

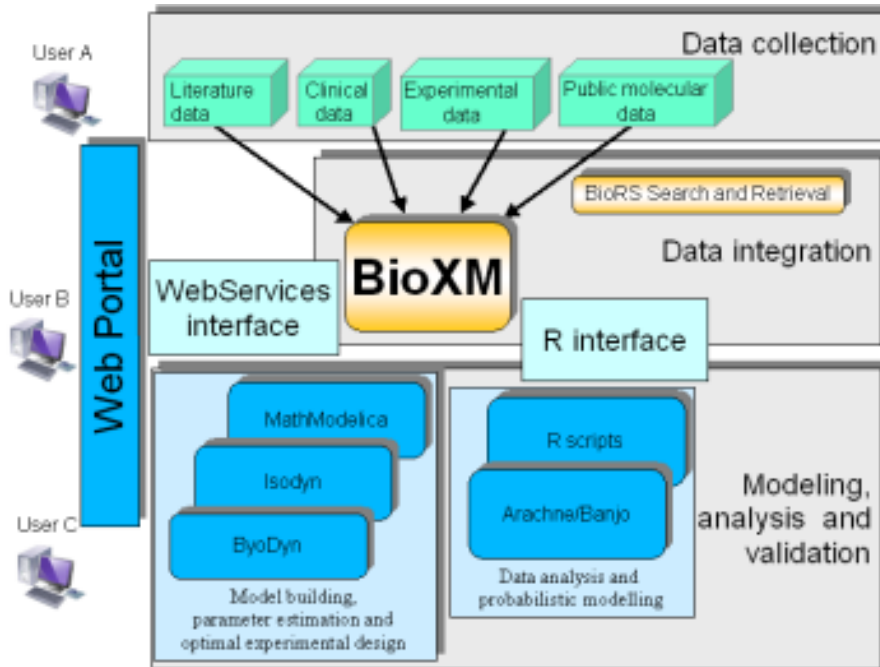
# Creating a Bridge between Modelica and the Systems Biology Community

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# The BioBridge project



1) structured **databases** including genomic, proteomic, and metabolomic information

2) integrated to model the underlying **metabolic networks**

3) a **simulation environment** for simultaneous analysis of multilevel data able to improve existing knowledge on complex disorders, such as COPD

*The BioBridge project is supported by the European Commission and is part of the Sixth Framework Programme.*



# SBML Translator

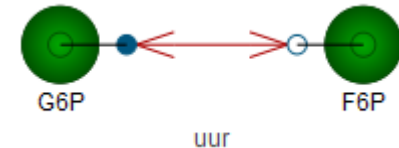
As the standard modeling language within systems biology applications SBML was chosen as “communication layer”.

By creating a translator to Modelica we can give the users access to a much richer language, offering new possibilities.



# SBML Translator

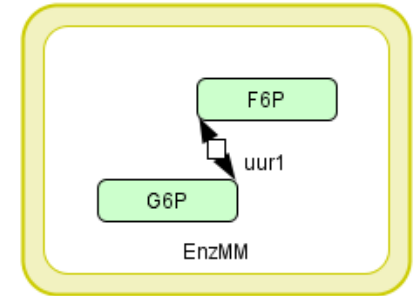
Example of a simple Modelica model:



```
model EnzMM "An enzymatic reaction with Michaelis-Menten kinetics"  
  extends BioChem.Compartments.Compartment;  
  Substances.Substance F6P(c.start=2) "Fructose-6-phosphate";  
  Reactions.MichaelisMenten.Uur uur(vF=1.5, KmS=0.1, KmP=0.05);  
  Substances.Substance G6P(c.start=1) "Glucose-6-phosphate";  
equation  
  connect(uur.p1,F6P.n1);  
  connect(G6P.n1,uur.s1);  
end EnzMM;
```



# SBML Translator



The same model exported to SBML:

```

<?xml version="1.0" encoding="UTF-8"?>
<sbml xmlns="http://www.sbml.org/sbml/level2" level="2" version="1">
  <model id="MyExample">
    <listOfCompartments>
      <compartment id="EnzMM" size="1"/>
    </listOfCompartments>
    <listOfSpecies>
      <species id="G6P" compartment="EnzMM">
        <notes>
          <html xmlns="http://www.w3.org/1999/xhtml">
            <p>
              A substance with variable concentration.
            </p>
          </html>
        </notes>
      </species>
      <species id="F6P" compartment="EnzMM">
        <notes>
          <html xmlns="http://www.w3.org/1999/xhtml">
            <p>
              A substance with variable concentration.
            </p>
          </html>
        </notes>
      </species>
    </listOfSpecies>
    <listOfReactions>
      <reaction id="uur1">
        <math xmlns="http://www.w3.org/1998/Math/MathML">
          G6P \rightleftharpoons F6P
        </math>
        <listOfParameters>
          <parameter id="KMS" name="Forward Michaelis-Menten constant" value="1"/>
          <parameter id="KMP" name="Reverse Michaelis-Menten constant" value="1"/>
          <parameter id="vF" name="Forward maximum velocity" value="1"/>
          <parameter id="vR" name="Reverse maximum velocity" value="1"/>
        </listOfParameters>
      </reaction>
    </listOfReactions>
  </model>
</sbml>
  
```



# Behind the scenes

A few things have been done to make this possible:

- Finding a mapping between SBML and the more expressive and general Modelica language and the pure
  - “Catch” Modelica constructs and map them
  - Restrict how the Modelica models are built
- BioChem library updated
- Wizards introduced



# Verification of translator

Models from BioModels database have been used to verify if models that are imported to *MathModelica* and exported from give the same result as the simulation published on the database.

