Data Integration and Mining for Synthetic Biology Design

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Engineering biological systems is challenging

C G A T → NNNNNNNNNN → 4^{10} ~ 1 million solutions

Order and layout

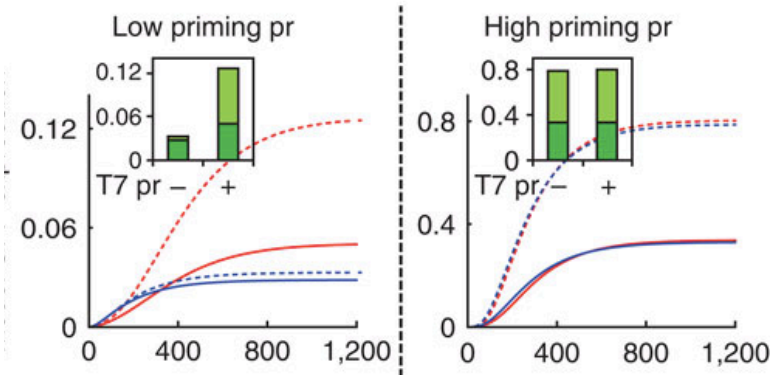
Regulatory elements

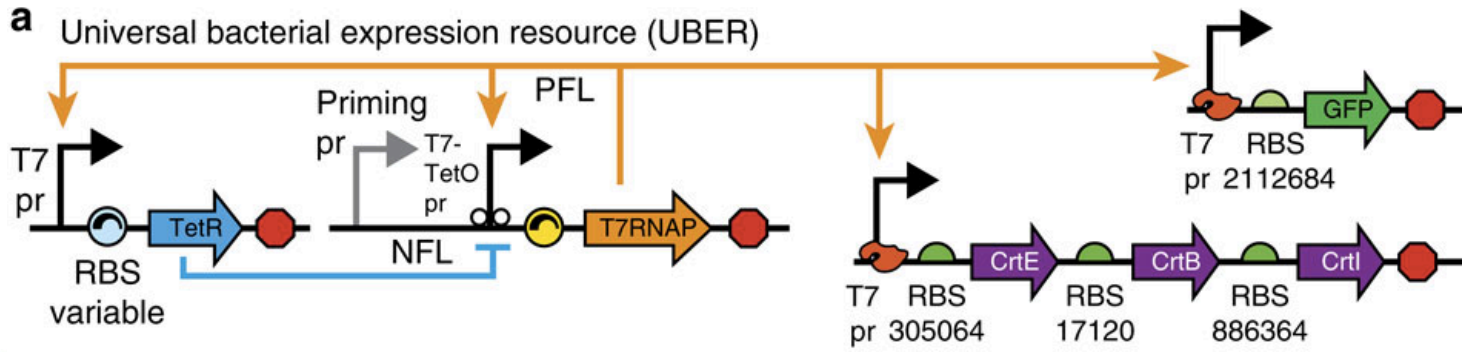
Molecular interactions

Strain/Host/Chassis

Biological Context

Experimental Conditions





Kushwaha and Salis, 2015

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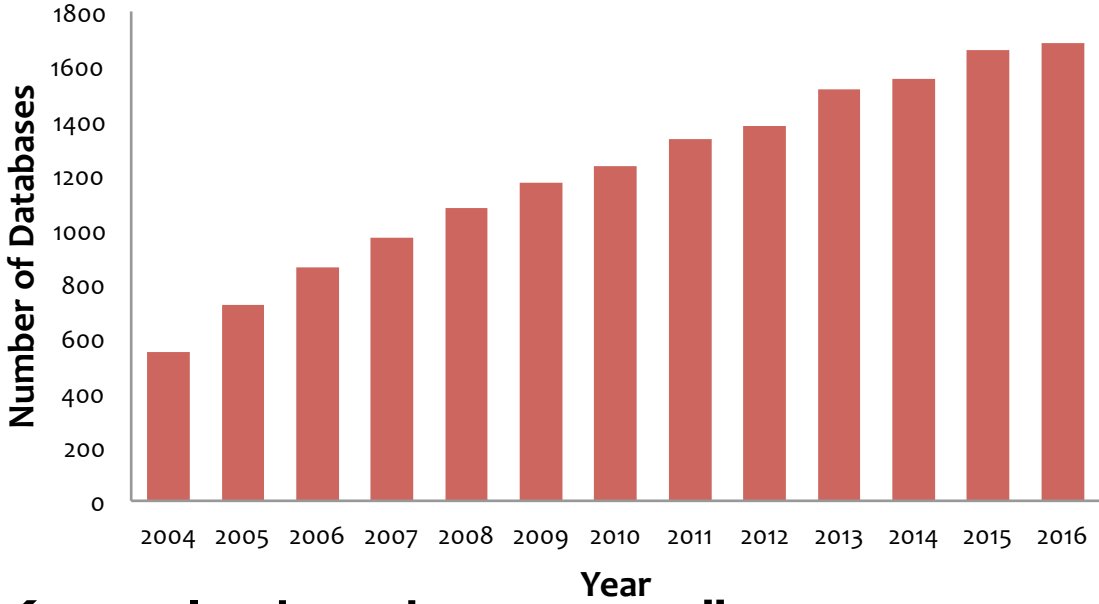
Data integration

