The Synthetic Biology Knowledge System (SBKS)

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Introduction

- Synthetic biology has a transformative potential.
- Many parts come from or are initially tested in *E. coli*.
- Many applications require different bacteria or higher-level organisms.
- Researchers currently use trial-and-error.
- Access to a wide range of data is essential to scale.
- The SBKS project is developing an open and integrated knowledge system.

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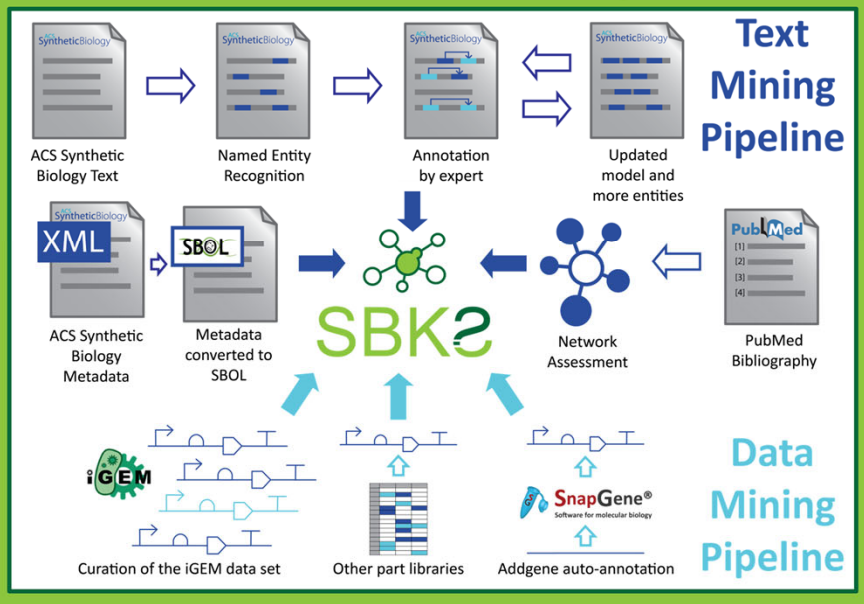
Synthetic biology has a transformative potential in applications from energy, agriculture, materials, and health.
Many parts come from or are initially tested in *E. coli*.
Many applications require different bacteria or higher-level organisms (i.e., yeast and other eukaryotic cells).
Researchers currently use trial-and-error, since reliable information about prior attempts is difficult to locate.
Access to a wide range of data is essential to scale.
The SBKS project is developing an open and integrated knowledge system to harness disparate, heterogeneous data sources to accelerate scientific exploration and discovery.

