PathVisio 3
New Features for Pathway Analysis and Visualization

Martina Kutmon
martina.kutmon@maastrichtuniversity.nl
Department of Bioinformatics, Maastricht University

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Outline

1. Introduction
   - Pathway Analysis
   - Characteristics of PathVisio 3

2. Use cases
   - What can you do with PathVisio 3?
   - PathVisio plugins

3. Example Applications
   - Toxicology
   - Other examples
Pathway Analysis

Quantify
Isolated Data Points

Slide adapted from Thomas Kelder
Pathway Analysis

Comparative statistics
Isolated lists

Clustering
Isolated groups
Pathway Analysis

Functional organization
Pathway lists

Slide adapted from Thomas Kelder
Pathway Analysis

A picture is worth a thousand words
- Intuitive
- Puts data into biological context
Pathway Analysis

- **A picture is worth a thousand words**
  - Intuitive
  - Puts data into biological context

- **Involvement in pathways**
  - Group genes, proteins and other biological molecules
  - Reducing complexity
  - Several hundreds pathways instead of thousands of genes
  - Analysis on functional level

Publication:

Ten Years of Pathway Analysis: Current Approaches and Outstanding Challenges


DOI: 10.1371/journal.pcbi.1002375
Pathway Analysis

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  - Several hundreds pathways instead of thousands of genes
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- Identification of active pathways
  - Pathways that are turned on/off in specific experiments

Publication: Ten Years of Pathway Analysis: Current Approaches and Outstanding Challenges
P. Khatri, N. Sirota, A.J, Butte, PLOS Computational Biology (2012)
DOI: 10.1371/journal.pcbi.1002375
PathVisio 3

Publication: Presenting and exploring biological pathways with PathVisio
Martijn P. van Iersel et al., BMC Bioinformatics (2008)
DOI: 10.1186/1471-2105-9-399
Website: http://www.pathvisio.org

Draw for presentation & publication

Easily install plugins for added features

Link to external databases for more information

Visualize quantitative data for integrative pathway analysis

Share on Wikipathways.org
What’s new?

1. New modular framework that can be extended with plugins
2. Plugin repository: central plugin collection
3. Plugin manager: one-click installation of plugins
PathVisio 3

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3. Plugin manager: one-click installation of plugins
4. Annotations of interactions and reactions
5. Visualization of data on lines
PathVisio 3

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1. New modular framework that can be extended with plugins
2. Plugin repository: central plugin collection
3. Plugin manager: one-click installation of plugins
4. Annotations of interactions and reactions
5. Visualization of data on lines
6. Interoperability with other standards
   - Draw pathways in SBGN or MIM
   - Import SBML models
   - Export in BioPAX
PathVisio Plugins

Current and soon to be released plugins

Check out the plugin repository on http://www.pathvisio.org/plugins/plugins-repo/
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PathVisio functionality

1. **Draw pathways**
   - Create new pathway
   - Share/Upload
   - WikiPathways
**PathVisio functionality**

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2. **Visualize data**
   - Load dataset
     - Transcriptomics, Proteomics, Metabolomics, Fluxomics
   - Create data visualization
     - Gradient / rule based
   - Visualize data on pathway
   - Export pathway image with data
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4. **Network analysis**
   - WikiPathways app for Cytoscape

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WikiPathways client plugin

- WikiPathways is a pathway database using the wiki system
  - everybody can create, edit, curate, discuss, download and use pathways (CreativeCommons 3.0 License)
  - community curation
  - new findings can be added immediately
**WikiPathways client plugin**

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  - everybody can create, edit, curate, discuss, download and use pathways (CreativeCommons 3.0 License)
  - community curation
  - new findings can be added immediately
- Plugin allows searching and browsing the database
- Users can create and upload pathways from PathVisio to WikiPathways
- Users can update pathways from WikiPathways in PathVisio

Publication: WikiPathways: building research communities on biological pathways
Thomas Kelder et al., Nucleic Acids Research (2011)
DOI: 10.1093/nar/gkr1074
Website: http://www.wikipathways.org
PathVisio plugins

**GeneSet Enrichment Analysis (GSEA) plugin**
- Perform gene set enrichment analysis in PathVisio
- Use pathways as gene sets

**PathwayLoom**
- Find known interactions for a selected gene or protein
- Interactions from online databases and text mining results
Export options
High-quality figures for presentations and publications

