Recent progress on SBGN in **Arcadia**

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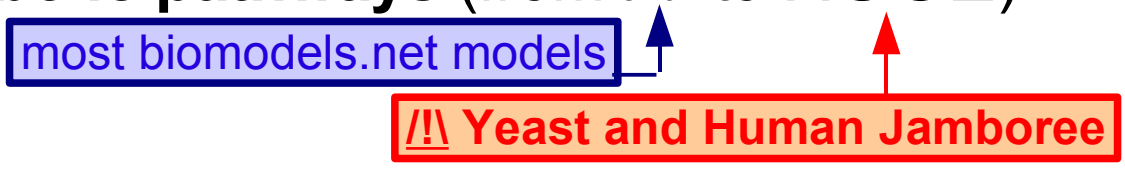
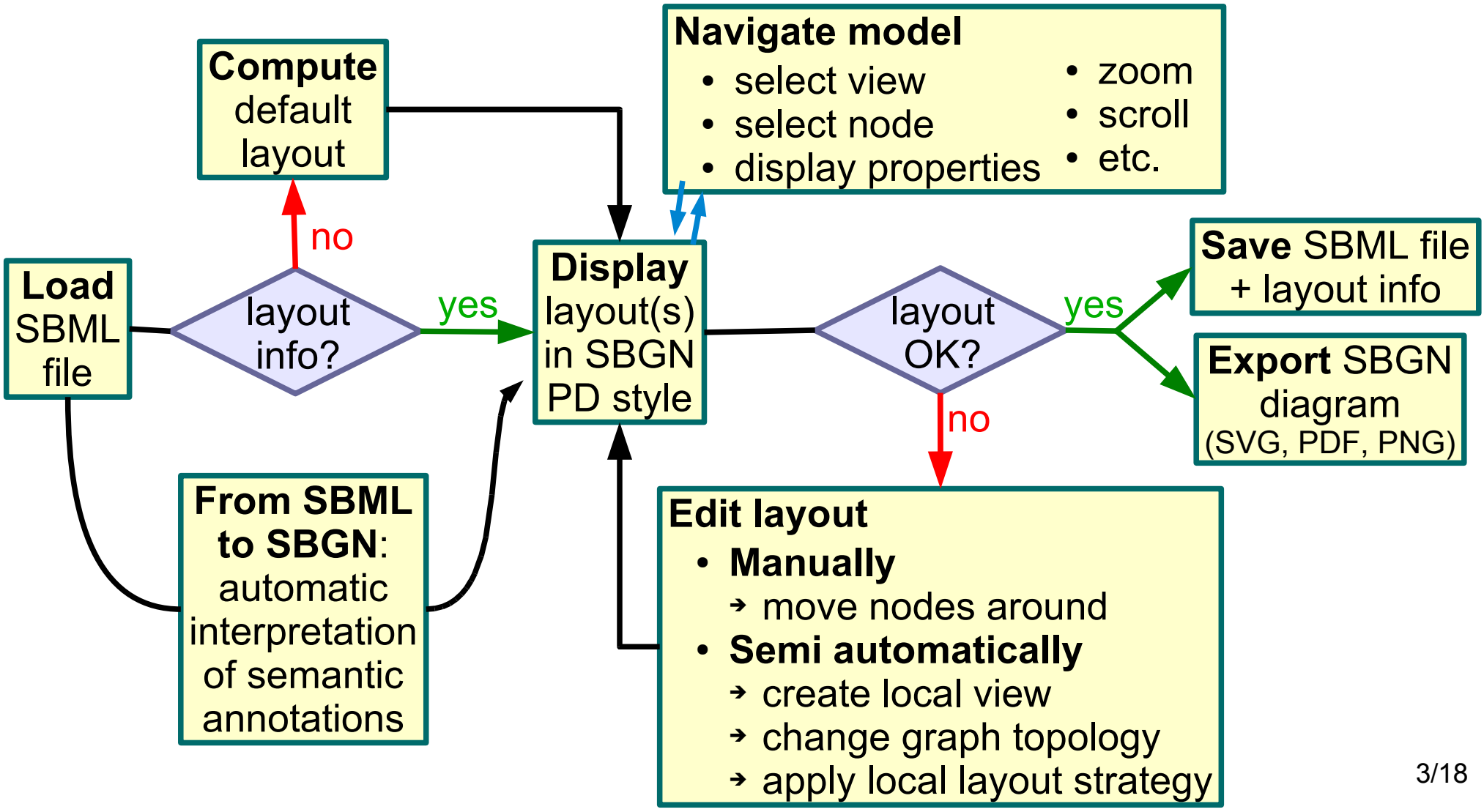
Arcadia in a nutshell

- What? systems biology model **viewer**/browser (≠ editor)
- Why? to visualise **metabolic pathways** (from small to HUGE)
- How?

