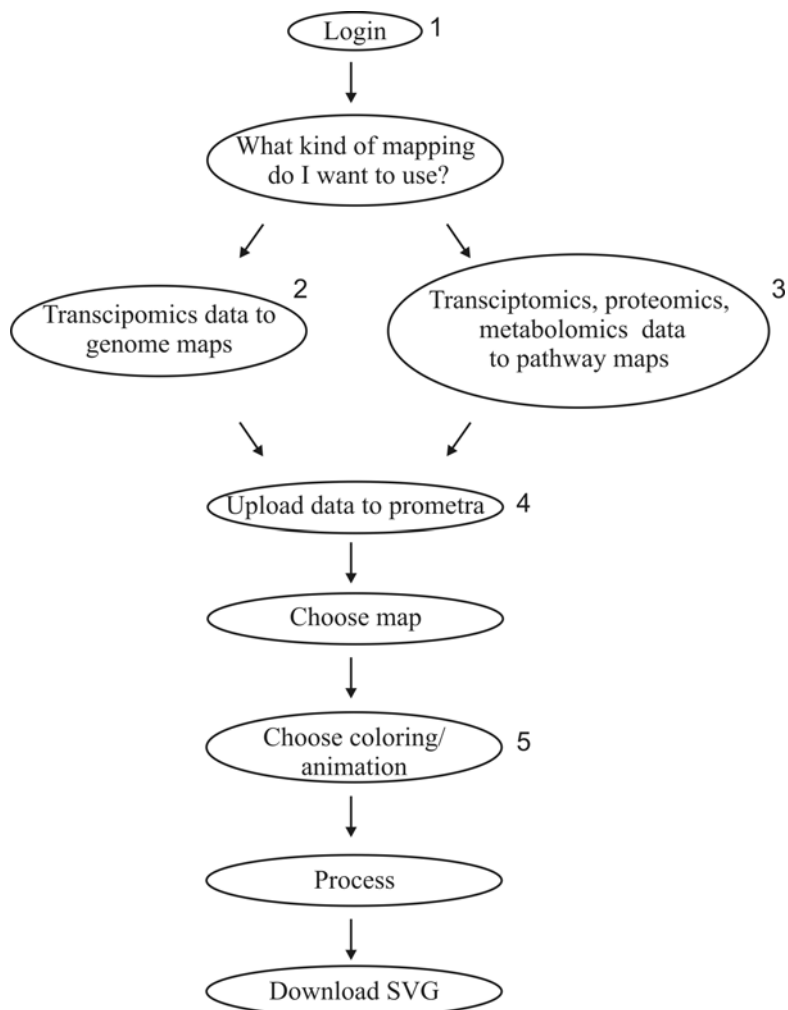


# ProMeTra - Multi-Omics Viewer

[http://www.cebitec.uni-bielefeld.de/groups/brf/software/prometra\\_info](http://www.cebitec.uni-bielefeld.de/groups/brf/software/prometra_info)

ProMeTra is a web based framework for the storage and visualization of user defined metabolic pathway maps and their visualization with experimental data from transcriptomics, genomics and proteomics.

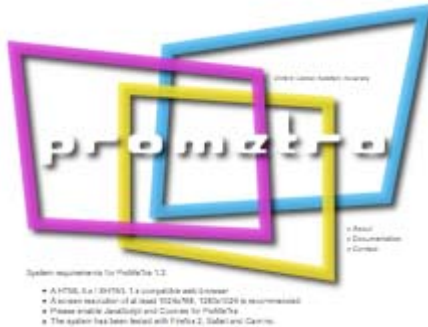
## Workflow



## 1. Login to ProMeTra

### 1.1 The public ProMeTra account

We provide free access to the ProMeTra functionality via the public 'prometra' account. By clicking on the main ProMeTra logo at the login page, a persistent ProMeTra session is generated for your web browser with the public account.



Using this public login, users can already access public metabolomics and transcriptomics experiments stored in Emma2 and MeltDB. Please have a look at the point 4.1 on how to use the web service access to these *Omic*s platforms.

Apart from the direct Web Service access, users may also upload their own datasets in Excel or simple CSV format and use the existing Pathway- or GenomeMaps to visualize their data. Every uploaded dataset is only stored temporarily and will be deleted automatically after the session is closed via the logout button.

Access to the uploaded experimental data is restricted to the active session. This is sufficient to present the data on various PathwayMaps and also ensures the privacy of the experimental datasets.