SBKS Curation Pipeline



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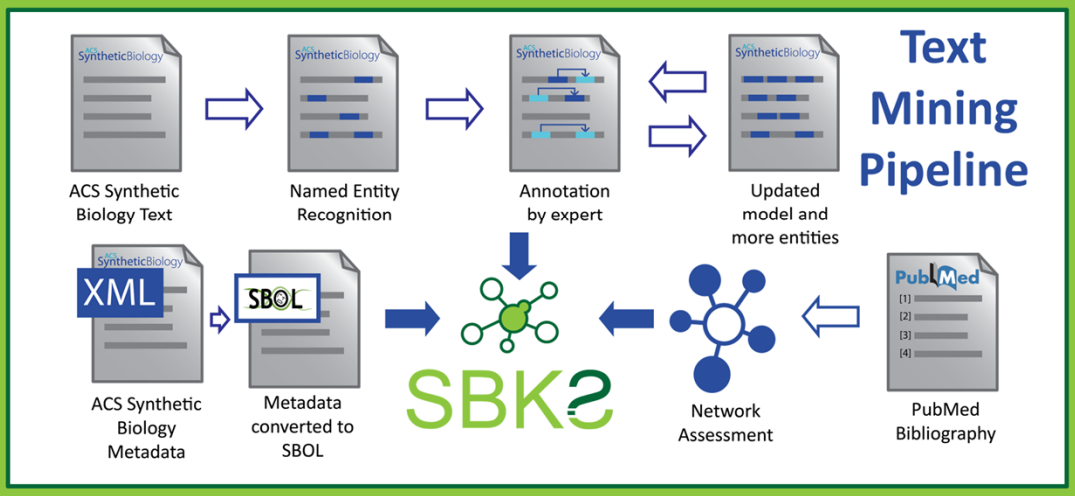
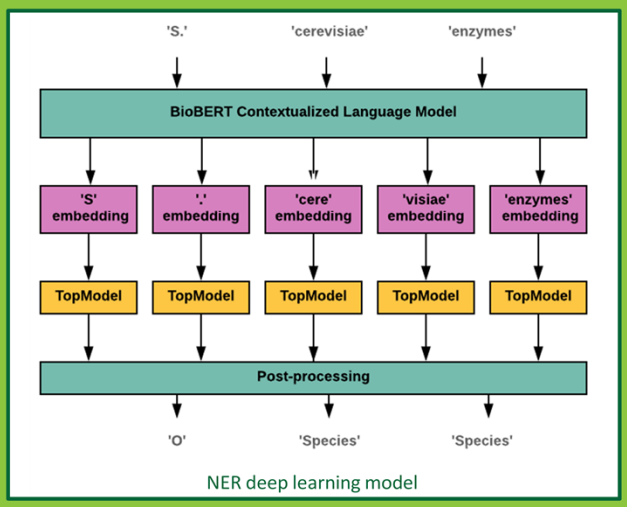
Text Mining Pipeline (Overview)



ACS Synthetic Biology provided full text in Journal Article Tag Suite (JATS) XML format.
Text extracted and annotated using Named Entity Recognition (NER) and validated by domain experts.
Metadata extracted and encoded into the Synthetic Biology Open Language (SBOL).
In parallel, full synthetic biology corpus found in PubMed is searched for articles on synthetic biology ethics.
Results are shared via the SBKS instance of SynBioHub.

Named Entity Recognition

- Parse XML formatted full articles into text.
- Process text with NER using deep learning models to identify synthetic biology related entities (e.g., gene names).



NER deep learning model

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We use a deep learning model for NER, specifically a BioBERT model. The figure gives a schematic view of the model. The model inputs text, tokenizes it, and generates embeddings for the tokenized text. The token embeddings are then classified into pre-specified entity types (e.g., Species), and additional processing is performed to assign a label to an entire entity (e.g., Species for S. cerevisiae). [Note: An embedding is a numeric vector representation of a token.]

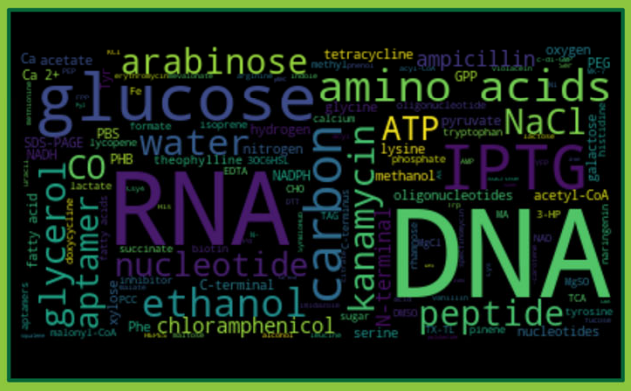
Named Entity Recognition

Species | Gene or Protein | Gene or Protein | Chemical

endogenous S. cerevisiae enzymes such as the reductase Oye2 and acetyltransferase Aft1 are known to degrade geraniol.

Annotations discovered by NER model in an ACS article

- NER-discovered annotations are validated by domain experts and corrected, as necessary.
- Refined annotations are used to fine tune models.
- Entities identified through this process are used to tag articles linked in SBKS.
- Analysis can also be carried out on tag frequency.