* There is a large amount of information about model organisms such as *B. subtilis* and *E. coli*
* This information may be spread in
  * Different databases
  * Different formats
  * Different semantics
* This information can be Integrated and used to inform & constrain biological designs



"Knowledge is power"

Marx, Nature, 2013

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What is an ontology?

The representation of the entities of a domain is consistent and unambiguous

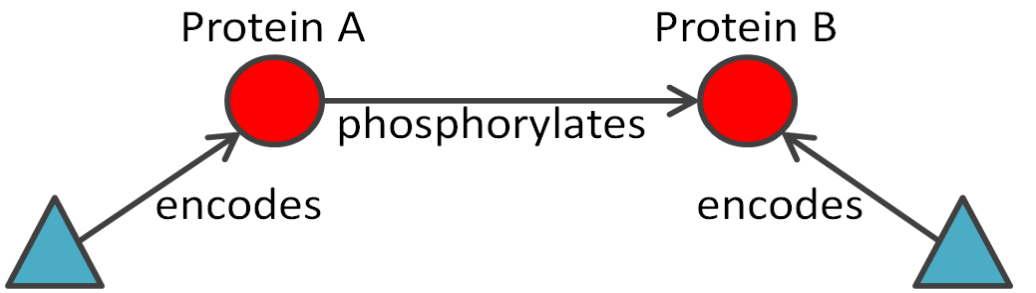
An abstract and simplified view of a domain being modelled

uses

captures

"***An explicit and formal specification of a conceptualisation***"
Gruber

Shared understanding of a domain



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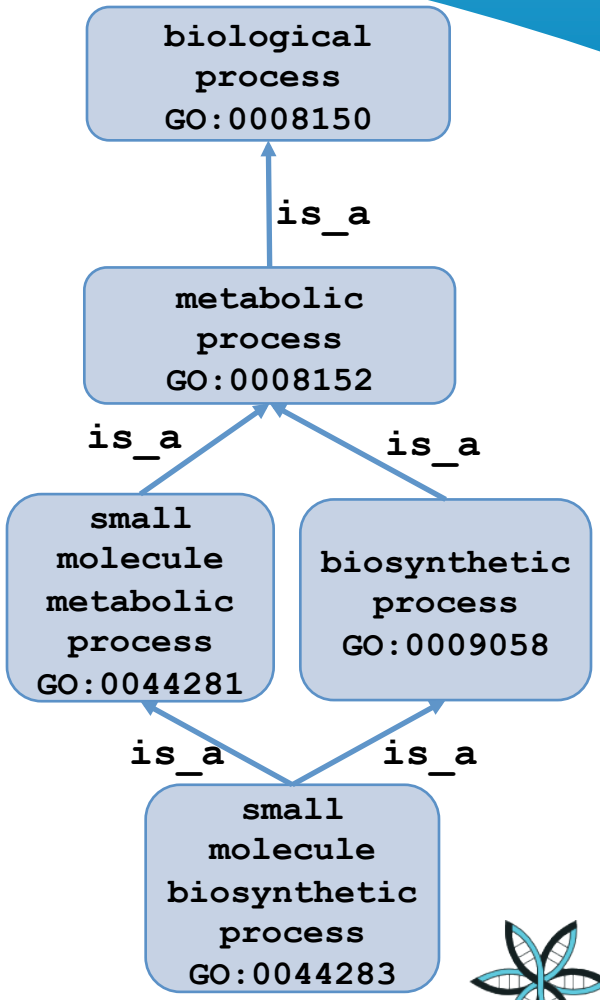
Semantic Web resources for synthetic biology

