# Synthetic Biology-

## **Owl: Electronic Datasheet Generator**

Evan Appleton,<sup>\*,†,§</sup> Jenhan Tao,<sup>‡</sup> F. Carter Wheatley,<sup>§</sup> Devina H. Desai,<sup>§,#</sup> Thomas M. Lozanoski,<sup>§,#</sup> Pooja D. Shah,<sup>§,#</sup> Jake A. Awtry,<sup>§</sup> Shawn S. Jin,<sup>§</sup> Traci L. Haddock,<sup>§,||</sup> and Douglas M. Densmore<sup>\*,†,§,||,⊥</sup>

<sup>†</sup>Graduate Program in Bioinformatics, Boston University, Boston, Massachusetts 02215, United States

<sup>‡</sup>Bioinformatics and Systems Biology Graduate Program, University of California, San Diego, La Jolla, California 92093, United States

<sup>§</sup>Center of Synthetic Biology, Boston University, Boston, Massachusetts 02215, United States

<sup>||</sup>Department of Biomedical Engineering, Boston University, Boston, Massachusetts 02215, United States

<sup>1</sup>Department of Computer and Electrical Engineering, Boston University, Boston, Massachusetts 02215, United States

**Supporting Information** 

**ABSTRACT:** *Owl* (www.owlcad.org) is a biodesign automation tool that generates electronic datasheets for synthetic biological parts using common formatting. Data can be retrieved automatically from existing repositories and modified in the *Owl* user interface (UI). *Owl* uses the data to generate an HTML page with standard typesetting that can be saved as a PDF file. Here we present the *Owl* software tool in its alpha version, its current UI, its description of input data for generating a datasheet, its example datasheets, and the vision of the tool's role in biodesign automation.



The Registry of Standard Biological Parts (http://parts.igem.org) is the largest open-source registry for synthetic biological parts. It is also the standard registry for the annual International Genetically Engineered Machine (iGEM) competition. As iGEM expands, many new entries and entry modifications are submitted each year. Given this already large and rapidly growing registry and other growing registries of synthetic genetic parts (JBEI https://registry.jbei.org/, JGI http://genome.jgi.doe.gov/, SynBERC registry.synberc.org, and BioFAB www.biofab.org), the question of how to best share and store data becomes very important to answer. It is critical that the synthetic biology community forms a concerted effort to share data on genetic parts and other biological components in a standard way.<sup>1-3</sup>

The Registry purposefully allows flexibility in the entries in both format and content, lending itself to a broad diversity of parts. One of the Registry's strengths is its ability to capture many types of synthetic biological parts, but it lacks consistent formatting and presentation that is required for machine readability and manual comparisons. The lack of a common format can also hinder new users and may impede them from adding useful information to the Registry. Furthermore, as a variety of software tools becomes available for biodesign automation, it is necessary to provide a unified format for a part datasheet so that the tools can leverage data stored in these sheets.

To address these problems, we have created an online tool called Owl (www.owlcad.org) to generate electronic datasheets with a common format automatically. This version of Owl (alpha) lays the groundwork for the automated generation of datasheets.

## RESULTS

Owl (www.owlcad.org) is a web-based tool that generates electronic datasheets for synthetic biological parts. A datasheet provides a quantitative and qualitative description of genetic device behavior that allows an engineer to determine if a part is suitable for a desired use.<sup>4</sup> *Owl* allows users to enter part information either automatically from pre-existing entries on the Registry or manually in the user interface. *Owl* currently uses Synthetic Biology Open Language visual (SBOLv) compliant images for part and device images and can link images from Pigeon<sup>5</sup> (www.pigeoncad.org) and Raven (www.ravencad.org)<sup>6</sup> onto a datasheet. *Owl* generates HTML pages in a standard format and can be saved as a PDF.