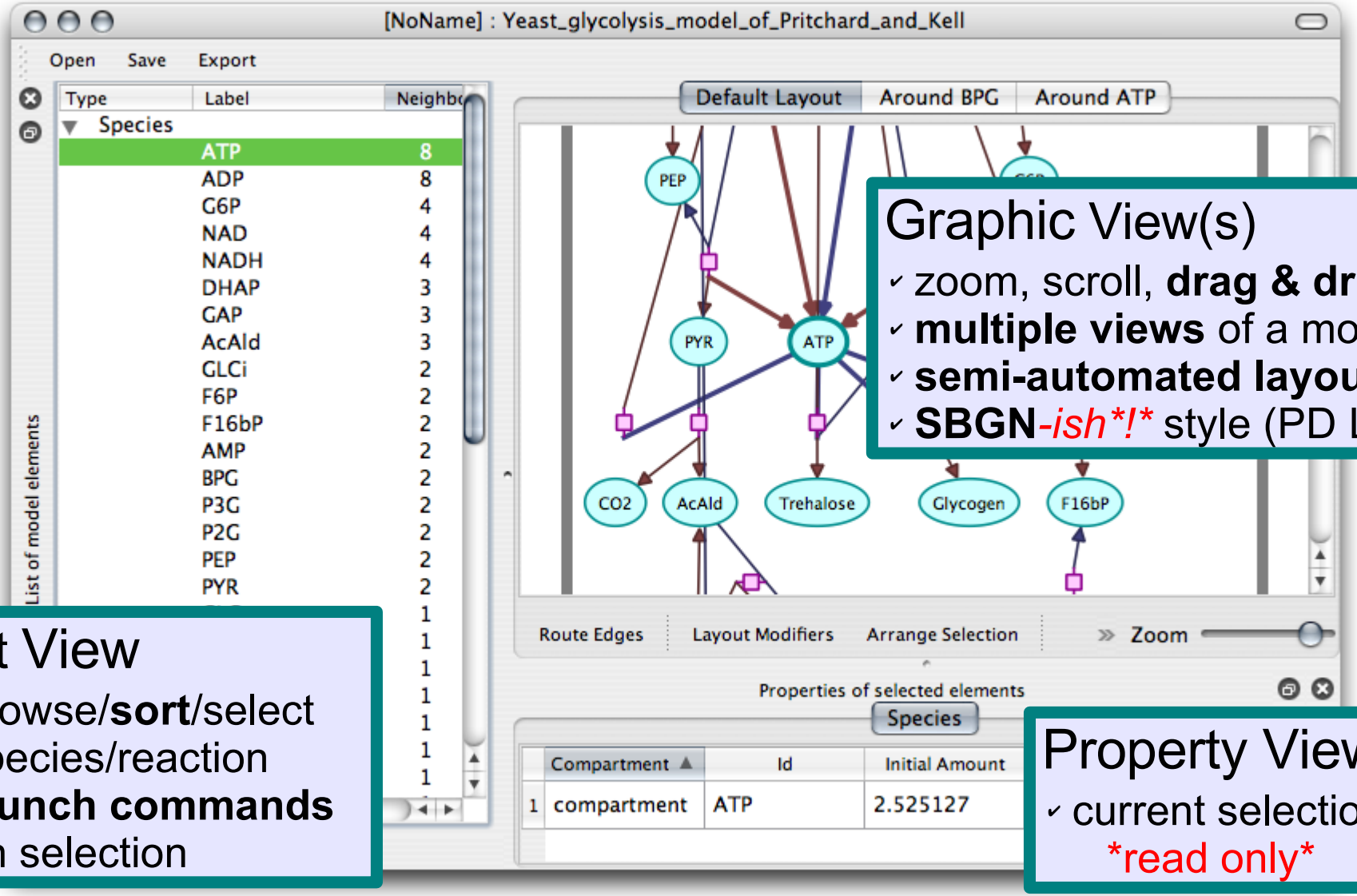


  - simple **navigation** interface between **multiple views**
  - light-weight, standalone, and **interoperable**
    - ➔ supports and promotes **standards** (SBML, SBGN, MIRIAM, SBO, ...)
  - **flexible** Model/View/Controller software architecture
    - ➔ **integration** of new file formats, **interaction** with external tools
  - **cross-platform**, **open-source** implementation (C++, Qt)
    - ➔ powered by existing libraries (libsbml, boost, graphviz, libavoid, ...)

Main features: typical workflow



GUI: interconnected views



Graphic View(s)

- zoom, scroll, **drag & drop**
- **multiple views** of a model
- **semi-automated layout**
- **SBGN**-*ish*!** style (PD L1r1)