Whereas the datasets are only temporarily stored, uploaded PathwayMaps remain available. Researchers can even make their uploaded PathwayMaps available to colleagues by setting the *public* flag.

**Upload annotated SVG Pathway**

**Name:** My ProMeTra Pathway Map

**Pathway SVG File:** /Users/heiko/Desktop/ProSe-MeTra.svg Durchsuchen...


**Description:** My new ProMeTra Pathway map created using Inkscape

**Access:**  public

**Owner:** prometra

Create

A PathwayMap will by default only be visible in ProMeTra to the account user who uploaded the file. By selecting an uploaded pathway map, appropriate actions to update, show or delete a map are provided in the left menu bar.

-  **Actions**
- 
- » Create
  - » List
  - » Show
  - » Update
  - » Delete
  - » DeSelect

## 1.2 The CeBiTec, Bielefeld University account

Users of CeBiTec software resources such as GenDB ([http://www.cebitec.uni-bielefeld.de/groups/brf/software/gendb\\_info/](http://www.cebitec.uni-bielefeld.de/groups/brf/software/gendb_info/)), Emma2 ([https://www.cebitec.uni-bielefeld.de/groups/brf/software/emma\\_info/](https://www.cebitec.uni-bielefeld.de/groups/brf/software/emma_info/)), ProSE ([http://www.cebitec.uni-bielefeld.de/groups/brf/software/prose\\_info/](http://www.cebitec.uni-bielefeld.de/groups/brf/software/prose_info/)) or MeltDB ([http://www.cebitec.uni-bielefeld.de/groups/brf/software/meltdb\\_info/](http://www.cebitec.uni-bielefeld.de/groups/brf/software/meltdb_info/)) can use their existing accounts to access the ProMeTra interface. This has the advantage that only a single login procedure has to take place and afterwards experimental data from the various *Omics* platforms of the CeBiTec are made available via data exchange by Webservice technology.

### Use CeBiTec login

**Username:**  ▶

**Password:**

The main interface of ProMeTra currently allows to access Emma2, ProSE and MeltDB and users will see the experiments and datasets they already have access to in the individual applications.

### **1.3 Data persistency and privacy**

ProMeTra takes care that the uploaded datasets remain private. They are only accessible during one user session. Even if multiple users access the ProMeTra web interface with the public account at the same time, they can only access their own datasets. Furthermore, the uploaded numerical data is only stored on the ProMeTra server temporarily. After the user logs out, all data files uploaded during the session are removed automatically. Additionally, if the ProMeTra session runs out before the user logs out, all data files older than 6 hours will be removed automatically. These mechanisms ensure the privacy of experimental data. Users who wish to reuse their data files are kindly asked to re-upload their datasets at later sessions.

### **1.4 Web Browsers compatible with ProMeTra**

A current web browser is required to use the SVG visualization features of the ProMeTra software. In case your browser does not support visualization of SVG images directly an error will be displayed stating “Your browser is not capable of viewing SVG images!” and a link to download the image is presented alternatively.

Nonetheless, all major modern web browsers except Microsoft Internet Explorer support and render SVG mark-up directly. In order to view SVG files in Internet Explorer (IE), users have to download and install a browser plugin. This plugin is provided for free by Adobe (<http://www.adobe.com/svg/viewer/install/>) and is available for various operating systems:

Win 98–XP, Mac 8.6–9.1, Mac 10.1–10.4, RedHat Linux, Solaris 8

### **Important information for users of Firefox 3**

Users of the recently released Mozilla Firefox version 3 can experience problems when trying to access web-sites using secure connections and certificates such as our software pages (e.g. GenDB, EMMA). When accessing the secure page for the first time, Firefox 3 could show an alert message "www.cebitec.uni-bielefeld.de:443 uses an invalid security certificate".

The reason for this is that we are using a certificate that is not issued by a Certification Authority (CA) included into Mozilla products. Certificates are used to identify and authenticate the server of a secure web-site. Instead of purchasing such a certificate from a commercial CA included into Mozilla products, we use a certificate signed by the CeBiTec.

