Biochemical Space: A framework for formal description and annotation of complex biological processes

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Frequent issues with models:

- reconstruction – get it working,
- understanding – what does it mean,
- interpretation – what are the results.
Biochemical Space (BCS) is a semi-formal knowledge-base providing

- description,
- annotation,
- public sharing

of domain-specific biological models.

**Motto:** formalization of biological description while annotating models.
Comprehensive Modeling Platform

Web-based framework for integration of biological knowledge with computational models and wet-lab experiments.

- e-photosynthesis.org
- e-cyanobacterium.org
<table>
<thead>
<tr>
<th>Rule name</th>
<th>NADPH oxidation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Equation</td>
<td>NADPH::cyt + 5 H{+}::cyt + pq::cym ⇒ NADP{+}::cyt + 4 H{+}::pps + pqh2::cym</td>
</tr>
<tr>
<td>Modifier</td>
<td>NDH1::cyt</td>
</tr>
<tr>
<td>Classification</td>
<td>reduction, oxidation</td>
</tr>
<tr>
<td>Description</td>
<td>Oxidation of NADPH and reduction of plastoquinone in the cytoplasmic membrane</td>
</tr>
<tr>
<td>Links</td>
<td>kegg::R01195, kegg::1.18.1.2</td>
</tr>
</tbody>
</table>
Why new language?

Biochemical Space Language (BCSL)

- internal representation easily editable and manageable,
- rule-based – decrease size of the space,
- completely textual – no graphical representation,
- human-readable – direct interpretation to the user,
- not just a notation – operational semantics suitable for analysis (translation to Kappa).
Advantages

- gives the model back its biological meaning
  - individual annotation for entities/reactions easily accessible
  - implemented model available online

- relating to BCS produces model described in BCSL
  - allows further analysis
  - provides qualitative formal description

- helps to reveal differences between models
KaiC(S\{u\}, T\{p\}) \cdot \text{KaiB}\{a\} :: \text{cell}

Compartment

Complex

Structure

Atomic

S\{u\}  T\{p\}  \text{KaiB}\{a\}

cell

KaiC

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Abstraction of the complex

Biology
- graph "isomorphism"
- 700 different deviations

BCS abstraction
- mixture → order not important
- 84 different deviations

- Unphosphorylated protein
- Serine residue phosphorylated protein
- Threonine residue phosphorylated protein
- Both residues phosphorylated protein
E + S $\leftrightarrow$ ES
ES $\rightarrow$ E + P

E + S\{i\} $\Rightarrow$ E.S\{u\}
E.S\{u\} $\Rightarrow$ E.S\{a\}
E.S $\Rightarrow$ E + S

R(enzyme\{avail\}) $\iff$ R(enzyme\{unavail\})
### BCS domain allows further abstractions

<table>
<thead>
<tr>
<th>Entity ID</th>
<th>KaiC</th>
</tr>
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<tbody>
<tr>
<td>Entity name</td>
<td>KaiC protein</td>
</tr>
<tr>
<td>Composition</td>
<td>S, T</td>
</tr>
<tr>
<td>Type</td>
<td>structure</td>
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</table>

<table>
<thead>
<tr>
<th>Entity ID</th>
<th>KaiC6</th>
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<tbody>
<tr>
<td>Entity name</td>
<td>KaiC complex</td>
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<tr>
<td>Composition</td>
<td>KaiC.KaiC.KaiC.KaiC.KaiC.KaiC</td>
</tr>
<tr>
<td>Type</td>
<td>complex</td>
</tr>
</tbody>
</table>

\[
S\{u\}::\text{KaiC}::\text{KaiC6}::\text{cyt} \Rightarrow S\{p\}::\text{KaiC}::\text{KaiC6}::\text{cyt}
\]

\[\downarrow\]

\[
\text{KaiC}(S\{u\})\cdot\text{KaiC} \ldots \cdot\text{KaiC}::\text{cyt} \Rightarrow \text{KaiC}(S\{p\})\cdot\text{KaiC} \ldots \cdot\text{KaiC}::\text{cyt}
\]
Conclusions

Summary

• *Biochemical Space* – framework for process modeling
• not strictly in the very same configuration
  • usage of alternative representation

Future work

• independent operational semantics / improved representation
• custom analysis tool for BCSL models
  • efficient static analysis
• *BCS numbers* extension
  • annotation of parameters