List View

- browse/**sort**/select species/reaction
- **launch commands** on selection

Property View

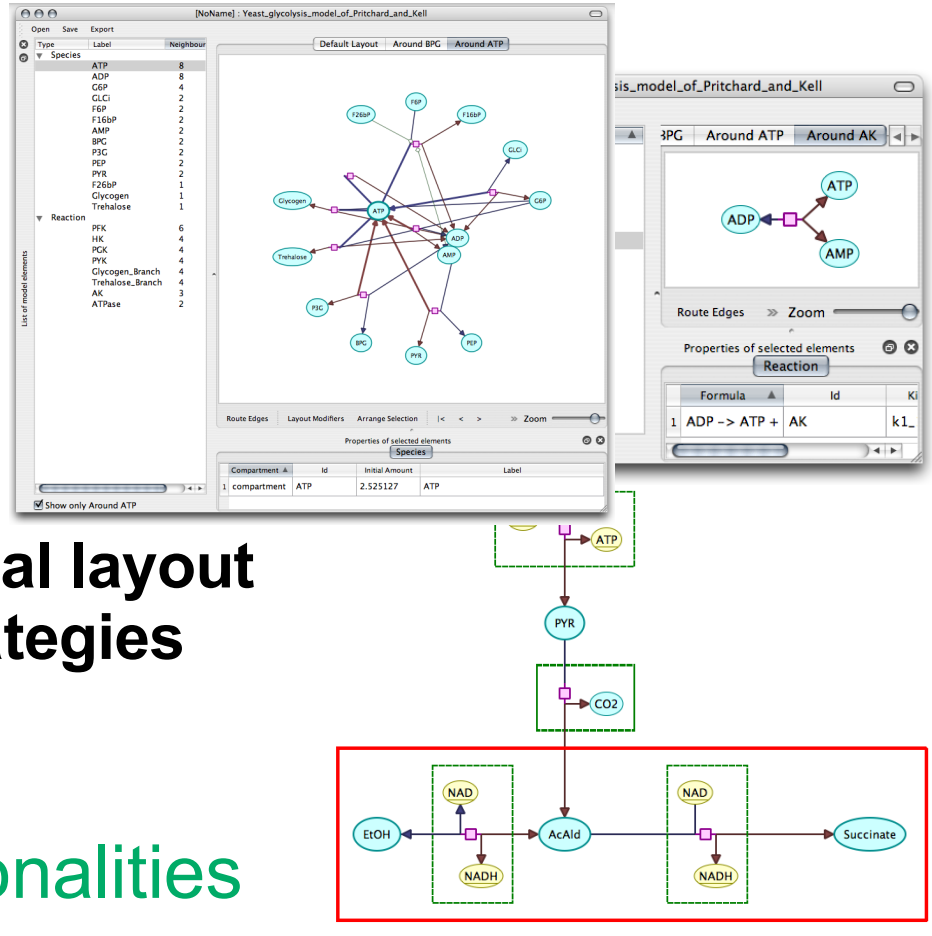
- current selection

read only

Dynamic semi-automated layout

- Simple controls
  - R-click: navigate **neighbourhood** views
  - 2-click: layout control
    - **update** layout
    - **clone** species
    - **branch** reaction

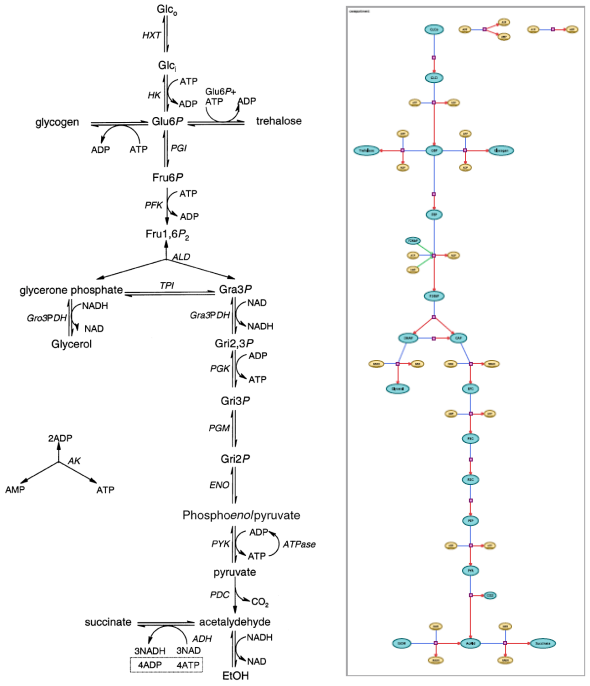
Local layout strategies



- Menu: advanced functionalities
  - ➔ clone all **modifiers**, **merge** similar reactions, ...

Current results

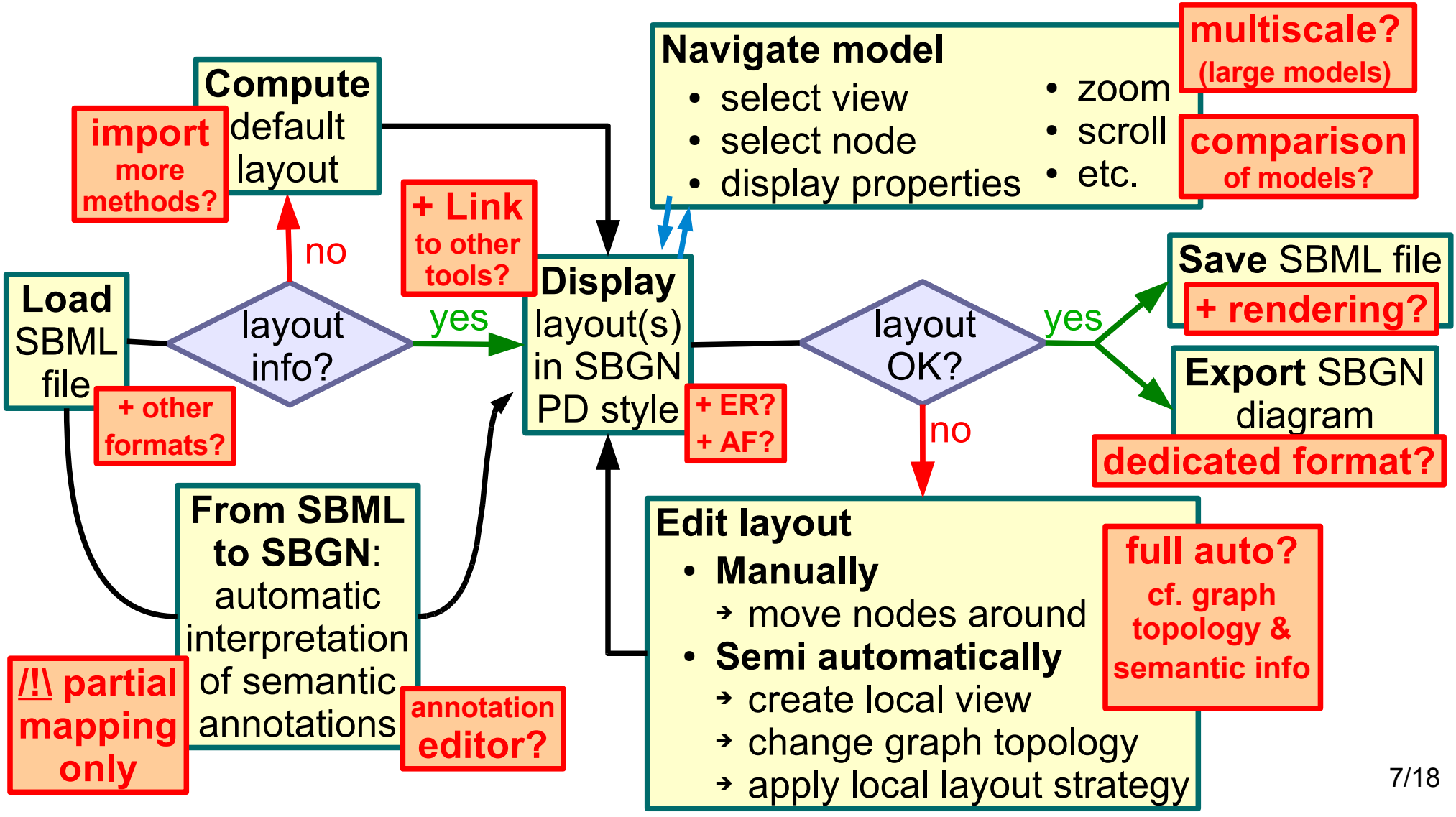
semi automated layout
similar to
hand-drawn diagram