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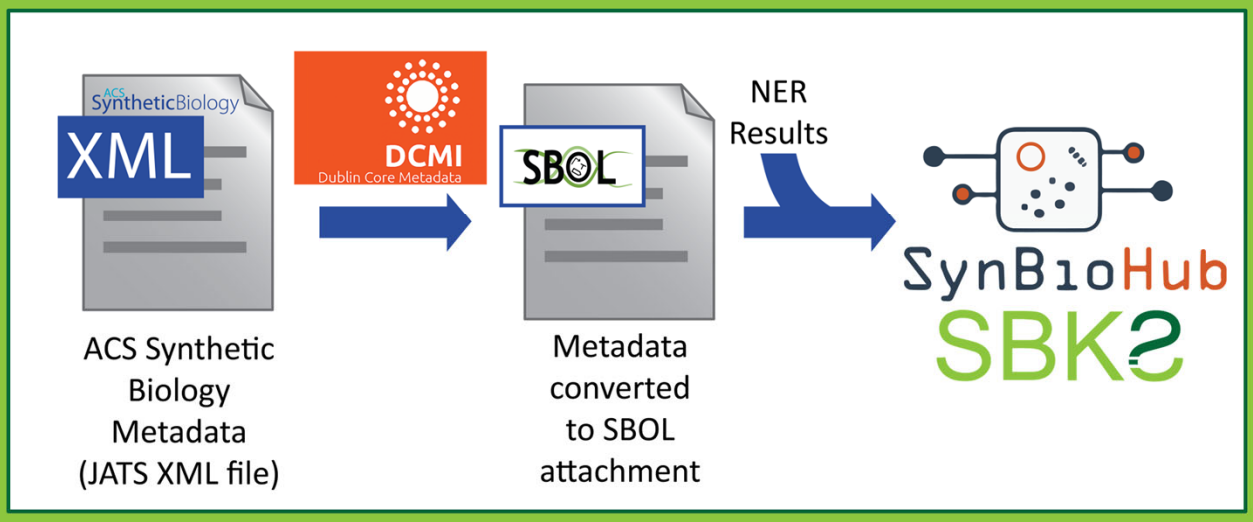
The lower figure is a word cloud showing how often the Chemical entity type was found in the ACS dataset. The larger the term is in the word cloud, the more often it was identified by the NER model in the set of ACS articles.

The top figure shows entity mentions found by the NER model in an ACS article. Each mention is associated with a single entity type. Note that when the NER-discovered terms are validated by the domain experts, "reductase Oye2" is split into two entities, "reductase" and "Oye2."

Metadata Harvesting



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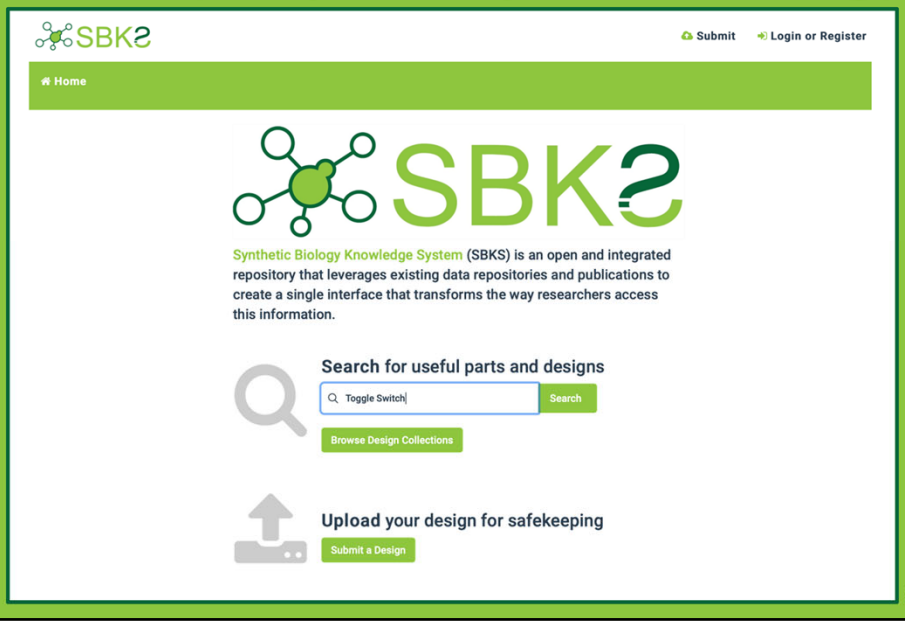
Create an SBOL Attachment object for each article in ACS Synthetic Biology.
Parse the metadata and reference sections from the JATS XML file, and map to SBOL and Dublin Core.
Results of NER added as keywords to these objects.
Results uploaded to the SBKS instance of SynBioHub.

