.org).

2.4 GlyGen docstore and web services
As mentioned earlier, the GlyGen data integration workflow creates glycan, protein and glycoprotein centric datasets. These datasets are used to generate glycan, protein and glycoprotein centric JSON objects, which are stored in a MongoDB docstore. The GlyGen docstore is used as a backend for various GlyGen web services that are used by the GlyGen frontend as well as other external application contexts. The GlyGen web services (https://api.glygen.org), which have been documented using the Swagger framework (https://swagger.io/) allow programmatic access of GlyGen data objects for glycan, proteins and glycoproteins. Some of these web services are generic and provide searching, listing and detailed record access functionalities for GlyGen data objects, while others are custom designed to respond to specific biological questions or use cases collected from the user community. The GlyGen API’s webpage is shown in the Supplementary Figure S2.

3 GlyGen data model, triplestore and SPARQL endpoint
All data in the GlyGen project are also available in the Resource Description Framework (RDF) format using namespace from various existing ontologies. The UniProt Core Ontology (Redaschi and UniProt Consortium, 2009) and GlyGen Ontology are used to describe protein-centric data whereas glycan-centric data are described using the GlycoRDF Ontology (Ranzinger et al., 2015). The GlyGen Ontology along with the Glycoconjugate Ontology (https://github.com/glycoinfo/GlycoCoO) provides the necessary namespace to represent glycoprotein data.

A partial view of the GlyGen data model is given in the Supplementary Figure S4, showing a glycoprotein entry linked to a protein sequence and one or many glycosylation sites. A glycosylation site consists of an exact or fuzzy position on a protein sequence that is known to have been glycosylated by a glycan or glycan set. An exact glycosylation site position is linked to the amino acid type that occupies it. The GlyGen knowledgebase uses a Virtuoso triplestore to store GlyGen triple data, and a SPARQL Protocol and RDF Query Language (SPARQL) endpoint (https://sparql.glygen.org) is built to provide programmatic access to the triplestore. The webpage for the GlyGen SPARQL interface and triplestore content statistics for release 1.5 are shown in the Supplementary Figure S3 and Table S1, respectively.

4 Conclusion
This application note has introduced the data model and processing workflow used for building the backend for the GlyGen knowledgebase. In this processing and integration workflow, data are retrieved
and extracted from a number of resources and then standardized and harmonized to create clean high-quality datasets. The dataset creation process is fully documented in a form of metadata by creating BCOs. These datasets are further processed to create JSON objects and RDF triples that populate MongoDB docstore and Virtuoso triplestore backend databases, respectively. The docstore is used by various GlyGen web services while the triplestore is accessed through the GlyGen SPARQL endpoint.

**Acknowledgements**

We would like to acknowledge the following people for their contributions: Jodie L. Abrahams, Yukie Akune, Sena Arpinar, Sanath Bhat, Judith A. Blake, Richard D. Cummings, Hayley Dingerdissen, Ten Feizi, Jeffrey Gildersleeve, Radoslav Goldman, Vinamra Jain, Johnathon G. Keeney, Radoslav Goldman, Vinamra Jain, Johnathon G. Keeney, Charles H. King, Akul Mehta, Sandeep Nakarakommula, Gareth Owen, Michael J. Pierce, Dacian Reece-Stremtan, Vijay Shankar, Tyler J. Stewart, Peng Su, Michael Tiemeyer, Robert J. Woods and Issaku Yamada.

**Funding**

This work was supported by the National Institutes of Health [1U01GM125267 - 01]; partly by the Australian Research Data Commons (ARDC); and Institute for Glycomics.

**Conflict of Interest:** none declared.

**References**

Altenhoff, A.M. *et al.* (2018) The OMA orthology database in 2018: retrieving evolutionary relationships among all domains of life through richer web and programmatic interfaces. *Nucleic Acids Res.*, 46, D477-D485.

Alterovitz, G. *et al.* (2018) Enabling precision medicine via standard communication of HTS provenance, analysis, and results. *PLoS Biol.*, 16, e3000099.

Berman, H.M. *et al.* (2000) The Protein Data Bank. *Nucleic Acids Res.*, 28, 233-242.

Bult, C.J. *et al.;* The Mouse Genome Database Group. (2019) Mouse Genome Database (MGD) 2019. *Nucleic Acids Res.*, 47, D801-D806.

Campbell, M.P. *et al.* (2014) UniCarbKB: building a knowledge platform for glycoproteomics. *Nucleic Acids Res.*, 42, D215-D223.

Cook, C.E. *et al.* (2018) The European Bioinformatics Institute in 2017: data coordination and integration. *Nucleic Acids Res.*, 46, D21-D29.

Dingerdissen, H.M. *et al.* (2018) BioMuta and BioXpress: mutation and expression knowledgebases for cancer biomarker discovery. *Nucleic Acids Res.*, 46, D1128-D1136.

Kibbe, W.A. *et al.* (2015) Disease Ontology 2015 update: an expanded and updated database of human diseases for linking biomedical knowledge through disease data. *Nucleic Acids Res.*, 43, D1071-D1078.

Kim, S. *et al.* (2016) PubChem substance and compound databases. *Nucleic Acids Res.*, 44, D1202-D1213.

Martin, A.R. *et al.* (2019) PanelApp crowdsources expert knowledge to establish consensus diagnostic gene panels. *Nat. Genet.*, 51, 1560-1565.

Mungall, C.J. *et al.* (2017) The Monarch Initiative: an integrative data and analytic platform connecting phenotypes to genotypes across species. *Nucleic Acids Res.*, 45, D712-D722.

O’Leary, N.A. *et al.* (2016) Reference sequence (RefSeq) database at NCBI: current status, taxonomic expansion, and functional annotation. *Nucleic Acids Res.*, 44, D733-D745.

Ranzinger, R. *et al.* (2015) GlycoRDF: an ontology to standardize glycomics data in RDF. *Bioinformatics*, 31, 919-925.

Redaschi, N. and UniProt Consortium (2009) UniProt in RDF: tackling data integration and distributed annotation with the semantic web. In: *Nature Precedings, 3rd International Biocurration Conference*. https://www.nature.com/articles/npre.2009.3193.1.

Sayers, E.W. *et al.* (2019) Database resources of the National Center for Biotechnology Information. *Nucleic Acids Res.*, 47, D23-D28.

Tiemeyer, M. *et al.* (2017) GlyTouCan: an accessible glycan structure repository. *Glycobiology*, 27, 915-919.

UniProt Consortium (2019) UniProt: a worldwide hub of protein knowledge. *Nucleic Acids Res.*, 47, D506-D515.

York, W.S. *et al.* (2019) GlyGen: computational and informatics resources for glycoscience. *Glycobiology*, 30, 72-73.