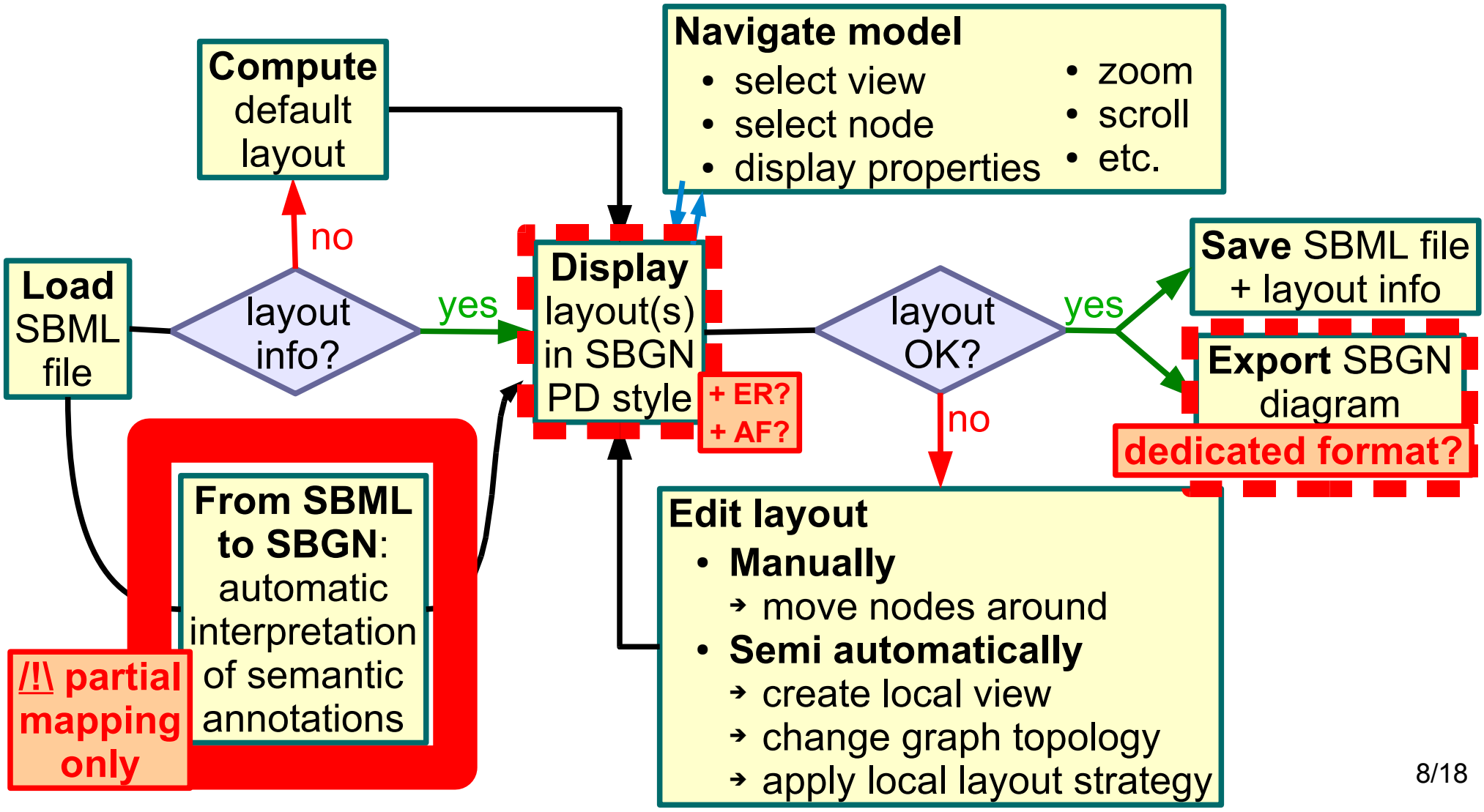
- Tested on a few real use cases
  - illustrate models (communication)
  - interpret experimental results
  - assist curation process
- Mostly SBGN compatible
  - ✔ fixed **transition** nodes problem
  - ✔ all the **glyphs** are supported
  - ✗ but **incomplete mapping** between SBML and SBGN
- Imminent first public release!

arcadiapathways.sourceforge.net

Areas for potential improvements...