SBKS (https://synbioks.org)



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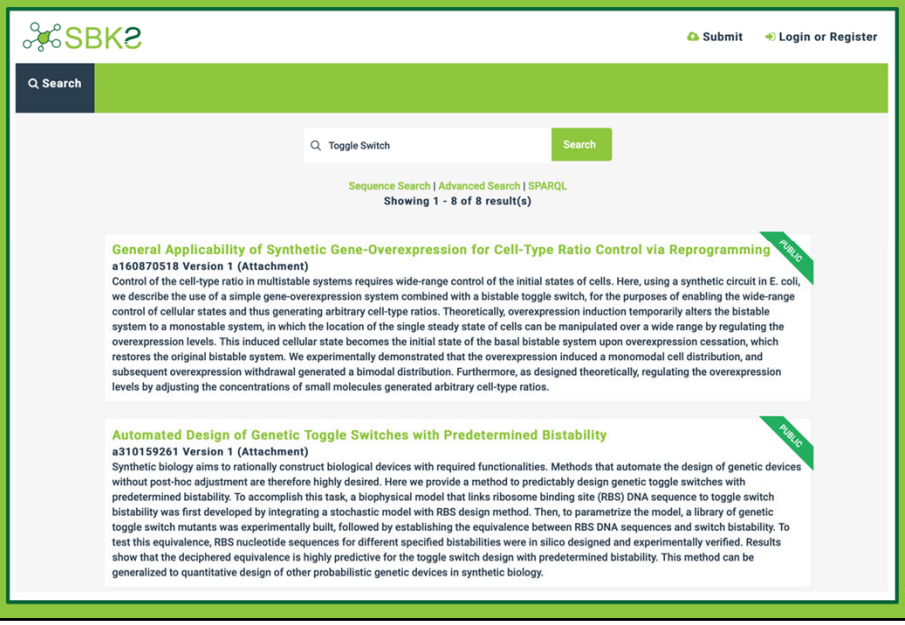
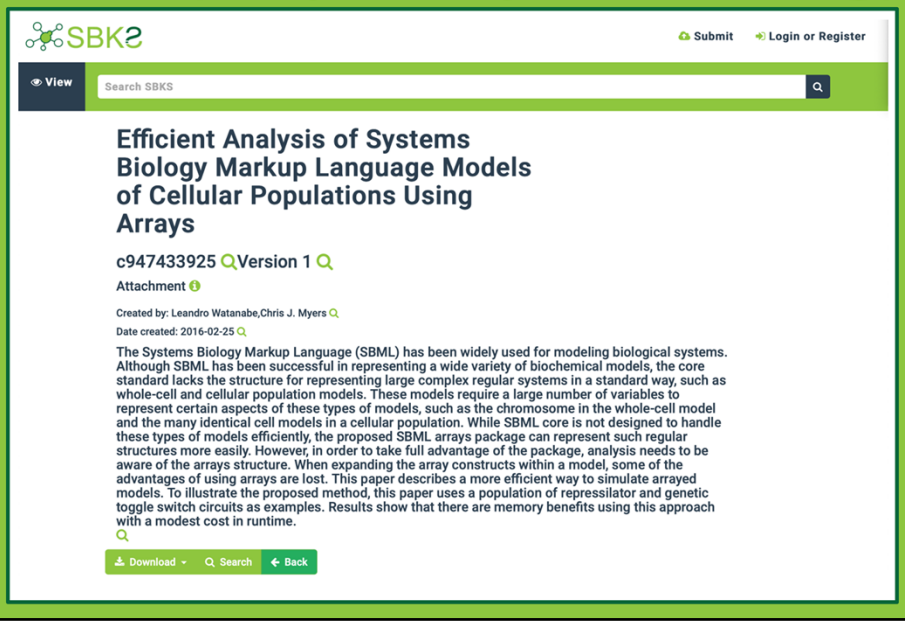
SBKS (https://synbioks.org)