* Gene Ontology
* Sequence Ontology
* Systems Biology Ontology
* Synthetic Biology Open Language
* Standard Biological Parts Knowledgebase
* SBOL Stack
* Ontologies are needed to
  * Capture different relationships between biological parts
  * Facilitate data mining



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Synthetic Biology Ontology (SyBiOnt)

ACS SyntheticBiology

Research Article

pubs.acs.org/synthbio

Data Integration and Mining for Synthetic Biology Design

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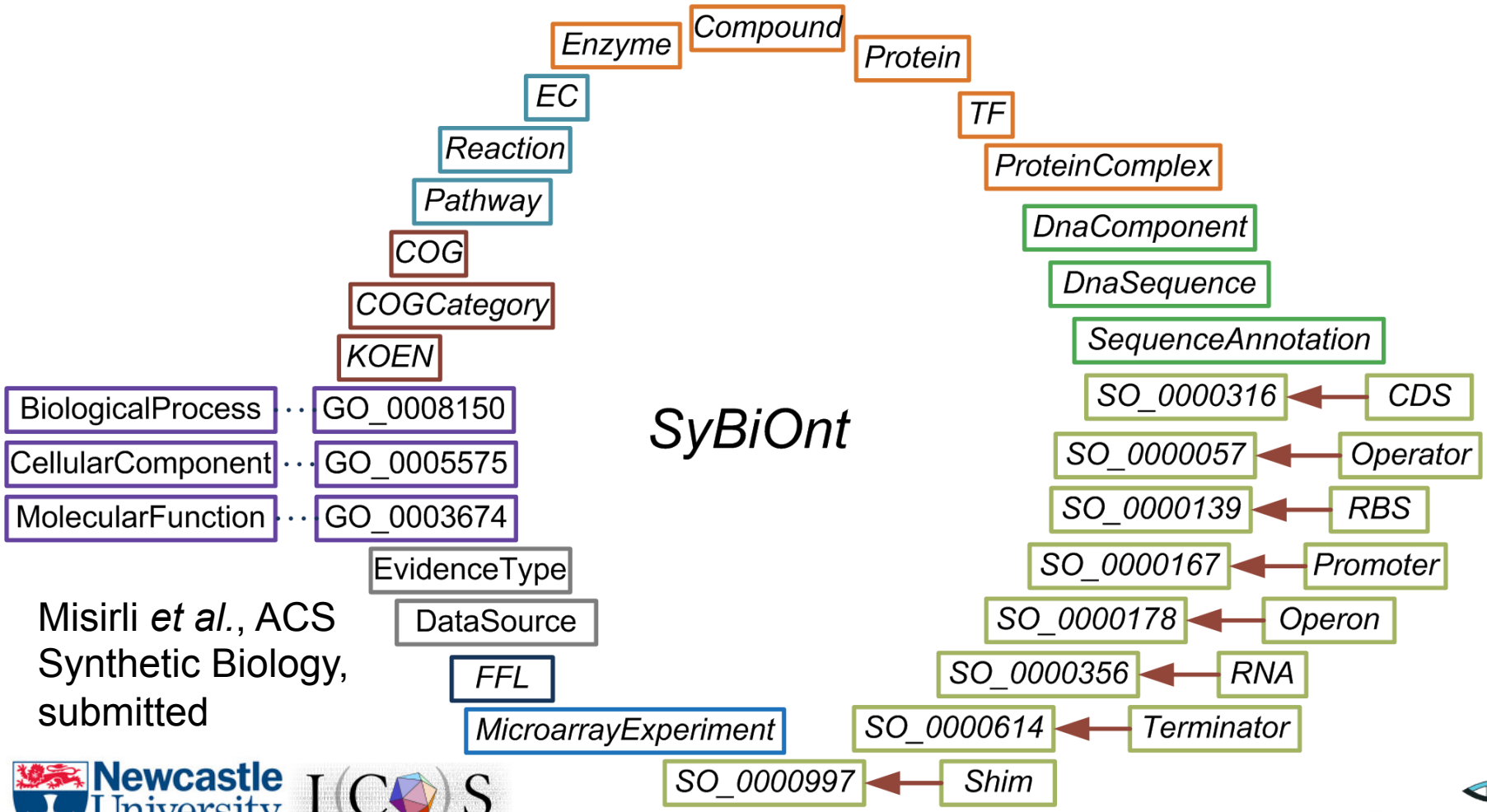
Open Access, available from ACS Synthetic Biology

w3id.org/synbio/ont

Synthetic Biology Ontology (SyBiOnt)