In consideration of previous datasheets<sup>2,4,7</sup> and common assays used to characterize biological systems, *Owl* datasheets are separated into five sections: (1) Basic Information, for part identification and visual representation; (2) Designer Information, for attributing authorship, providing contact information and the date; (3) Design Details, for detailed information about part function; (4) Assembly Information, for describing how the part was made; and (5) Assays, for presenting characterization data. We have provided three sections for assays: restriction mapping, flow cytometry, and a section where users can add their own type of assay.

To demonstrate our format's ability to represent a diversity of parts, we created several example datasheets for a variety of functionally different parts (Table 1; datasheets are available

Received: January 19, 2014 Published: December 19, 2014

Special Issue: iGEM 2013

#### **ACS Synthetic Biology**



| Input Fields   | Input Information  | Basic Information   |   |
|--|--|---|---|
| Basic Information<br>Part Name*<br>Sequence*<br>Part Type<br>Pigeon Image<br>Plasmid Map<br>Part Summary*<br>Related Parts | Part name (e.g., BBa_R0040, pTetR)<br>DNA sequence for the part<br>Basic or composite part<br>Graphic to visualize the part<br>Graphic to visualize the entire plasmid with the part<br>Short written description of the part<br>List of related Part Names if applicable        | Part Name Sequence Part Type Basic Part Part Summary                      | Pigeon Image<br>Choose File  No file chosen<br>Plasmid Map Image<br>Choose File  No file chosen |
| Designer Information<br>Author(s)*<br>Date*<br>Team  | List all researchers who worked on creating this part<br>Date the part was created<br>iGEM team name; can also be used as Lab Name   | Related Parts Back Next   |   |
| Affiliation<br>Contact   | Researchers who collected data for this part<br>University or company affiliation<br>Contact person and email for questions about the part   | Designer Information  |   |
| Design Details<br>Type<br>Design<br>Components<br>Vector<br>Additional   | Descriptive part type (e.g., inducible promoter; NOR gate)<br>Components used in the part (e.g., basic parts within a<br>composite, restriction sites, sequence direction)<br>Plasmid backbone the part is cloned into<br>Any other comments (e.g., plasmid resistance, required | Author(s) Date Team Back Next   | Data Collectors Affiliation Contact   |
| Comments   | growth conditions)   | Design Details  | Vector  |
| Assembly Information<br>Assembly<br>Method(s)<br>Assembly RFC<br>Scars   | List any methods used to create this part (e.g., BioBricks,<br>MoClo, Gibson)<br>If available, list the Request For Comments number (e.g.,<br>RFC10)<br>Assembly scars remaining within or flanking the part   | Design Components Back Next   | Additional Comments   |
| Assembly   | once assembled (e.g., BioBricks mixed site)<br>Items required for proper assembly (e.g., restriction   | Assembly Informatio   | n   |
| Components<br>Assembly<br>Graph<br>Chassis<br>Strain   | enzymes, oligonucleotides)<br>Assembly graph or plan used to create this part (e.g.,<br>Raven assembly graph)<br>Organism the plasmid containing the part was cloned<br>into (e.g., <i>E. coli, S. cerevisiae</i> )<br>Specific strain of the organism (e.g., DH5-alpha, MG1655) | Assembly Methods(s)<br>Assembly RPC<br>Scars (y/n)<br>Assembly Components | Assembly Graph Image<br>Choose File No file chosen<br>Chassis                                   |
| Additional<br>Comments   | Any other comments needed to understand how this part<br>was assembled   |   | Additional Comments   |
| * indicates required fi  | eld  | Back Next   |   |

Figure 1. The *Owl* UI sections for Basic Information, Designer Information, Design Details, and Assembly Information. The input fields for each section are outlined on the left with descriptions for the input information for each field. The images on the right show the web interface UI from www.owlcad.org.

online at www.owlcad.org). These datasheets represent several parts created by the CIDAR lab (www.cidarlab.org) as well as examples from literature to demonstrate *Owl's* applicability to a diverse assortment of parts.