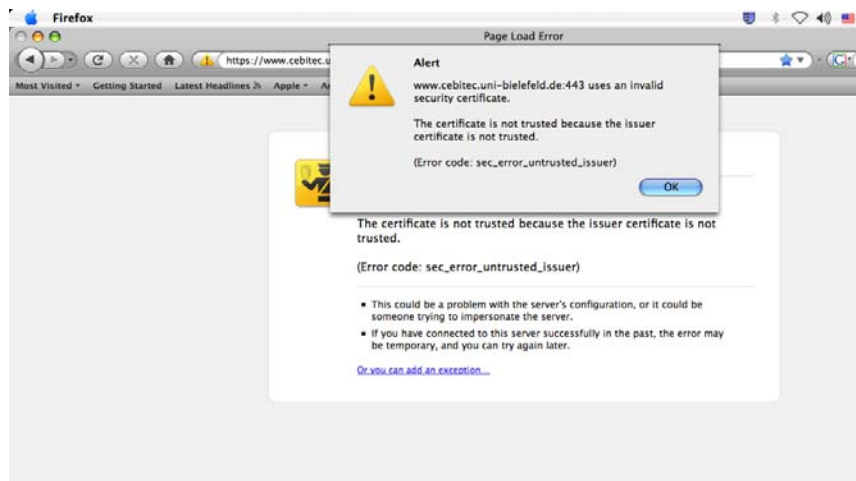
User who have just upgraded from Firefox 2 and used our software before will most likely not be affected.

Due to reasons of cost efficiency we do not intend to purchase a certificate from a commercial vendor for our servers. However, Firefox 3 is much more restrictive when it comes to unrecognized CAs and thus more complicated to configure for this than Firefox 2. We intend to obtain a certificate from the CA of the Deutsche Forschungs-Netz (DFN). Unfortunately, this CA (or better German Telekom which is the root CA for DFN) is, up to now, not included into Mozilla. See the Mozilla bug report ([https://bugzilla.mozilla.org/show\\_bug.cgi?id=378882](https://bugzilla.mozilla.org/show_bug.cgi?id=378882)) to get an impressive overview of the bureaucratic process of getting a root certificate into this product.

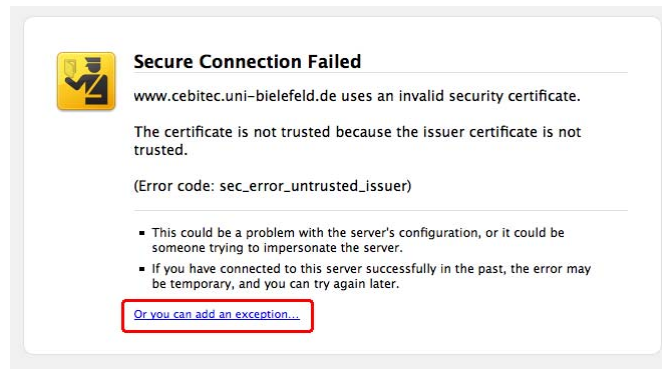
## Solution

To access our software you may want to follow the procedure outlined below. This has to be done only once. We apologize for any complication caused by this.

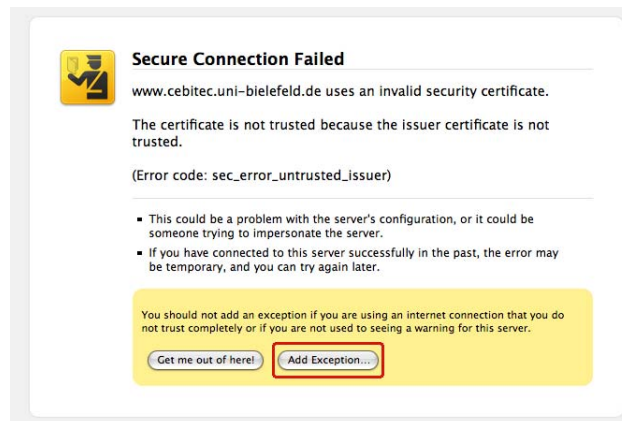
In the alert box, click **OK**



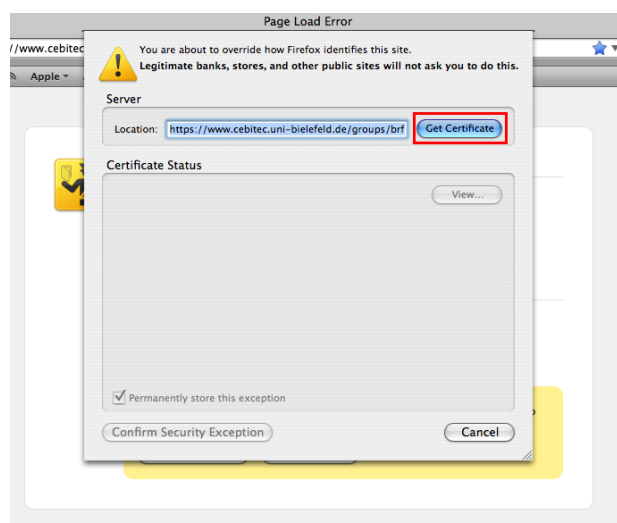
Click **Or you can add an exception...**



