

# SBPAX: Turning Bio Knowledge into Math Models, Automated

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Virtual Cell, BioPAX, SBPAX  
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[www.sbpax.org](http://www.sbpax.org)

# Qualitative Bio Knowledge on Web

- **Pathway Commons** (BioPAX Level 2):
  - BioGRID, MSKCC Cancer Cell Map, HPRD, HumanCyc, SBCNY, IntAct, MINT, NCI/Nature PID, Reactome
  - 1,623 pathways, 585,000 interactions, 106,000 physical entities, 564 organisms
  - BioPAX Level 3 being tested
- **UniProt**: 531,473 SwissProt, 16,504,022 TrEMBL
- **ChEBI**: 26,091 entries
- **NCBI Taxonomy**: 814,119 taxons
- **Foundational Model of Anatomy**: 120,000+ terms

# Quantitative Bio Knowledge on Web

- **SABIO-RK**: SBML export, rich on SBO; BioPAX L3, SBPAX3 interest;
- **Signaling Gateway Molecule Pages**: 672 curated pages (interactions), large diversity of quantitative values, BioPAX L3 export, SBPAX3 export (test)
- **MetaCyc, EcoCyc**: started to collect enzymatic rate constants recently; SBML, BioPAX L3 export; SBPAX3 plans;

# Bio Knowledge from Web into VCell

- **Virtual Cell (VCell)**: mature, rich modeling platform; visual model editor, simulations, parameter fitting, model db, etc; SBML import/export
- **SBPAX at VCell**: Grab Bio Knowledge from Web to build and annotate models
  - **Qualitative**: Queries Pathway Commons, UniProt, ChEBI; imports BioPAX (since years)
  - **Quantitative**: in process (SGMP) via BioPAX + SBPAX3

# Quantitative Bio versus Modeling

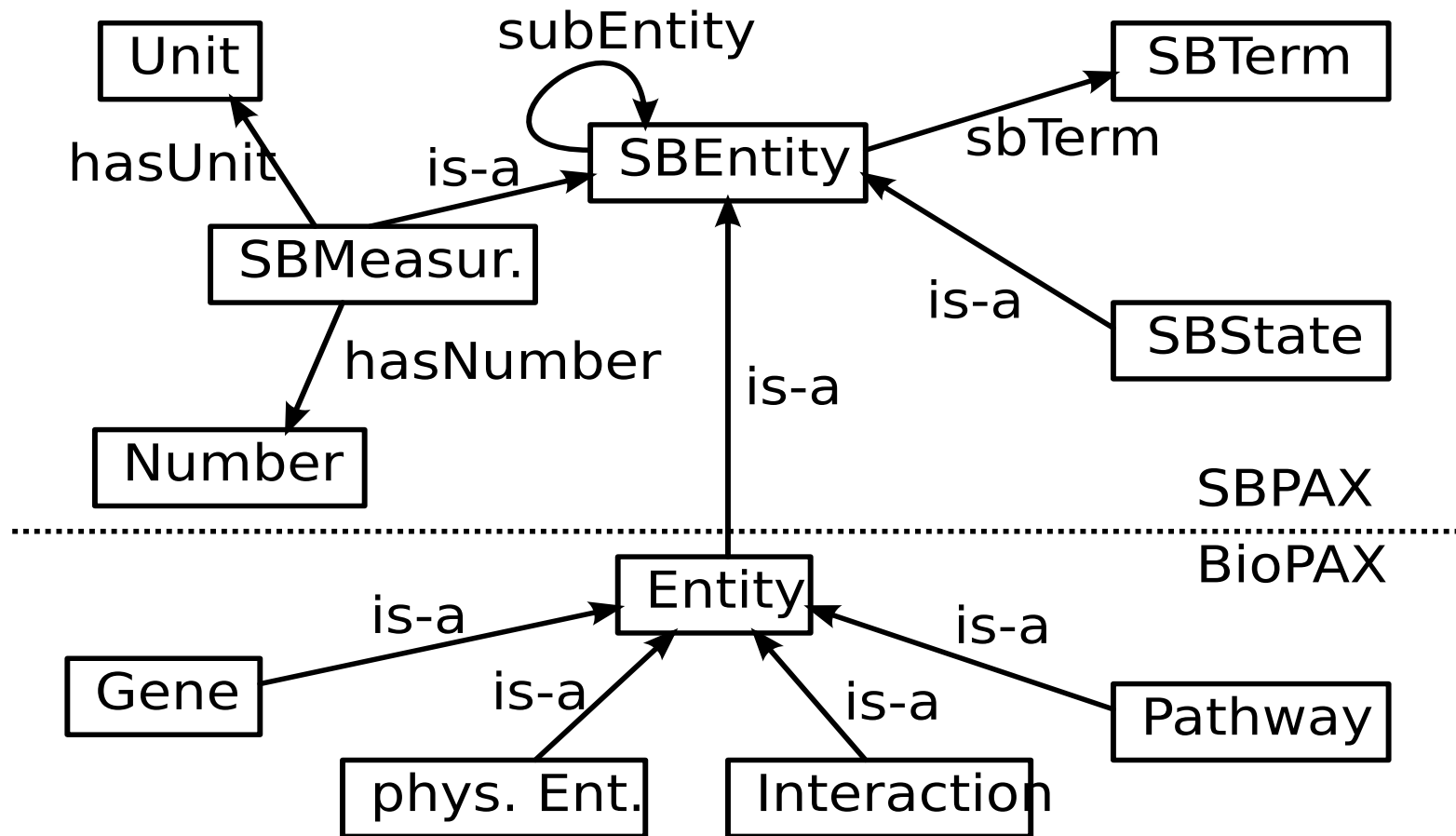
## **Model = Biology + Method**

- **Biology:** biological reality; qualitative + quantitative; general + specific ( => BioPAX, SBPAX)
- **Method:** cropping, filtering, merging, requirements, assumptions, simplifications, omissions, artifacts ( => VCell)
- **Model:** Math (=> SBML, CellML)

