

Software for Molecular Interaction Maps (MIMs): Editor, API, and Validation

COMBINE 2010
10/8/2010

Augustin Luna
augustin@mail.nih.gov

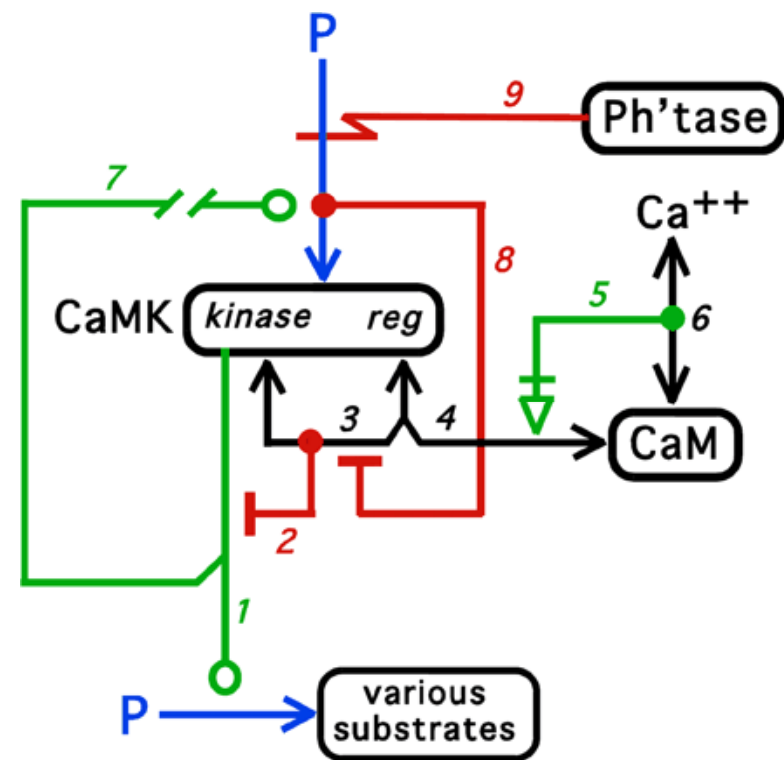
Bioinformatics Dept., Boston University,
Boston, MA, USA

Laboratory of Molecular Pharmacology,
National Cancer Institute, Bethesda, MD, USA



Molecular Interaction Maps (MIMs)

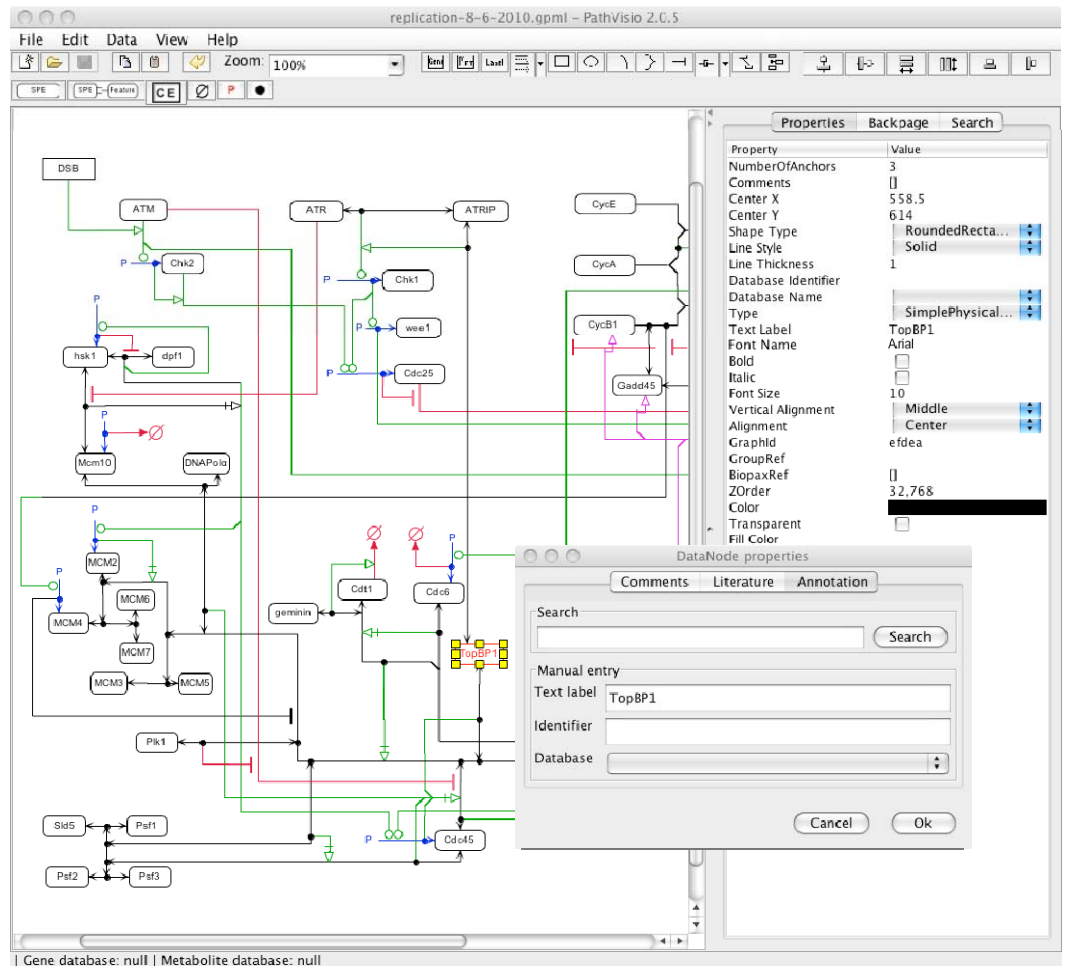
- A graphical notation for bioregulatory networks created by Kurt Kohn in 1999
- Creation of large diagrams that remain intuitive for use by biologists by minimizing redundant elements
- Tools for biologists and programmers