Click **Add Exception**



In the following dialogue click **Get Certificate**

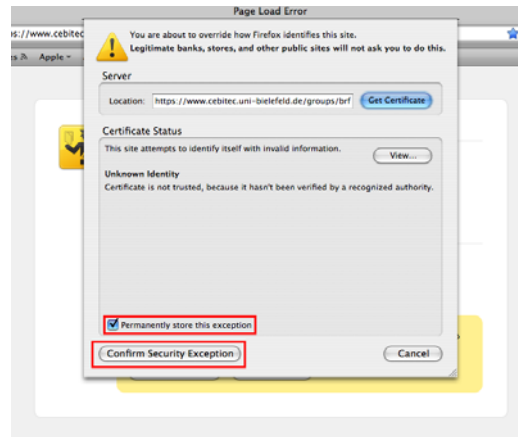


After the certificate has loaded, check the **Permanently store exception checkbox**.

Otherwise, the procedure has to be repeated after each browser start.

## Click **Confirm Security Exception**

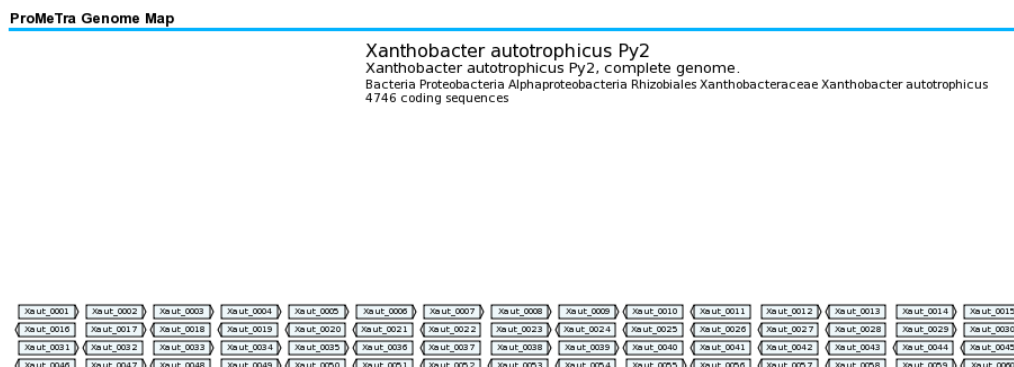
The software page should appear; this has only to be done once for all CeBiTec pages.



## 2. GenomeMaps in ProMeTra

The replicons of prokaryotic genomes present in the NCBI genome database (as of Dez. 2008) have been converted into so called GenomeMaps for the ProMeTra web interface. A GenomeMap in the ProMeTra context is a SVG based representation of the coding sequences (CDS) identified and annotated in the GenBank files of the individual prokaryotic database entries. GenomeMaps represent CDS in a grid by individual rectangles labelled with the locus tag (or if available the gene name). The order of the CDSs in the Grid representation is determined by the base number of the stop codon counted from the origin of replication. The grid is filled by row, i.e. the first CDS is in first row, first column, the second CDS is located at first row second column and so forth. A triangle at the right side of a rectangle indicates that the corresponding CDS is located on the forward strand, a triangle at the left indicates the location on the reverse strand.