**Required and Optional Fields.** *Owl* datasheets have required fields based on the Registry's data model (Figure 1). This information is meant to represent the minimum information required to define a part with which data can be experimentally associated. Specifically, *Owl* requires that a DNA part be described sufficiently such that an assay could be performed upon it. Thus, all fields needed to describe a part's composition are required. *Owl* datasheets have five required fields, namely: Part Name, Sequence, Part Summary, Author(s), and Date. Completion of all other relevant fields is encouraged but optional.

Automated Population of Fields from Registry Pages. When generating a new datasheet from an existing Registry page, *Owl* parses information from the Registry's XML pages and autopopulates fields on the datasheet, namely: Part Name (ex: BBa\_B0034), Part Description, Part Type (ex: RBS), Date entered, Part Author, and Sequence. The user can then go through each section manually and add to or change the existing information.

#### DISCUSSION

While *Owl's* goal is to automate the creation of datasheets, the task inherently poses the question of what a datasheet for synthetic biological parts should display. The default format of *Owl's* datasheet may not be ideal for all cases; however, it is flexible and provides fields similar to those described in previous work<sup>2,4,7</sup> such as identifying information, circuit visualization, author contact information, assembly information, and characterization by gel electrophoresis and flow cytometry. Further considerations include the ability to present four kinds of data proposed in previous work:<sup>4</sup> static behavior, dynamic behavior, compatibility with other devices, and reliability of the device measured by the number of generations the device can uphold desired functionality (Figures S1 and S2, Supporting Information).

# Table 1. Twenty Biological Parts Used to Generate Owl Datasheets

| part description                       | datasheet name           | chassis                     | source                             |
|--|--------------------------|-----------------------------|------------------------------------|
| Fungus promoter                        | BBa_K678001              | Aspergillus<br>nidulans     | The Registry                       |
| BioBrick Inverter                      | BBa_K783067              | Escherichia coli            | The Registry                       |
| Cas9                                   | BBa_K1179002             | E. coli                     | The Registry                       |
| Coexpression device<br>for RFP and GFP | CoxRG_AF                 | E. coli                     | CIDAR Lab,<br>Boston<br>University |
| Constitutive<br>promoter               | BBa_J23100               | E. coli                     | The Registry                       |
| 5' UTR                                 | BBa_K1114107             | E. coli                     | The Registry                       |
| RFP                                    | BBa_K1114211             | E. coli                     | The Registry                       |
| Transcriptional<br>terminator          | BBa_B0015                | E. coli                     | The Registry                       |
| MoClo destination<br>vector            | BBa_K1114400             | E. coli                     | The Registry                       |
| BioBrick vector                        | BBa_pSB1K3               | E. coli                     | The Registry                       |
| RFP reporter (1)                       | BBa_K1114500             | E. coli                     | The Registry                       |
| RFP reporter (2)                       | BBa_K1114502             | E. coli                     | The Registry                       |
| RFP reporter (3)                       | BBa_K1114503             | E. coli                     | The Registry                       |
| RFP reporter (4)                       | BBa_K1114504             | E. coli                     | The Registry                       |
| RFP reporter (5)                       | pJ054m1Rm_AE             | E. coli                     | CIDAR Lab,<br>Boston<br>University |
| Alternative splicing device            | BBa_K1051900             | Saccharomyces<br>cerevisiae | The Registry                       |
| T1S1 RNAi                              | T1S1                     | HEK 293                     |                                    |
| Toggle switch                          | Collins Toggle<br>Switch | E. coli                     |                                    |
| Arteminisic acid<br>producer           | CYP71AV1                 | S. cerevisiae               |                                    |
| NOR Gate                               | NOR Logic Gate           | E. coli                     |                                    |

*Owl* is intended to serve the community by streamlining the creation of electronic datasheets that can be used to exchange important biological part information in a visually intuitive and user-friendly manner. Although other platforms formalize data exchange between machine users,<sup>3,8</sup> there is a need for a consistently structured way to present data to a human user with which they can make decisions. We believe that *Owl* can help fill this gap.