# Systems Biology Pathway Exchange (SBPAX)

- Integrated with BioPAX classes
  - Extension to BioPAX L3 as SBPAX3
  - Proposal for BioPAX L4
- Arranges Systems Biology terms (e.g. Systems Biology Ontology), numbers and units into hierarchies
- Units based on Units of Measurement Expressions (UOME)

# SBPAX3: Classes + Properties



# SBPAX3 Sub-Elements

| Entity type             | Sub entity type          | Entity example                       | Sub-entity example     |
|-------------------------|--------------------------|--------------------------------------|------------------------|
| Material object         | Component                | Hemoglobin                           | Hb subunit, heme group |
| Process                 | Partial process          | $A \rightarrow B \rightarrow C$      | $A \rightarrow B$      |
| Object                  | Property                 | Conductor                            | Conductance            |
| Entity                  | Mathematical description | Reaction                             | Rate law               |
| Mathematical expression | Partial expression       | Rate law                             | Rate law parameter     |
| Index-able              | Index                    | Michaelis constant for substrate ATP | ATP                    |



# Systems Biology Ontology (SBO)

- Project by BioModels.net, curator Nick Juty
- Comprehensive collection of SB-relevant terms, hierarchical
- Includes terms for many rate laws, parameters and quantities
- For rate laws, includes math expression and references to SBO terms of the parameters (e.g. term for Michaelis-Menten rate law refers to term for Michaelis constant)

# Units of Measurement Expressions (UOME)

- UOME core: ontology to define units:
  - By scaling, exponentiation, offset, product or quotient of other units
  - By reference to controlled vocabulary (e.g. UO)
- UOME list: long list of predefined units (e.g. micro mole per milligram per minute)
- Can convert to SBML/VCell units

# SBPAX3: Dissociation Constant

**SBEntity: C5a receptor-ligand binding**

**SB Term:** SBO 526: protein complex formation

**BioPAX Class:** complex formation

**SBMeasurable: Dissociation constant**

**SB Term:** SBO 282: dissociation constant

**Number:** 0.001      **Unit:** micro molar

# SBPAX3: Multi-Ion Channel

|   |                           |
|---|---------------------------|
| <b>SBEntity: Polycystein 2 Ion Channel</b>      |                           |
| <b>SB Term:</b> SBO 252: polypeptide chain      |                           |
| <b>BioPAX Class:</b> protein                    |                           |
| <b>SBMeasurable: Conductance for Calcium</b>    |                           |
| <b>SB Term:</b> SBO 257: conductance            |                           |
| <b>Number:</b> 88.0                             | <b>Unit:</b> pico Siemens |
| <b>SBEntity: Calcium</b>                        |                           |
| <b>SB Term:</b> SBO 327: non-macromolecular ion |                           |
| <b>BioPAX Class:</b> small molecule             |                           |
| <b>SBMeasurable: Conductance for Sodium</b>     |                           |
| <b>SB Term:</b> SBO 257: conductance            |                           |
| <b>Number:</b> 18.0                             | <b>Unit:</b> pico Siemens |
| <b>SBEntity: Sodium</b>                         |                           |
| <b>SB Term:</b> SBO 327: non-macromolecular ion |                           |
| <b>BioPAX Class:</b> small molecule             |                           |

# SBPAX3: Multi-Substrate Enzyme

|   |
|---|
| <b>SBEntity: Phosphatidylinositol-4-kinase type III beta</b>          |
| <b>SB Term:</b> SBO 216: phosphorylation                              |
| <b>BioPAX Class:</b> catalysis  |
| <b>SBEntity: Michaelis-Menten kinetics 3</b>                          |
| <b>SB Term:</b> SBO 432: Michaelis-Menten kinetics for two substrates |
| <b>SBMeasurable: Michaelis constant 3a</b>                            |
| <b>SB Term:</b> SBO 322: Michaelis constant for substrate             |
| <b>Number:</b> 400.0 <b>Unit:</b> micro molar                         |
| <b>SBEntity: ATP</b>  |
| <b>SB Term:</b> SBO 247: simple chemical                              |
| <b>BioPAX Class:</b> small molecule                                   |
| <b>SBMeasurable: Michaelis constant 3b</b>                            |
| <b>SB Term:</b> SBO 322: Michaelis constant for substrate             |
| <b>Number:</b> 1000.0 <b>Unit:</b> micro molar                        |
| <b>SBEntity: phosphatidylinositol</b>                                 |
| <b>SB Term:</b> SBO 247: polypeptide chain                            |
| <b>BioPAX Class:</b> protein  |
| <b>SBMeasurable: maximal velocity 3</b>                               |
| <b>SB Term:</b> SBO 324: maximal velocity                             |
| <b>Number:</b> 0.6 <b>Unit:</b> micro mole per minute per milligram   |
| <b>SBMeasurable: catalytic rate constant 3</b>                        |
| <b>SB Term:</b> SBO 320: catalytic rate constant                      |
| <b>Number:</b> 0.9 <b>Unit:</b> per second                            |

# Outlook

- **Next few weeks:**
  - User does keyword query, selects entities
  - User removes, merges or splits entities
  - VCell creates, annotates model, simulates
  - (above works already except for kinetics)
- **Eventually:**
  - User asks biological question (“Cure cancer?”)
  - VCell answers (“Use 570mg/day of drug X.”)

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