Please see the following example of a GenomeMap for clarity:



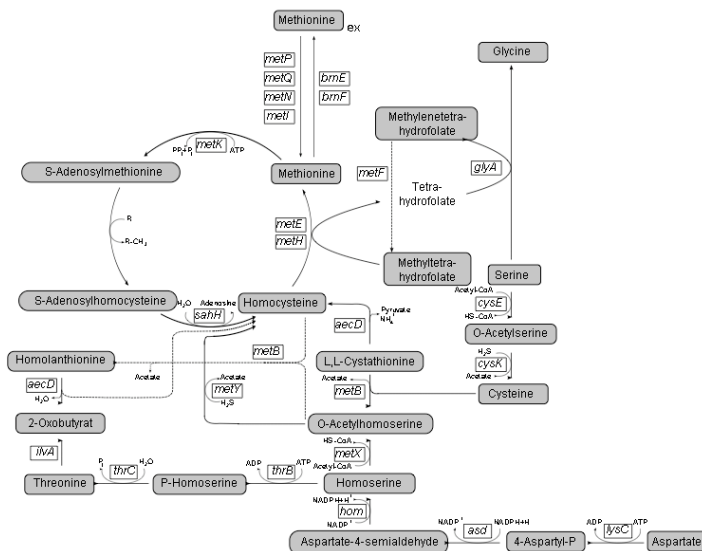
### 3. PathwayMaps in ProMeTra

#### 3.1 Which software can I use to draw my own pathway maps?

Inkscape is a Vector Graphics Editor that is SVG compliant, open source, responsive and extensible. The project homepage (<http://www.inkscape.org/>) contains the links to the free download (<http://www.inkscape.org/download/?lang=en>) of the latest release and extensive tutorials. Inkscape will help you to design your own PathwayMaps for ProMeTra and can also be used to review the generated results of PathwayMaps that you have colored with your experimental datasets using the ProMeTra web interface.

#### 3.2 How do I create my own PathwayMap for ProMeTra?

A PathwayMap in ProMeTra is a SVG image designed using e.g. Inkscape which additionally contains some labelled rectangles. The labelling defines which experimental data associated to entities from functional genomics (transcripts, proteins, metabolites) can be represented inside the image. Users can add other graphical elements such as lines, shapes, and text to SVG PathwayMaps, only the specially labelled elements will be modified by ProMeTra.

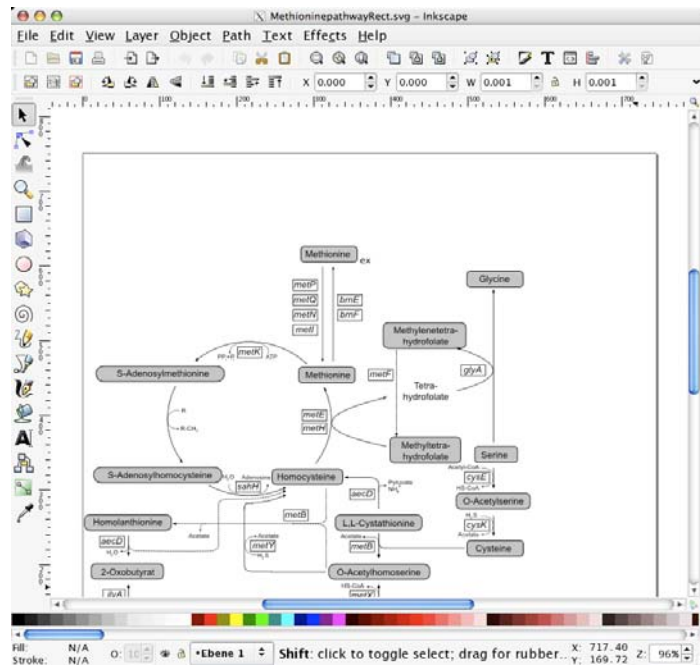


#### 3.3 How do I annotate SVG elements using Inkscape?

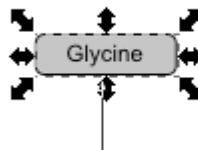
To add such a label to a graphical element in the SVG image, functionality of Inkscape can be used.