Newer versions of the tool will be integrated with additional platforms and registries<sup>3,8</sup> to generate datasheets automatically as a user moves through experimental workflows. The current datasheet sections and fields may not be the best way to represent information for every type of part so the fields and sections of a datasheet will be editable in human-readable "configuration files." Since the stylistic formatting of the datasheets may not suit all users, style files will be used to automatically typeset datasheets.

### ASSOCIATED CONTENT

#### **S** Supporting Information

Figure S1: The *Owl* UI sections for the Restriction Digest and Flow Cytometry Assays. The input fields for each section are outlined on the left with descriptions for the input information for each field. The images on the right show the web interface UI from www.owlcad.org. Figure S2: The *Owl* UI sections for the Other Assay. The input fields for each section are outlined on the left with descriptions for the input information for each field. The images on the right show the web interface UI from www.owlcad.org. This material is available free of charge *via* the Internet at http://pubs.acs.org.

#### AUTHOR INFORMATION

#### **Corresponding Author**

\*E-mail: dougd@bu.edu.

\*E-mail: eapple@bu.edu.

#### Author Contributions

<sup>#</sup>D.H.D., T.M.L., and P.D.S. contributed equally.

#### Notes

The authors declare the following competing financial interest(s):D.M.D. is the co-founder and President of Lattice Automation, Inc., a company that creates bio-design automation software.

#### ACKNOWLEDGMENTS

The authors acknowledge Dr. Jacob Beal, Dr. Swapnil Bhatia, Dr. Ernst Oberortner, Zachary Chapasko, and Sonya Iverson for useful discussions. This work has been funded by the Office of Naval Research under Grant No. N00014-11-1-0725.

#### REFERENCES

(1) Peccoud, J., Anderson, J. C., Chandran, D., Densmore, D., Galdzicki, M., Lux, M. W., Rodriguez, C. A., Stan, G. B., and Sauro, H. M. (2011) Essential information for synthetic DNA sequences. *Nat. Biotechnol.* 29, 22–22.

(2) Arkin, A. (2008) Setting the standard in synthetic biology. Nat. Biotechnol. 26, 771–774.

(3) Galdzicki, M., Clancy, K. P., Oberortner, E., Pocock, M., Quinn, J. Y., Rodriguez, C. A., Roehner, N., Wilson, M. L., Adam, L., Anderson, J. C., Bartley, B. A., Beal, J., Chandran, D., Chen, J., Densmore, D., Endy, D., Grunberg, R., Hallinan, J., Hillson, N. J., Johnson, J. D., Kuchinsky, A., Lux, M., Misirli, G., Peccoud, J., Plahar, H. A., Sirin, E., Stan, G. B., Villalobos, A., Wipat, A., Gennari, J. H., Myers, C. J., and Sauro, H. M. (2014) The Synthetic Biology Open Language (SBOL) provides a community standard for communicating designs in synthetic biology. *Nat. Biotechnol.* 32, 545–550.

(4) Canton, B., Labno, A., and Endy, D. (2008) Refinement and standardization of synthetic biological parts and devices. *Nat. Biotechnol.* 26, 787–793.

(5) Bhatia, S., and Densmore, D. (2013) Pigeon: A design visualizer for synthetic biology. *ACS Synth. Biol.* 2, 348–350.

(6) Appleton, E., Tao, J., Haddock, T., and Densmore, D. (2014) Interactive assembly algorithms for molecular cloning. *Nat. Methods* 11, 657–662.

(7) Lee, T. S., Krupa, R. A., Zhang, F., Hajimorad, M., Holtz, W. J., Prasad, N., Lee, S. K., and Keasling, J. D. (2011) BglBrick vectors and datasheets: A synthetic biology platform for gene expression. *J. Biol. Eng.* 5, 12.

(8) Xia, B., Bhatia, S., Bubenheim, B., Dadgar, M., Densmore, D., and Anderson, J. C. (2011) Developer's and user's guide to Clotho v2.0 A software platform for the creation of synthetic biological systems. *Methods Enzymol.* 498, 97–135.