SBKS (https://synbioks.org)



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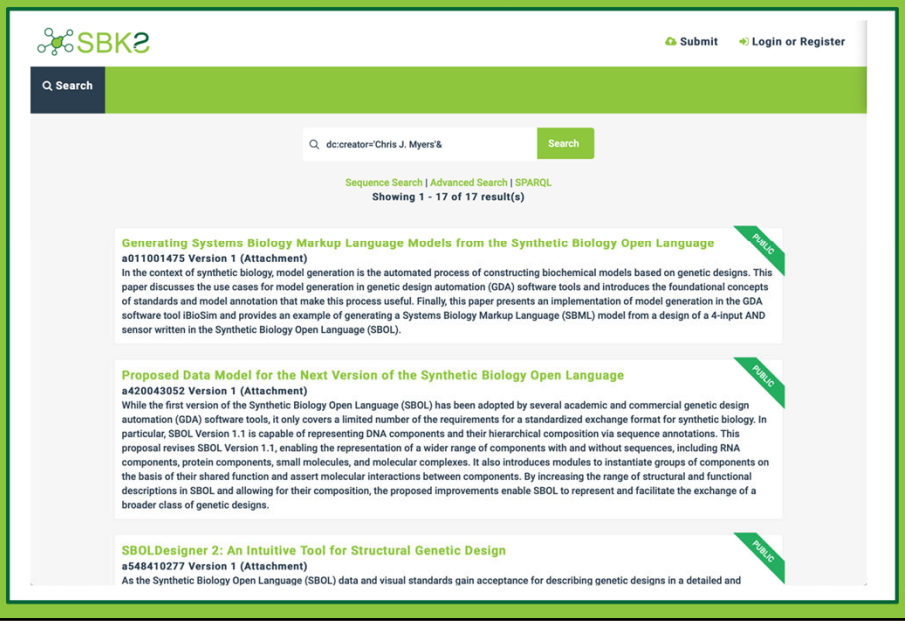
SBKS (https://synbioks.org)



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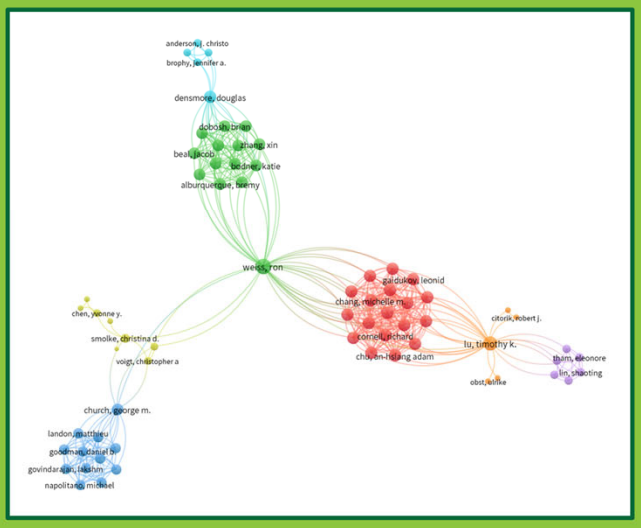
Synthetic Biology Ethics Literature

- Only ~4% of synthetic biology texts discuss ethical issues.
- Ethics gets little attention until 2010, 10 years after field began.
- Social networks among ethically-concerned researchers differ greatly from the overall synthetic biology collaboration network.
- Topics discussed range from concrete (e.g., food technology) to abstract (e.g., moral principles, defn of life).
- Analytical results from NLP will link SBKS queries with ethical issues.