Open a SVG Pathway image in Inkscape

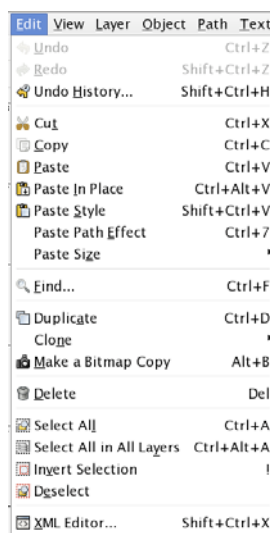




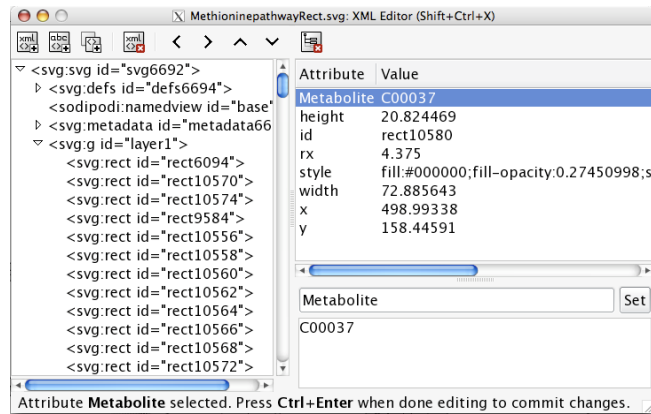
Select a rectangular image element (e.g. the Glycine rectangle as in the example)



Select XML Editor from the Edit Menu ...

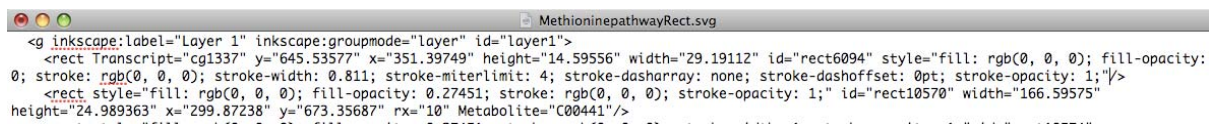


Add the *Metabolite* attribute and set the value to e.g. C00037 (KEGG-Nr.)



### 3.4 Annotate SVG elements using a text Editor

You may also edit the SVG file (XML Format) with any text editor and add the *Protein*, *Metabolite* or *Transcript* identifiers to the rectangle elements manually. In the following example the *Transcript* element for the *C. glutamicum* gene identified by the locus tag cg1337 is defined and another rectangle is connected to a *Metabolite* (KEGG Compound C00441).



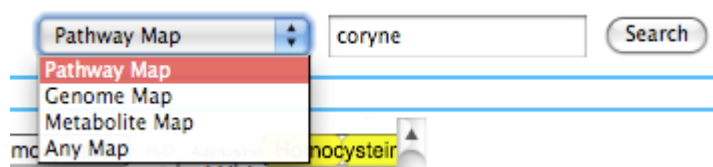
### 3.5 Data connection

ProMeTra will be able to identify the attributes *Protein*, *Metabolite* or *Transcript* in your rectangular SVG elements and use the associated identifiers (e.g. C00037) to connect to experimental datasets that users upload or obtain from MeltDB, ProSE or Emma2 via WebServices.

### 3.6 How can I download existing pathway maps from ProMeTra?

After logging in to ProMeTra you can use the *Search Bar* at the top of the interface to find all PathwayMaps and/or GenomeMaps that contain e.g. 'coryne' in their name, filename or description.

Simply enter your query string in the Search field and press the Search button.



ProMeTra will search the internal object relational database containing the Pathway descriptions and present a list with matching pathways.

Map::Pathway list

Show	Name $\Delta\nabla$	Owner $\Delta\nabla$	Filename $\Delta\nabla$	Description $\Delta\nabla$	Public $\Delta\nabla$
<input type="checkbox"/>	<a href="#">Coryne pathway rect</a>	prometra	Coryne_pathway_rect.svg	Coryne pathway rect public pathway map	Yes
<input type="checkbox"/>	<a href="#">Coryne pathway fixed</a>	prometra	Coryne_pathway_fixed.svg	Coryne pathway fixed public pathway map	Yes
<input type="checkbox"/>	<a href="#">Corynepathway all</a>	prometra	Corynepathway_all.svg	Corynepathway all public pathway map	Yes

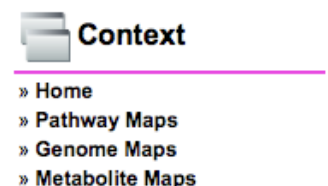
Click on one of the pathway name and the associated SVG image will be displayed in your browser window. Below the SVG image is a download link.



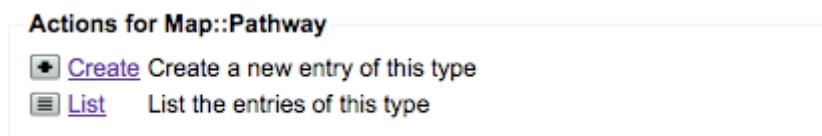
Store the image on your computer and edit it according to your needs using the Inkscape software.