Pathway Export
*with or without data*

- PNG
- SVG
- PDF
- HTML5
Integration into workflows

Use PathVisio functionality from different programming languages
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PathVisio in Toxicology

Study 1

Title: Biotransformation pathway maps in WikiPathways enable direct visualization of drug metabolism related expression changes
Authors: D.G.J. Jennen et al.
Journal: Drug Discovery Today

- Biotransformation pathway map suitable for multi-omics analysis and data visualization
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Biotransformation pathway map suitable for multi-omics analysis and data visualization
PathVisio in Toxicology

Study 1

Compare expression profile in different cell types.
Study 2

Title: RNA-Seq Provides New Insights in the Transcriptome Responses Induced by the Carcinogen Benzo[a]pyrene
Authors: van Delft J. et al.
Journal: Toxicological Sciences

Transcriptomic responses in HepG2 cells upon exposure to benzo[a]pyrene, pathway analysis with WikiPathways collection.

<table>
<thead>
<tr>
<th>12h pathway name</th>
<th>Z-score</th>
<th>24h pathway name</th>
<th>Z-score</th>
</tr>
</thead>
<tbody>
<tr>
<td>BaP metabolism</td>
<td>6.33#</td>
<td>BaP metabolism</td>
<td>7.38#</td>
</tr>
<tr>
<td>Oxidative stress</td>
<td>5.09#</td>
<td>Cholesterol biosynthesis</td>
<td>6.08</td>
</tr>
<tr>
<td>Keap1-Nrf2</td>
<td>4.63#</td>
<td>Codeine and morphine metabolism</td>
<td>4.16</td>
</tr>
<tr>
<td>GPCRs, class A rhodopsin-like</td>
<td>3.67</td>
<td>Keap1-Nrf2</td>
<td>3.85#</td>
</tr>
<tr>
<td>Metapathway biotransformation</td>
<td>3.47#</td>
<td>Urea cycle and metabolism of amino groups</td>
<td>3.66</td>
</tr>
<tr>
<td>Myometrial relaxation and contraction</td>
<td>3.12#</td>
<td>Metapathway biotransformation</td>
<td>3.65#</td>
</tr>
<tr>
<td>Nucleotide GPCRs</td>
<td>3.06</td>
<td>Oxidative stress</td>
<td>3.34#</td>
</tr>
<tr>
<td>Hypertrophy model</td>
<td>2.96</td>
<td>Statin pathway</td>
<td>3.26</td>
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<tr>
<td>Estrogen metabolism</td>
<td>2.94#</td>
<td>Estrogen metabolism</td>
<td>3.13#</td>
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<tr>
<td>Focal adhesion</td>
<td>2.88</td>
<td>Tryptophan metabolism</td>
<td>2.74#</td>
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<tr>
<td>DNA damage response</td>
<td>2.82</td>
<td>Adipogenesis</td>
<td>2.31</td>
</tr>
<tr>
<td>Blood clotting cascade</td>
<td>2.77</td>
<td>Inflammatory response pathway</td>
<td>2.30</td>
</tr>
<tr>
<td>Biogenic amine synthesis</td>
<td>2.70</td>
<td>Myometrial relaxation and contraction</td>
<td>2.16#</td>
</tr>
</tbody>
</table>
PathVisio in Toxicology

Study 2
Visualization of the effects in the DNA damage response pathway demonstrates that especially the network of genes around TP53 is upregulated.
Tisoncik et al. "Into the eye of the cytokine storm". Microbiology and Molecular Biology Reviews (2012).
PathVisio is a free, open source pathway editing, visualization and analysis tool

- http://www.pathvisio.org
Summary

1. PathVisio is a free, open source pathway editing, visualization and analysis tool
   - http://www.pathvisio.org
2. Extended functionality through plugins
PathVisio is a free, open source pathway editing, visualization and analysis tool

- [http://www.pathvisio.org](http://www.pathvisio.org)

2. Extended functionality through plugins

3. PathVisio is the pathway editor integrated in WikiPathways, new JavaScript version under development
PathVisio is a free, open source pathway editing, visualization and analysis tool

- http://www.pathvisio.org

2. Extended functionality through plugins

3. PathVisio is the pathway editor integrated in WikiPathways, new JavaScript version under development

4. Pathways drawn in PathVisio can be uploaded and shared on WikiPathways

- http://www.wikipathways.org
Acknowledgements

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- Thomas Kelder

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- Google Summer of Code students
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Thank you for your attention.

Questions?