Misirli *et al.*, ACS Synthetic Biology, submitted

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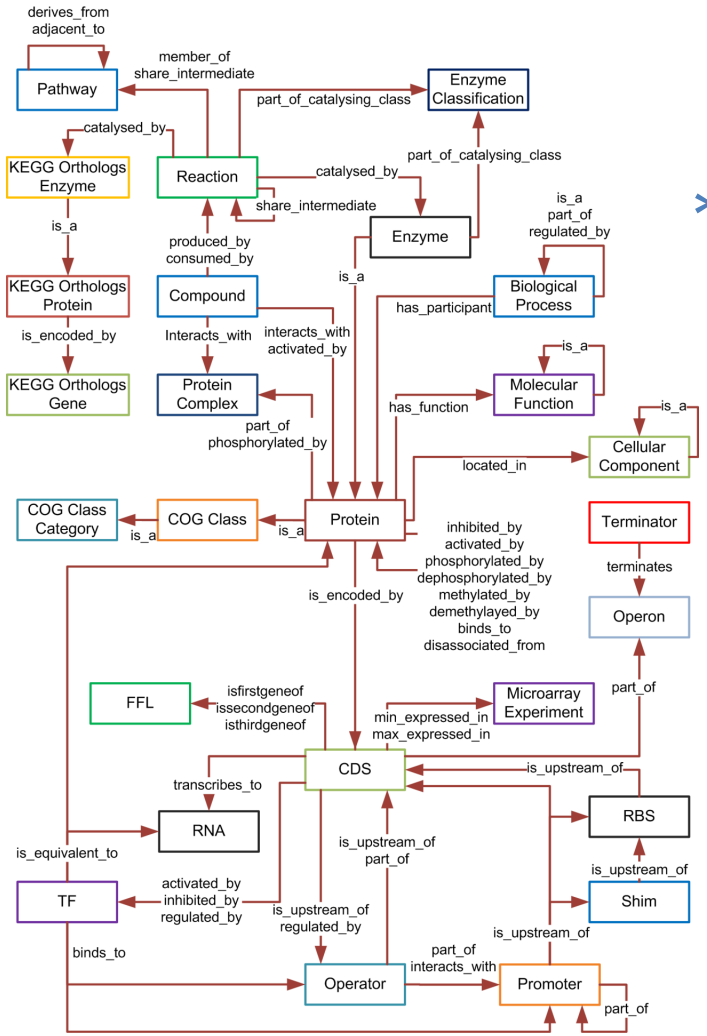
SyBiOntKB knowledge base



* The knowledge base includes information about
  * Sequences, annotations
  * Metabolic pathways
  * Gene regulatory networks
  * Protein-protein interactions
  * Gene expression