What I will be talking about now



From SBML to SBGN through SBO

- General idea behind the conversion

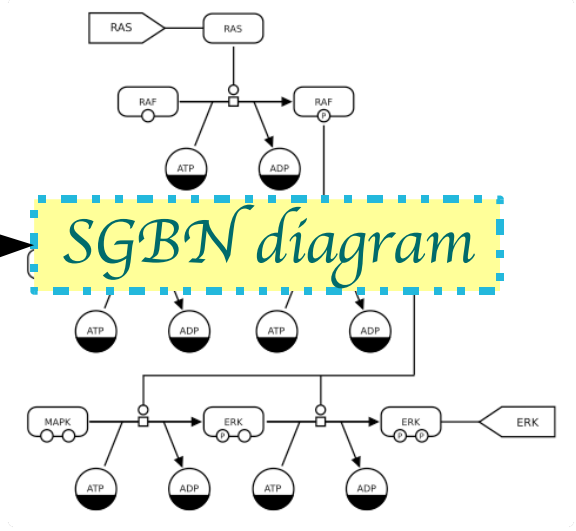
(annotated, structured content + stylesheet)
x rendering engine = visual representation

SBML
with SBO and MIRIAM annotations

stylesheet???

model browser?

External
resources?
(via URI)

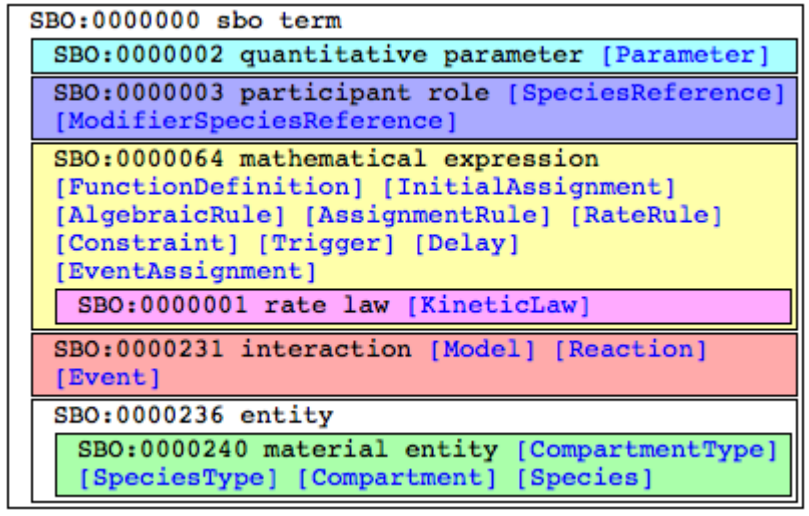


SBO = missing link?

- SBML x SBO (SBML L2v4r1)

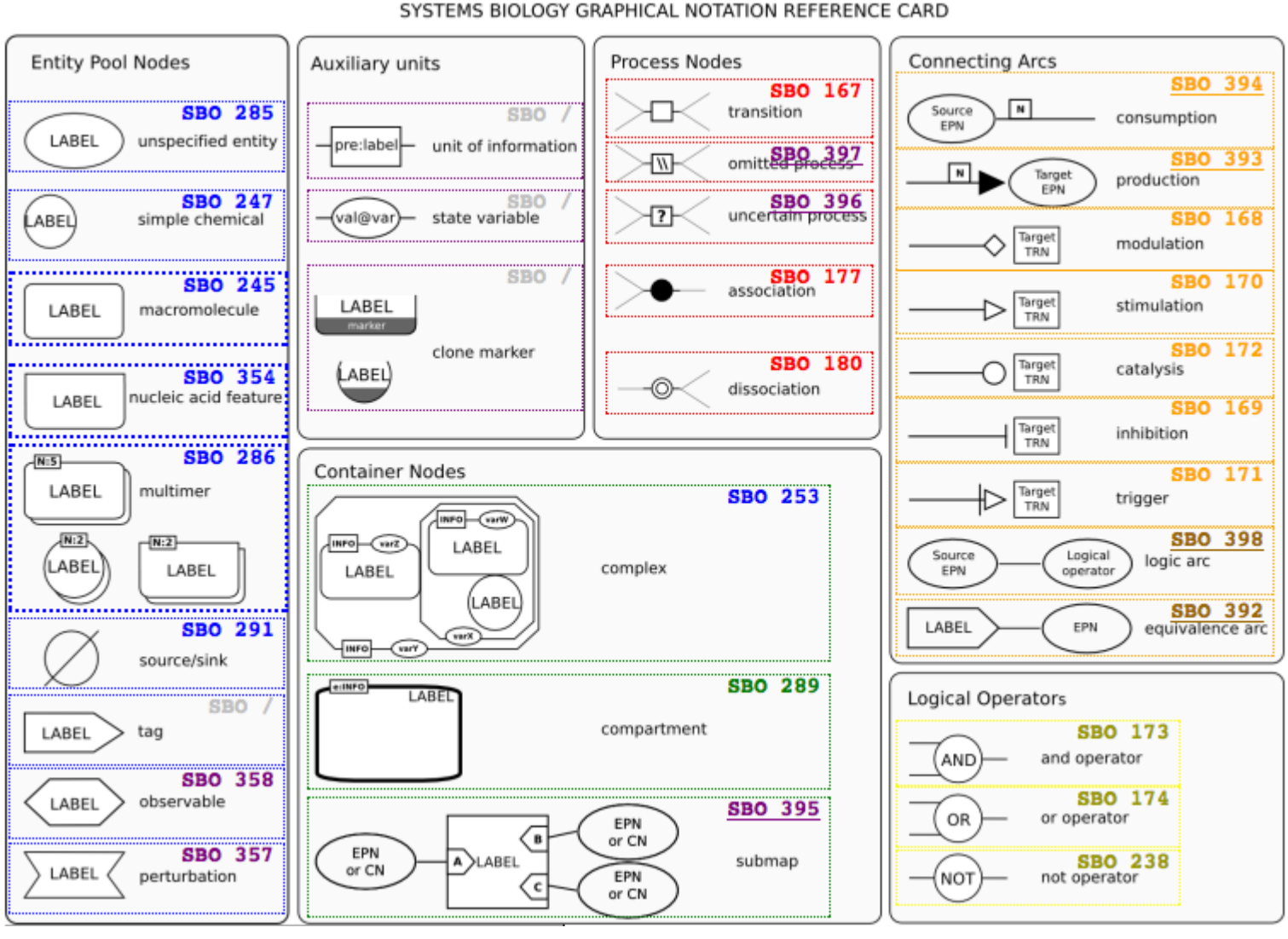
SBML Component	SBO Branch	Branch Identifier
Model	interaction	SBO:0000231
FunctionDefinition	mathematical expression	SBO:0000064
CompartmentType	material entity	SBO:0000240
SpeciesType	material entity	SBO:0000240
Compartment	material entity	SBO:0000240
Species	material entity	SBO:0000240
Reaction	interaction	SBO:0000231
Parameter	quantitative parameter	SBO:0000002
SpeciesReference	participant role	SBO:0000003
ModifierSpeciesReference	participant role	SBO:0000003
KineticLaw	rate law	SBO:0000001
InitialAssignment	mathematical expression	SBO:0000064
AlgebraicRule	mathematical expression	SBO:0000064
AssignmentRule	mathematical expression	SBO:0000064
RateRule	mathematical expression	SBO:0000064
Constraint	mathematical expression	SBO:0000064
Event	interaction	SBO:0000231
Trigger	mathematical expression	SBO:0000064
Delay	mathematical expression	SBO:0000064
EventAssignment	mathematical expression	SBO:0000064