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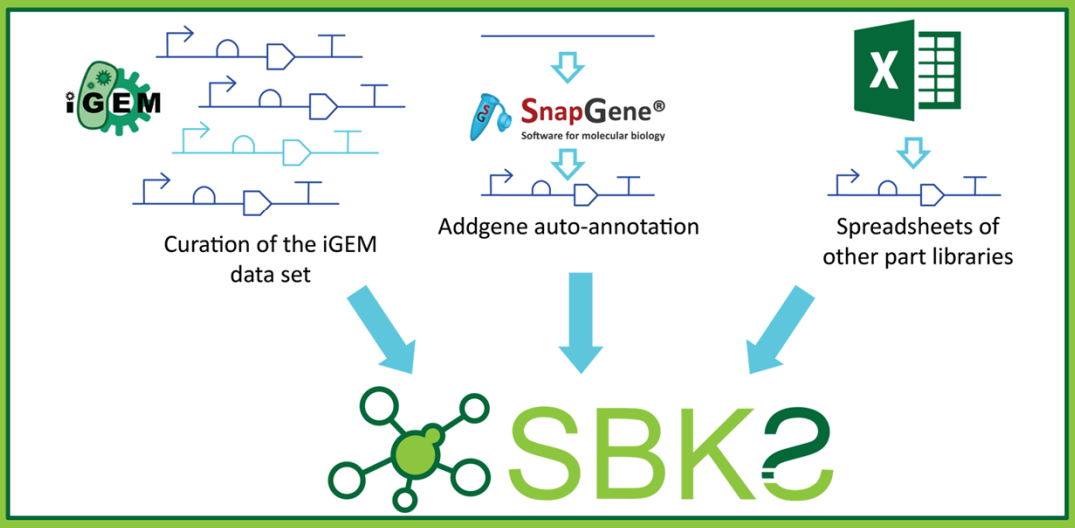
- Overview
  - Innovations within synthetic biology offer a lot of promises (e.g., medicine, food technologies), but they nonetheless bring about many ethical questions. CRISPR is probably the most well-known example, but actually most research deals in some way with issues that concern the public. Pew Research Center pretty consistently publishes public opinion data showing this.
  - Our SBKS doesn't attempt to resolve these questions but rather seeks to inform researchers about known ethical concerns surrounding their research/query. Researchers will then be able to look into the concerns on their own or to turn to ethical experts identified by SBKS results.
  - In order to to this well, we need to know what is being discuss and who is discussing each topic.
    - Without knowing the communities in which certain concerns tend to focus, information retrieval systems can easily collect a biased sample of the ethical literature. This can happen because such systems do not consistently identify the ways in which certain communities discuss ethical issues (and thus fail to learn new ways they should be querying literature).
- Findings
  - Ethics currently represents a very small proportion of synthetic biology literature.
  - Synthetic biology literature started to grow exponentially around 2000, but it wasn't until closer to 2010 that people started to publish consistently on ethics.

