Creating a model pathway

The instances of glycolysis in A. thaliana and E. coli are combined to create a Model Pathway. The operation occurs at two levels:

1. Structure: the model pathway includes all the reactions and compounds present in either of the original pathway instances.
2. Catalysts: each model reaction is annotated with all the catalysts of all the corresponding instance reactions.

Predicting pathways

By creating a model pathway, we combine all the known organism-specific variants of a pathway into one general, organism-independent pathway.

What are those reactions?

Here is a listing of the enzymatic reactions used in the examples:

<table>
<thead>
<tr>
<th>EC</th>
<th>Official enzyme name</th>
</tr>
</thead>
<tbody>
<tr>
<td>EC 5.3.1.9</td>
<td>Glucose-6-phosphate isomerase</td>
</tr>
<tr>
<td>EC 2.7.1.11</td>
<td>β-phosphoglucomutase</td>
</tr>
<tr>
<td>EC 2.7.1.90</td>
<td>Diphosphate-fructose-6-phosphate 1-phosphotransferase</td>
</tr>
</tbody>
</table>

Predictions

Input:
- model pathway (computed on-demand)
- proteome of the target organism (Organism X)

Algorithm:

For each of the pathway’s reactions:
- Search for catalysts in the proteome
  - If any found?
    - add reaction to predicted pathway
    - annotate with catalysts found

The challenge: how to search for catalysts in the proteome?

Current Approach:
- BLAST model reaction’s catalysts against Organism X’s proteome

Future:
- Train HMM for each model reaction
- additional evidence (e.g. subcellular localization and GO)

Web Interface

We are developing a web interface for Pathway Analyst. It will allow users to:
- submit analyses
- examine their results
- easily search our DB of precomputed analysis results

For each reaction in the model pathway, we make a reaction-specific prediction like this one:

[Diagram showing model catalyst information passed to the predictor]