### 3.7 How can I upload my own pathway maps?

Select the *Pathway Maps* context in the left menu bar.



Select the *create* action to upload one of your SVG pathways and create a new entry in the ProMeTra Pathway Database.



Fill out the form, select the SVG file to upload and choose an unique and descriptive name for your pathway. You can add additional text to the description field that will help you and others to find your pathway. If you want to share the pathway with other ProMeTra users, check the *public* attribute.

**Upload annotated SVG Pathway**

**Name:**

**Pathway SVG File:**

**Description:**




**Access:**  public

**Owner:** prometra

You can later delete or update the entries of your pathway object.

## 4. Upload data to ProMeTra

### 4.1 Accessing datasets via the ProSE, Emma2 or MeltDB web services

-  **Connect to MeltDB**  
Visualize metabolomics datasets on the selected Pathway Map via the MeltDB web service.
-  **Connect to ProSE**  
Visualize quantitative proteomics datasets on the selected Pathway Map via the ProSE web service.
-  **Connect to Emma2**  
Visualize transcriptomic datasets on the selected Pathway Map via the Emma2 web service.

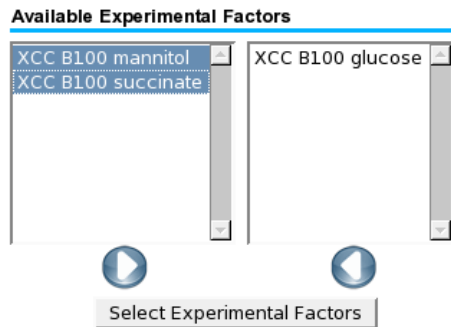
To request a dataset a user initially has to select a project.

<p><b>Available MeltDB Projects</b></p> <ul style="list-style-type: none"> <li>MeltDB_Public</li> <li>MeltDB_AC</li> <li>MeltDB_CO</li> <li>MeltDB_CellCulture</li> <li>MeltDB_Test</li> <li>MeltDB_SysMap</li> <li>MeltDB_Heart</li> <li>MeltDB_Sorangium</li> </ul> <p><input type="button" value="Select MeltDB Project"/></p>	<p><b>Available MeltDB experiments</b></p> <ul style="list-style-type: none"> <li>Supported raw formats</li> <li>XCC Xylem</li> <li>Three carbon sources</li> <li>XCC Xylem (Timepoints)</li> </ul> <p><input type="button" value="Select MeltDB Experiment"/></p>	<p><b>Available Reference Groups</b></p> <ul style="list-style-type: none"> <li>XCC B100 glucose</li> <li>XCC B100 mannitol</li> <li>XCC B100 succinate</li> </ul> <p><input type="button" value="Select Reference Group"/></p>
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For the given project all available experiments are listed and ...

... a reference group or state can be selected afterwards.

The groups or states that are selected in the last dialog will be compared to the references, and the resulting m-values will be used for the pathway or genome map visualizations.



#### 4.2 Which format should the experimental data in my Excel files have?

Please upload only Excel files in the .xls format (Office 1997-2004). ProMeTra does not yet support Office 2008 documents. Only the data in the first spreadsheet of your Excel document will be retrieved. The ProMeTra parser automatically reads the experimental factors from the first row and the individual identifiers of the proteins, transcripts or metabolites from the first column. ProMeTra does only support numerical data matrices. Please make sure that no text elements occur elsewhere than in the first row and column.

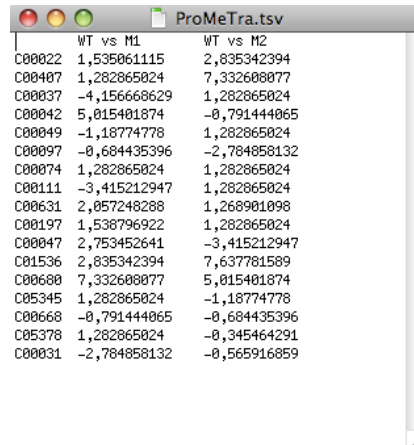
The following image shows a typical Excel sheet that can be uploaded via the ProMeTra interface.