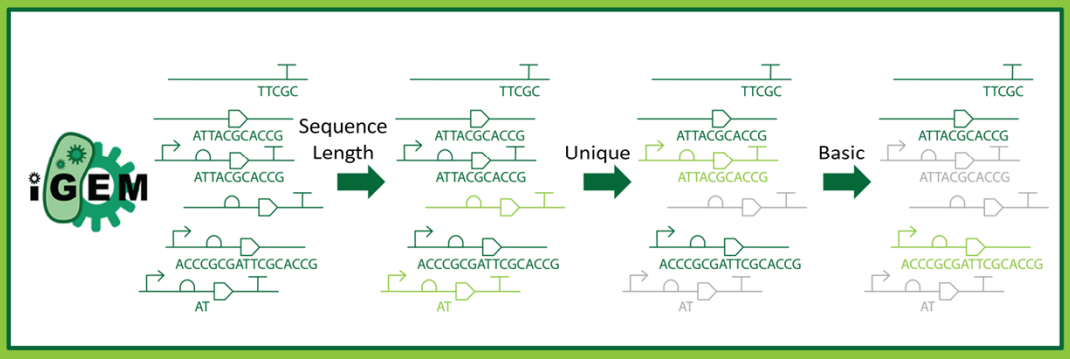
    - Among ethics publications, collaboration groups tend to be isolated. Individuals might co-publish very frequently with the same individuals, but these collaboration groups tend not to collaborate with others.
    - At the institutional level, collaborations tend to revolve around a handful of core institutions.
    - The included image presents the largest connected component in the collaboration graph. Even within this community, one can see that subgroups are pretty distinct and tend to be connect by one to few individuals.
    - Topic modeling uncovers a wide range of ethical concerns. Some topics are very concrete, e.g., CRISPR; other topics are policy related, i.e., regulation of these technologies and the allocation of new resources; still other topics are very abstract and philosophical, e.g., the definition of life.
- Linking back to non-ethics results
    - The next set of tasks will involve using many of the same NLP methods other project components have used so far (e.g., NER and custom embeddings) to connect these ethical concerns among frequently distinct communities to SBKS queries.

Data Mining Pipeline (Overview)



SBOL iGEM library was created, now being curated and validated.
Coarse and manual filtering, machine learning, and auto-annotation applied for poorly annotated sequences.
iGEM curation method will be applied to additional part libraries.
Developing methodology to add other part libraries to SynBioHub via Excel Spreadsheets.

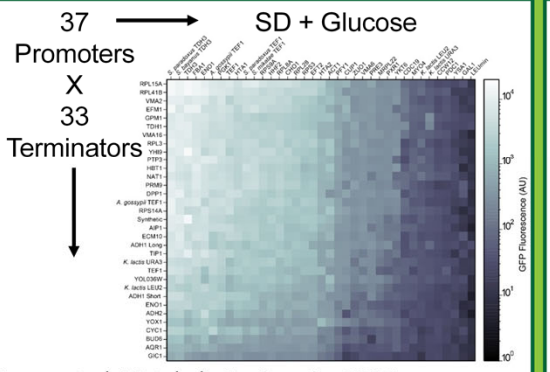
iGEM Dataset Curation



Further refinement performed using Snapgene auto annotation.

Other Libraries addgene

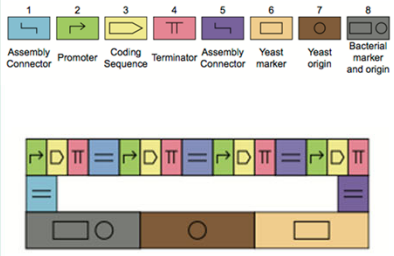
Foundry Yeast Parts



Young, *et al. Metabolic Engineering* 2018

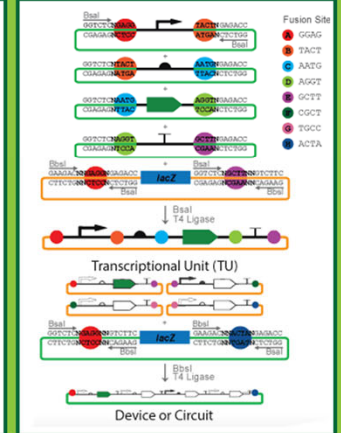
Casini, *et al. JACS* 2018

YTK



Lee, *et al. ACS Synthetic Biology* 2015

CIDAR



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We would like to include libraries that meet several criteria:

1. Published with characterization data
2. Available on Addgene for easy access and distribution
3. Modular, particularly TypeIIS assembly

The foundry parts library is a set of yeast parts developed by Eric Young at the MIT-Broad Foundry for massively parallel combinatorial design in yeast. This was applied to itaconic acid (met eng 2018) and several other molecules (JACS 2018)

The YTK parts library is a set of yeast parts developed by John Dueber that is on Addgene and used by the community.