	Test models	Succeeded
Import	216	212 (98%)
Simulation	212	208 (98%)
Export	18	18 (100%)



# Comparison with other tools

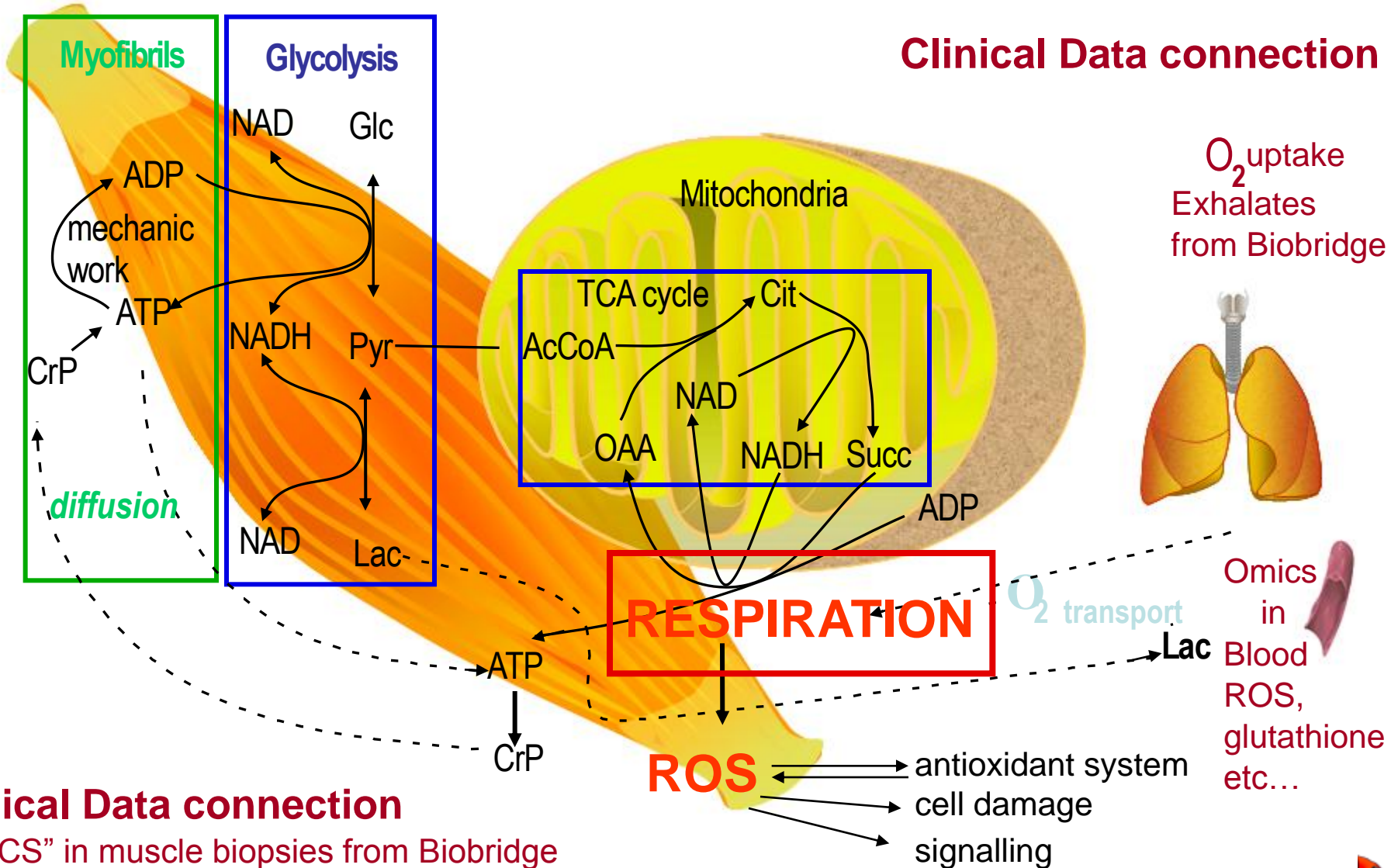
Models from BioModels database have been used to verify if different tools give the same result as the simulation published on the database.