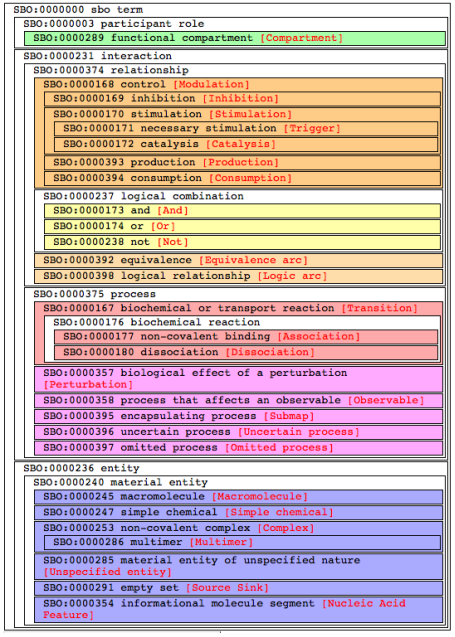
Table 6, page 90, SBML L2v4r1



SBO ∩ SBML

SBGN x SBO (PD L1r1)





SBO ∩ SBGN

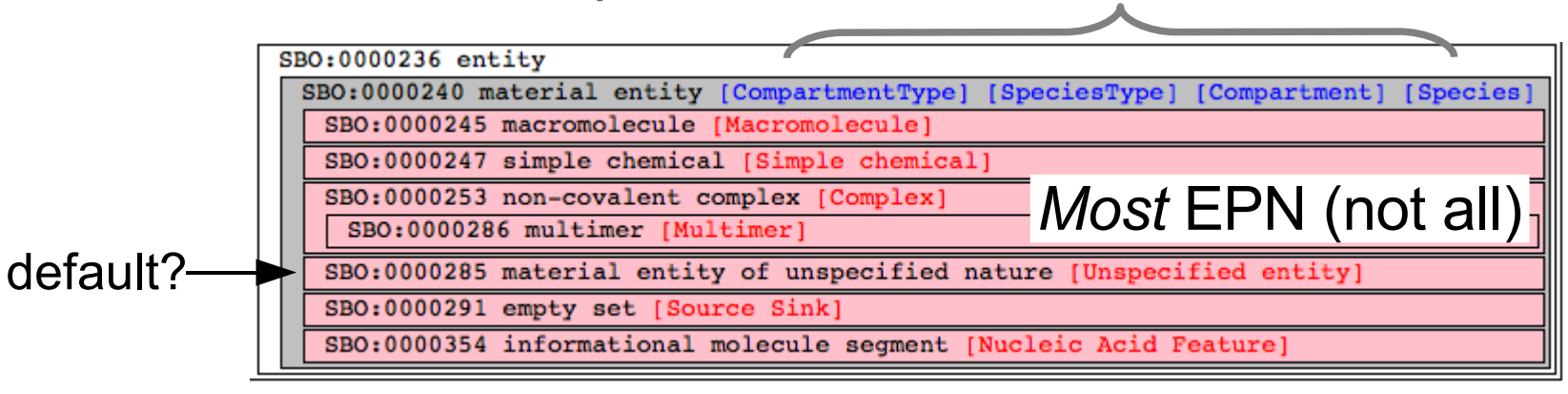
Converting SBML to SBGN

- Relevant SBML elements → Look at SBO term
  - Obvious ones
    - Species[Type]
    - Compartment[Type]
    - Reaction (reactants, products)
    - [Modifier]SpeciesReference
  - Less obvious ones?
    - Parameter
    - Event
    - ...?
  - While no equivalence with SBGN, go up in the SBO tree
  - If glyph found, display it
  - If no match found (or no SBO term), pick up a default SBGN glyph, e.g.:
    - Compartment (SBML) = Compartment (SBGN)
    - Reaction = Transition
    - Modifier = Modulation
    - etc.