The CIDAR MOclo kti is a set of E. coli parts developed by Doug Densmore that is on Addgene and used by the community, and easily adapted to other bacteria.

SynBioHub Sequence Search

- The ability to search becomes increasingly important as parts repositories grow.
- SBOLExplorer uses VSEARCH, a global alignment algorithm which is more effective at comparing similarities over entire sequences.

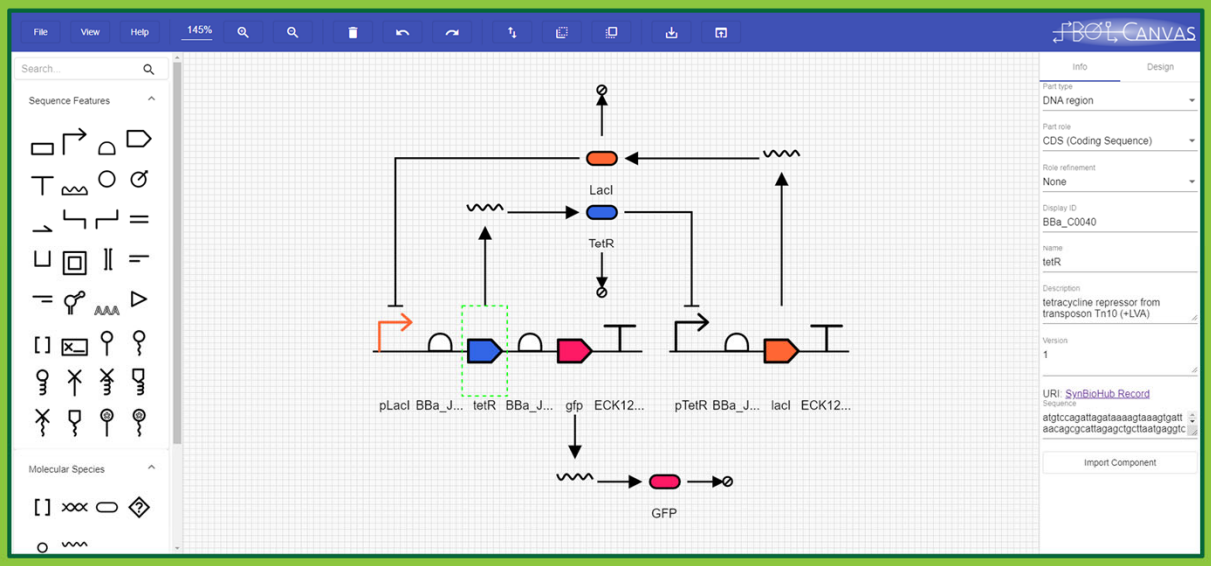
Searching by sequence will become a critical tool as repositories such as SynBioHub grow in size. Prior to this project, users could only search by keyword, or filters such as creator, or date.

The addition of a new sequence search tool allows users to search by a text sequence or FASTA/FASTQ file.

This was implemented using VSEARCH, an open-source tool using a global-alignment algorithm which is faster than BLAST for short sequences.

A command line API is also available for those who want to search via a GET request. More information can be found at the later poster session.

SBOLCanvas



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Discussion

- The SBKS project began less than a year ago, and it is being executed by a team that met only a few months before that.
- While the scope is ambitious, the progress so far is very promising.
- We look forward to feedback from the community about the needs and potential applications for SBKS.

More Information (Poster Session II)

- Room 1
  - *Discovering Content through Text Mining for a Synthetic Biology Knowledge System,* M. Nguyen, et. al.
  - *The Social and Conceptual Organization of Synthetic Biology Ethics,* B. Sepulvado, et. al.
- Room 2
  - *Analysis of the SBOL iGEM Data Set,* J. Mante, et. al.
  - *Sequence-based Searching For SynBioHub Using VSEARCH,* E. Yu, et. al.
  - *VisBOL 2.0 - Improved Synthetic Biology Design Visualization,* B. Hatch, et. al.

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