	Test models
<i>MathModelica 2.1b4</i>	98% (42 of 43)
Systems Biology Workbench 2.7.9	56% (24 of 43)
CellDeisgner 4.01	40% (17 of 43)



# Model of muscle energy metabolism

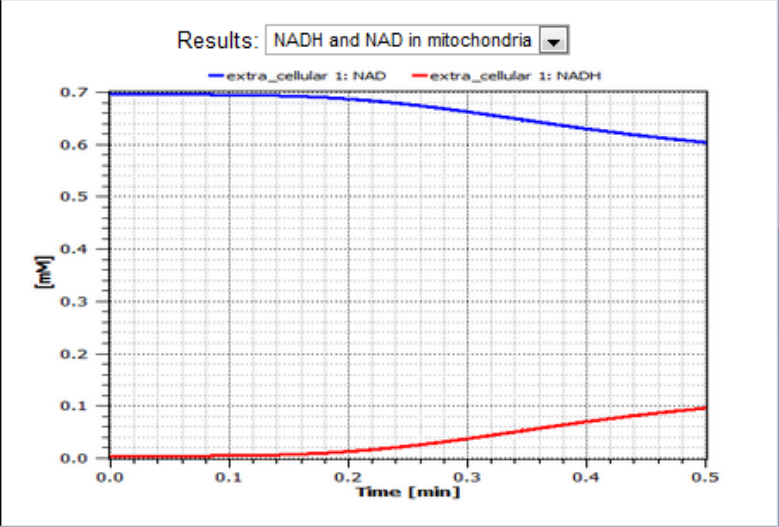
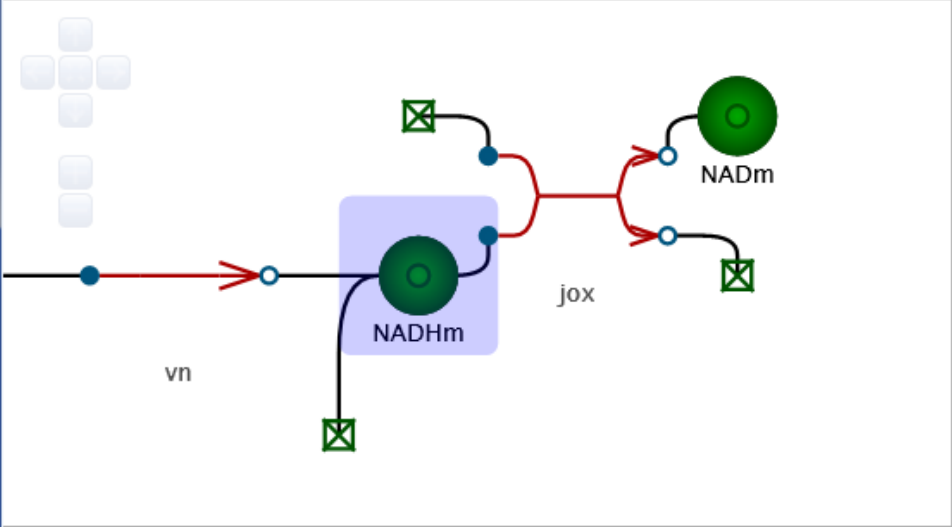
## Clinical Data connection



## Clinical Data connection

"OMICS" in muscle biopsies from Biobridge





- Information
- Revisions
- Parameters
- Variables
- Constants
- Components

7423  
21902

**Alias CAS:**  
**Alias KEGG:** C00004  
**SMILES:** NC(=O)C1=CN(C=CC1)[C@@H]2O[C@H](COP(O)(=O)OP(O)(=O)OC[C@H]3O[C@H]([C@H](O)[C@@H]3O)n4cnc5c(N)ncnc45)[C@@H]2O

**Metabolite Structural Information**

**C00004**

**Object:** C00004  
**Formula:** C<sub>21</sub>H<sub>29</sub>N<sub>7</sub>O<sub>14</sub>P<sub>2</sub>  
**Structure:**

C00004



# BioXM

- BioXM directly, or by access to their WebService query interfaces, integrates more than 20 different public databases and ontologies representing a total of
  - 80 793 genes (30 246 human, 27 237 mouse, 23 310 rat)
  - 1 307 pathways
  - 78 528 compounds,
  - 1 525 474 protein interactions
  - a total of 3 666 313 connections within the knowledge network and the entire Gene Expression Omnibus database



# Limitations

- Translator currently in beta stage and lacks support for...
  - unit conversion
  - initial assignments
  - graphical annotations
- The database connection to BioXM is a test implementation
- More advanced wizards needed
- Parameter estimation, model reduction and stochastic simulations could be added



# Conclusion

- We believe that modeling and simulation has a strong future for understanding complex biological processes, and that *MathModelica*, in combination with SBML-based software and models, has the potential of taking a leading role in such an effort.
- The BioBridge portal offers a possibility to simplify the task of understanding complex disorders such as diabetes and COPD.
- Soon available as beta from MathCore.