	1	2	3	4	5	6
1	KEGG	T1 vs T2	T1 vs T3	T1 vs T4	T1 vs T5	T1 vs T6
2	C00022			1,53506111		
3	C00407					1,26294659
4	C00037			-4,1566686		
5	C00042		1,17220984	2,06183511	1,84187549	
6	C00049		1,21571828			
7	C00097			1,2689011		
8	C00074					4,44519685
9	C00111			-3,4152129		
10	C00631			2,05724829		4,90297985
11	C00197			1,53879692		
12	C00047			2,75345264	2,23192866	1,47989945
13	C01536			2,83534239		
14	C00680			7,33260808	7,63778159	5,01540187
15	C05345				-0,3454643	-1,1877478
16	C00668			-0,7914441	-0,5659169	-0,6844354
17	C05378		1,28286502			
18	C00031			-2,7848581	-2,4881792	-4,8589779
19						
20						
21						

The number of factors should be adjusted to the width of the rectangular elements in your Pathway- and GenomeMaps. For the standard GenomeMap up to ten factors are a reasonable number, the more factors ProMeTra has to visualize, the smaller the individual divisions of the rectangular elements become in the generated images.

### 4.3 Which other data files can I upload?

ProMeTra supports the simple file formats CSV and TSV (comma separated and tab separated values). The first line of these files contains the experimental factors that will be used in the legend of the generated image. Every following line contains an identifier and a tab or comma separated list of values.



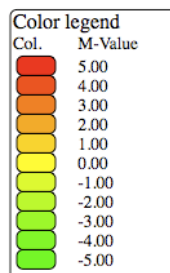
	WT vs M1	WT vs M2
C00022	1,535061115	2,835342394
C00407	1,282865024	7,332600077
C00037	-4,156668629	1,282865024
C00042	5,015401874	-0,791444065
C00049	-1,18774778	1,282865024
C00097	-0,684435396	-2,784858132
C00074	1,282865024	1,282865024
C00111	-3,415212947	1,282865024
C00631	2,057248208	1,268901098
C00197	1,538796922	1,282865024
C00047	2,753452641	-3,415212947
C01536	2,835342394	7,637781589
C00680	7,332600077	5,015401874
C05345	1,282865024	-1,18774778
C00668	-0,791444065	-0,684435396
C05378	1,282865024	-0,345464291
C00031	-2,784858132	-0,565916859

Only put one type of *Omic*s data into a single file.

## 5. Coloring and Animation of datasets

### 5.1 Which methods are employed to colorize the pathway maps?

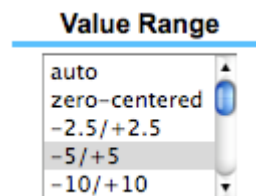
ProMeTra visualizes numerical values from *Omic*s-experiments by mapping them onto several predefined color gradients (e.g. Red-to-Green, Yellow-to-Blue, etc). Elements representing transcripts, proteins, or metabolites in Pathway- or GenomeMaps are highlighted with the respective colors. The following color legend shows an M-value mapping that can for example be used for transcriptomics datasets.



Various color gradients have been defined and are available via the web interface.



Users can select the numerical range of the color gradient mapping. Experimental values that are outside the range will be mapped to the colors at the respective end of the gradient. Alternatively, an automatic computation of maximal and minimal values can be employed ('auto'). The color gradient range is then dynamically adapted to the submitted experimental data.



The 'zero-centered' option computes the maximal absolute value found in the dataset and defines a symmetric range. The value 0 is always at the center of the color gradient. If the minimal value of the experimental data is -8.9 and the maximal value is 5.6, 'zero-centered' will set the range from -8.9 to 8.9.

## 5.2 What exactly is the "Animation" feature of ProMeTra?

ProMeTra can animate Pathway- and GenomeMaps using ColorAnimation defined in the SVG specification. During the animation, the background color of an *Enzyme* or *Metabolite* element changes and the current timepoint / factor is being highlighted in the legend. This is useful if large time series of *Omics* data need to be visualized.

Please bear in mind that currently only the Opera Browser (tested with Version 9.64) supports these animations features natively. The Adobe SVG Plugin (<http://www.adobe.com/svg/viewer/install/>) provides animation features for other browsers as well.

The following example SVG image was created with ProMeTra and contains the color animation of metabolite pool sizes in the Methionine pathway of *C. glutamicum*. Click on the link to download the image and/or open it in your browser.

Animation.svg: <http://www.cebitec.uni-bielefeld.de/groups/brf/software/wiki/ProMeTraWiki/Animation?action=AttachFile&do=get&target=animation.svg>

If your browser displays changing background colors for some of the metabolites in this SVG, you may also use the *Animation* feature of ProMeTra to visualize your data.