SBO ∩ (SBML ∪ SBGN)

- SBO:0000236 entity = SBML Species and Compartment
  - ✔ Species/SpeciesType maps well to *most* EPN
  - ✗ But SBGN Compartment are not here! ⇒ change specs?

Used to span all entities in SBML L2v3

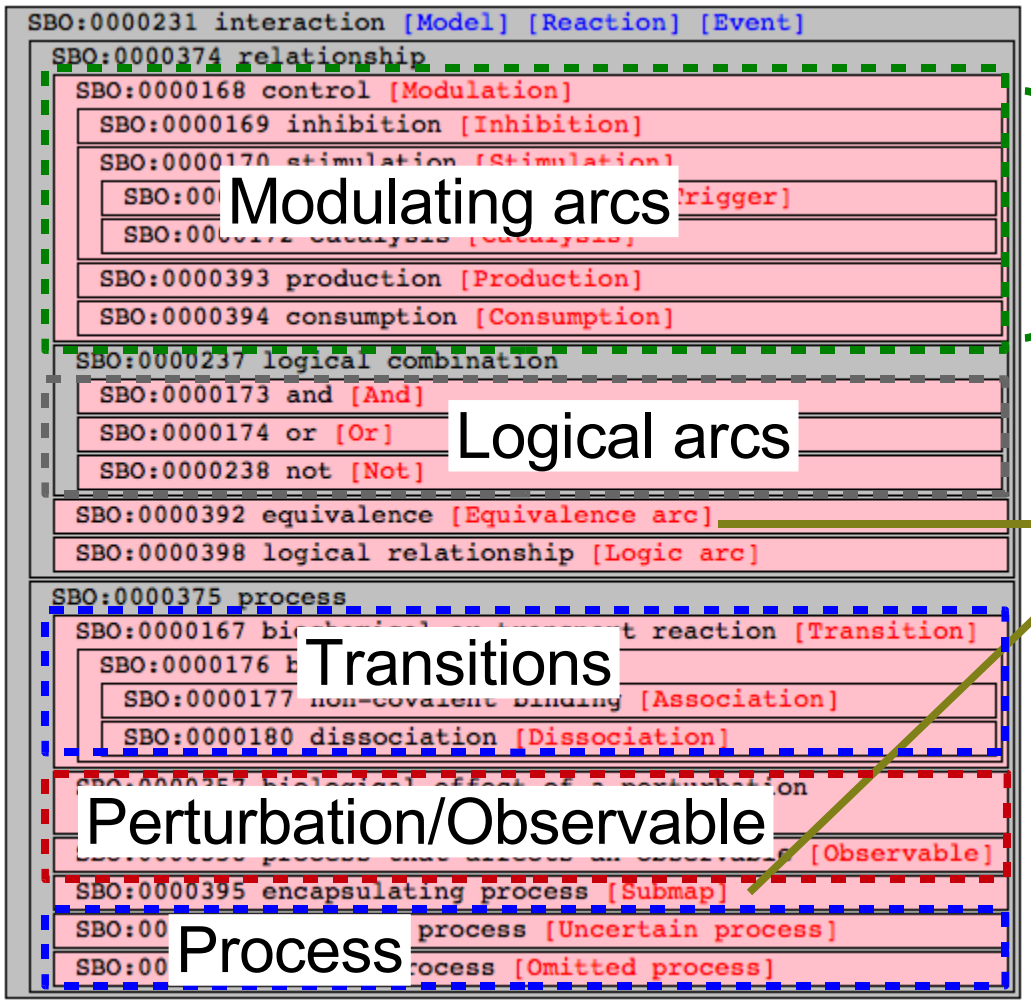


Q: is it ok to assume any unqualified Species is an unspecified EPN by default?
Should the unspecified EPN be associated to SBO:0000240 material entity?

SBO:0000231 interaction

= SBML Model, Reaction, Event

? Maps quite well ?



Problem! In SBML,
Species Reference is SBO:0000003
⇒ can be solved by changing
current SBGN specs (next slide)

Not in SBML?

Equivalence arc and **Submap**
= Layout information only?