Misirli *et al.*, the Journal of Integrative Bioinformatics, 2013

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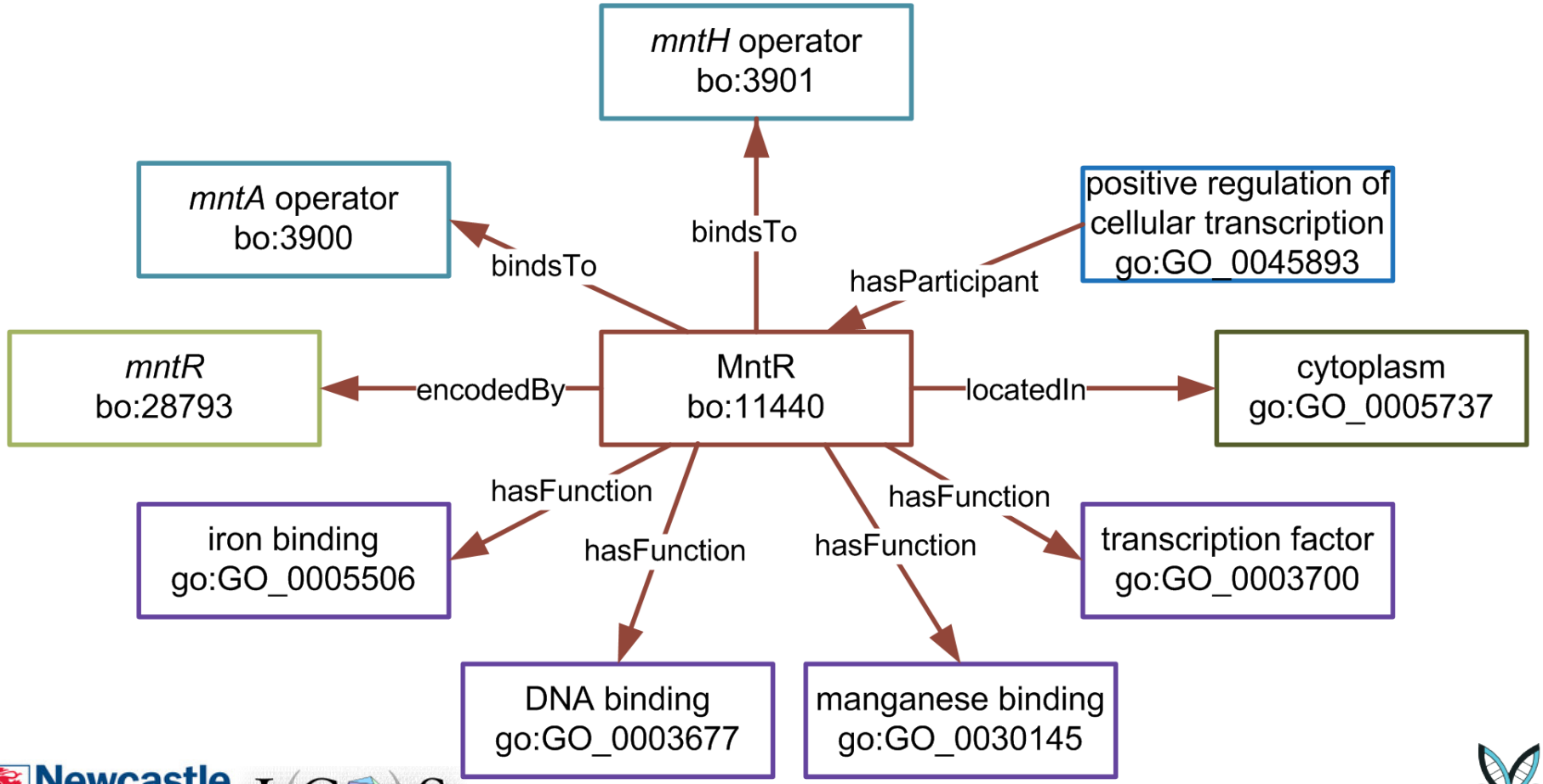
An example network from SyBiOntKB



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Testing the ontology with competency questions

* *Which parts can be used as inducible promoters?*

* **`Operator`**s have **`regulation type`** restrictions to indicate whether they are used positively or negatively in regulating gene expression. A **`Promoter`** with one **`Operator`** part that has the `Positive' **`regulation type`** restriction is an **`Inducible Promoter`**.