Kohn KW. et al., 2006

Choosing Pathvisio for MIM Diagrams

- Open-source
- Java
- Plugins
 - Cytoscape
 - BioPAX
 - SBGNML



Pathvisio: van Iersel M. et al. 2008; MIM-specific additions: Margot Sunshine

Pathvisio-MIM Plugin

The screenshot displays the PathVisio 2.0.5 interface with a metabolic pathway diagram. The diagram includes various entities and interactions, with MIM-specific annotations. A callout box labeled "MIM entity glyphs" points to a specific entity in the diagram. Another callout box labeled "MIM interactions glyphs" points to a specific interaction in the diagram. A third callout box labeled "Import/export MIM-specific format" points to the "File Format" dropdown in the "Export pathway" dialog box, which is set to "MIM Markup Language (MIM)". The "Export pathway" dialog box also shows a file list on the Desktop and "Cancel" and "Export" buttons. The Properties panel on the right shows the selected interaction's properties, including "mim-binding" for both Start Line Type and End Line Type.

Property	Value
Comments	
Start X	170
Start Y	331
End X	169.75
End Y	416
Start Line Type	mim-binding
End Line Type	mim-binding
Line Style	Solid
Line Thickness	1
GraphId	id86600dfb
StartGraphRef	d05ee
EndGraphRef	bd16b
GroupRef	
BiopaxRef	
ZOrder	12,288

MIM Schemas/API

- MIM diagrams have different interpretation modes
 - MIM-Visual (MIM-Vis): Symbols used in MIM syntax and graphical properties (width, height, color, etc)
 - MIM-Biological (MIM-Bio): Semantic objects in MIM and annotation properties (comments, references, etc)
- API being generated with XMLBeans for Java
- Syntactic validation using Schematron
 - Makes assertions about the presence or absence of patterns in XML documents using XPath
 - Processed into XSLT
 - Schematron is being used by CellML and SBML

Schematron Validation Example

```
<iso:pattern name="check-int-visref" id="check-int-visref">
  <iso:rule context="mimVis:InteractionGlyph">
    <iso:let name="vis-id" value="@visId"/>
    <iso:assert test="mimVis:Point[1]/@visRef"
      diagnostics="vis-id">The start of an
      interaction should be possess a visRef
      attribute.</iso:assert>
    <iso:assert test="mimVis:Point[last()]/@visRef"
      diagnostics="vis-id">The end of an
      interaction should be possess a visRef
      attribute.</iso:assert>
  </iso:rule>
</iso:pattern>
```

```
<svrl:active-pattern id="check-int-visref" />
<svrl:failed-assert
  test="mimVis:Point[1]/@visRef"
  location="...">
  <svrl:text>The start of an interaction should be
  possess a visRef attribute.</svrl:text>
  <svrl:diagnostic-reference diagnostic="vis-
  id">idcd72516b</svrl:diagnostic-reference>
</svrl:failed-assert>
</svrl:active-pattern>
```

Validation Schematron File

SVRL Validation Output

Projects Based on MIM

- Mathematical formalisms
 - Stochastic Concurrent Constraint Programming Language (Bortolussi L., et al., 2007)
 - Process Calculus (Barbuti R., et al., 2009)
 - Stochastic Calculus of Looping Sequences (Barbuti R., et al., 2010)
- Evaluation set for information retrieval from full-text articles (McIntosh, T. and Curran, J, 2007)
- Network analysis of MIMs

Acknowledgements

- National Cancer Institute (MIM)
 - Kurt Kohn
 - Mirit Aladjem
 - Sohyoung Kim
 - Lucas Chang
 - Margot Sunshine
- U of Maastricht (Pathvisio)
 - Martjin van Iersel
 - Pathvisio developers
- Bogazici University and NCI-Frederick (Schema and Network Analysis)
 - Itir Karac
 - Mine Edes
 - Ruth Nussinov
 - Can Ozturan
- MSKCC (BioPAX)
 - Emek Demir
 - BioPAX community
- SBGN Community