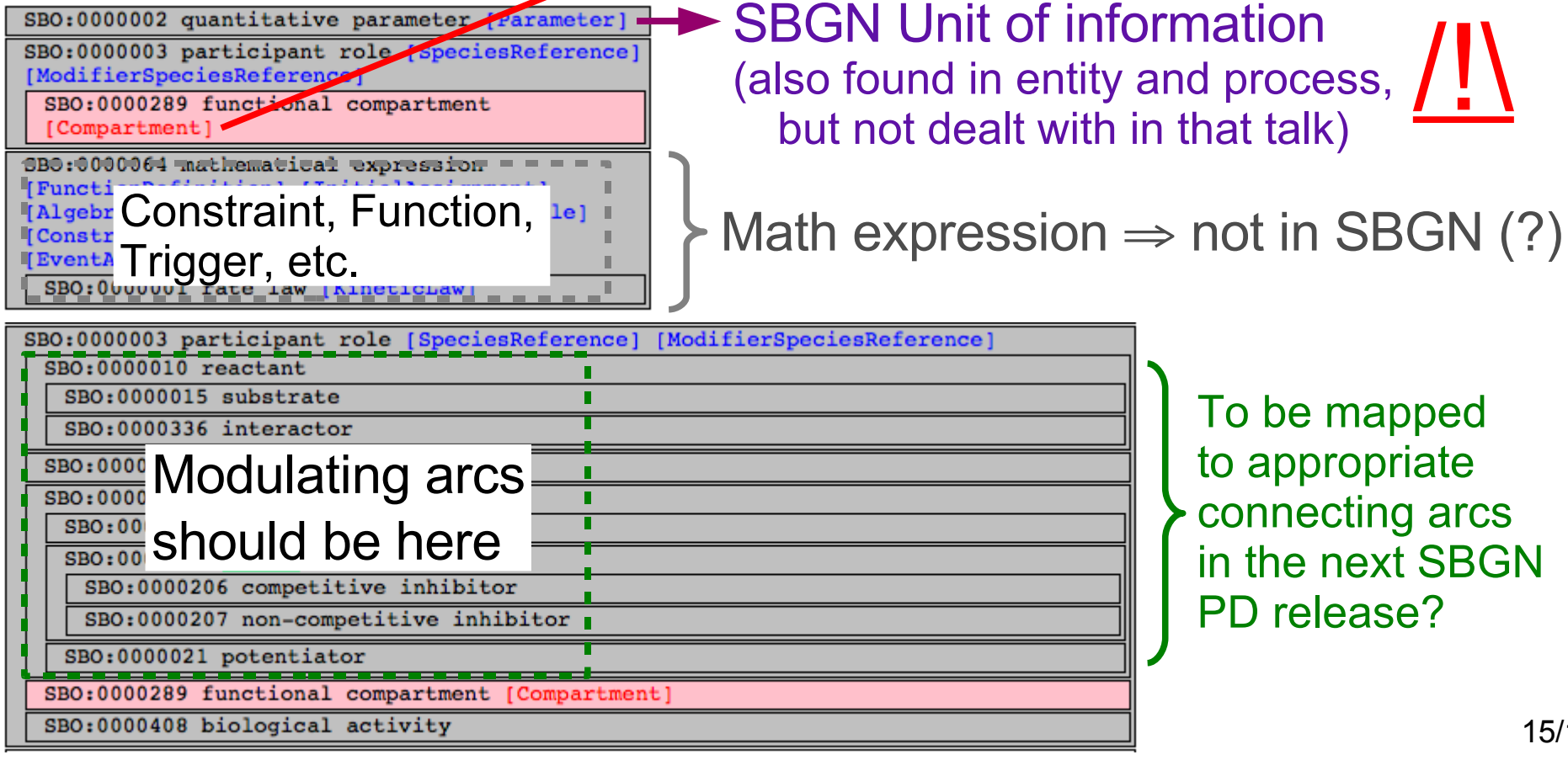
Reaction ⇒ transition

Reaction/Event ⇒ EPN??

Reaction ⇒ [?] [//] process?
(could be layout info?)

Other SBO terms

= Parameter, **SpeciesReference**, Rules, Law, Assignments, Delay, etc.



Tentative summary

✓ in Arcadia
✗ not yet
/ does not apply?

KineticLaw, FunctionDefinition, InitialAssignment, AlgebraicRule, AssignmentRule, RateRule, Constraint, Trigger, Delay, EventAssignment — no SBGN equivalent? /

Model — no SBGN equivalent? / (maybe Submap in SBML L3?) ✗

Compartment
CompartmentType — **Compartment** (but SBO mismatch) ✓
could be interpreted as Submap? ✗

Species, SpeciesType — Most EPN: ✓ **Unspecified entity**, Simple chemical, Macromolecule, Nucleic Acid Feature, Multimer, Source/Sink, + Complex (?) ~

Product/Reactant SpeciesReference
ModifierSpeciesReference — **Production**, **Consumption**
Modulation, Stimulation, Catalysis, Inhibition, Trigger (after patch) ✓

Reaction — **Transition**, Association, Dissociation ✓
Event? — Uncertain process? ✓, Omitted process? ✓ (could be layout info?) ✗
Perturbation, observable? (should be PN, not EPN?) ✗

Layout info? — **clone marker** ✓, equivalence arc ✗, tag ✗, submap ✗

Does not apply? — and, or, not, logic arc /

Parameter (among others) — Unit of information (not fully studied yet) ✗

??? — State variable ✗

Problems to solve

- Need machine readable expression of:
  - SBML x SBO
  - SBGN x SBO

  } XML file, other format, web service?
- Few models have appropriate SBO annotations
  - ➔ Generate a test case file covering all SBGN glyphs?
  - ➔ MIRIAM to SBO conversion? (e.g. on biomodels.net DB)
- Ad-hoc conversion in Arcadia ⇒ not reusable
  - ➔ Define a SBML to SBGN “stylesheet”? (PD, + ER, AF?)
  - ➔ Open question: SBGN file format...?

Thank you!

More information:

http://arcadiapathways.sourceforge.net

http://personalpages.manchester.ac.uk/staff/Alice.Villeger

Questions, comments, suggestions, etc.:
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Also feel free to ask me for a demo during the meeting!