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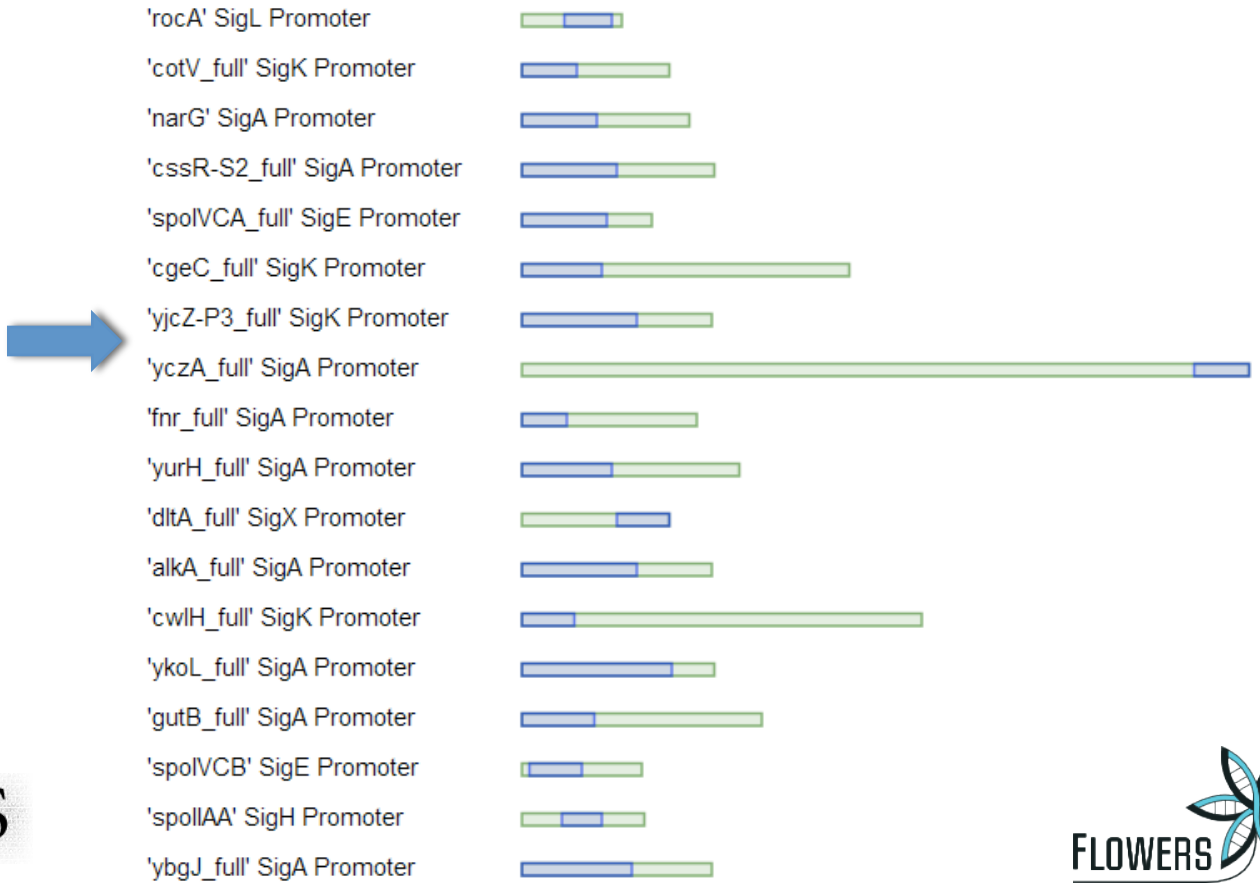
InduciblePromoter query and the results

QUERY:

```
Promoter
and (has_part exactly 1 Operator)
and (has_part exactly 1 PositivelyRegulatedOperator)
```

RESULTS: In total, 51 promoters were classified



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Examples about the automated identification of biological parts

Part type	Count
Activator sites	222
Repressor sites	333
Inducible promoters	51
Repressible promoters	85
Inducible promoters with two inputs (AND/OR gates)	15
Repressible promoters with two inputs (NAND/NOR gates)	25

Part type	Count
SigA promoters	465
SigB promoters	67
Constitutive promoters	311
Repressor encoding CDSs	55
Activator encoding CDSs	44
Response regulator encoding CDSs	40
Kinase encoding CDSs	38

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More examples

* *Which pathways should be targeted for the over-production of ammonium?*

'Ammonium' is **produced by Reaction**s that are **member of** 'Arginine and proline metabolism' and 'Purine metabolism' **Pathway**s.

* *Which parts can be used to upregulate the production of ammonium?*

The Compound 'Ammonia' with the **accession** of 'C00014' is **produced by** the **Reaction** 'RN:R00131', which **consumes** the **Compound** 'Carbamide' (C00086). 'Carbamide' is **produced by** a **Reaction** that is **catalysed by** an **Enzyme**, which is a subclass of a **Protein encoded by** the *argI* CDS with the **accession** of 'BSU40320'.

* How can the SpoOA protein, the master regulator of sporulation, be phosphorylated to trigger sporulation?

'SpoOA' is **phosphorylated by** the 'KinC' and 'SpoOB' **Protein**s. The 'SpoOB' **Protein** is **phosphorylated by** 'SpoOF' **Protein** which is further **phosphorylated by** the 'KinA' and 'KinB' **Protein**s.

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Summary

* SyBiOnt to capture complex biological data for synthetic biology computationally
* Facilitates semantic reasoning
* Complementary to existing standards and ontologies
* Open access and available at **w3id.org/synbio/ont**
* Extendible with new terms

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Thanks

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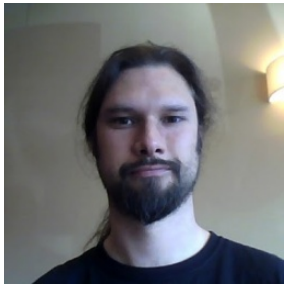
Prof. Anil Wipat

Dr Jennifer Hallinan



Dr Matthew Pocock

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