

# Proteus Guideline

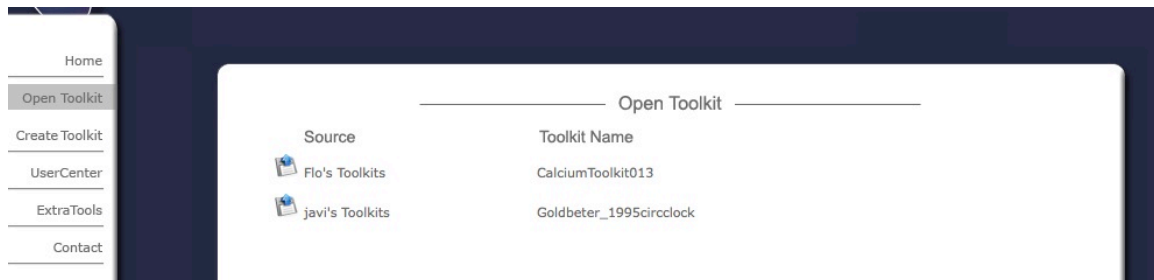
In addition to the online help section, this guideline is supposed to help users to use a toolkit, to create mechanisms and to combine mechanisms to build toolkits.

## 1. How to use a toolkit

A toolkit in Proteus is a collection of components. Each component provides a representation of a biological context. Users pick and choose components and, for each component, choose from different mechanisms. Each mechanism describes a different instantiation of the component's mechanism.

To open an existing toolkit, click on "Open Toolkit" in the main menu of Proteus. This yields the listing of all available toolkits as provided by the user community.

For this guideline, we select "CalciumToolkit013" which has been created by the user "Flo".



Initially the main design of the toolkit is shown. All toolkit components are listed along with dropdown lists and "target" buttons. For each component, you can select any assigned mechanism in the dropdown menu. If you intend to exclude certain components, you can set the assigned mechanism to be "none". In addition you can visualize each component via the corresponding "target" button. Picking and choosing mechanisms in the dropdown lists yields automatic creations of ODEs.

Design

Model Name

Redef. Values

Matlab

Fortran

SBML File

Upload

Model Design

Math Files

Save

Main Menu

Toolkit Components

Toolkit Component	Select Mechanism
IP3Receptor	DeYoung92_IP3Receptor
CalciumPump	DeYoung92_CalciumPump
PLC	DeYoung92_PLC
Phosphatase	DeYoung92_Phosphatase
Mitochondria	Meyer88_Mitochondrium
Leak	Atri93Class1_Leak
LeakER	none

Once a set of mechanisms has been selected, you can download the resulting Matlab files in the “Matlab” section:

Design

Model Name

Redef. Values

Matlab

Fortran

SBML File

Upload

Model Design

Math Files

Save

Main Menu

**Execution File**

```
function sol = _run()
%Main File for

[tspan,u_0,para,speciesname,paramname] =
_parameterset();
sol = ode23s(@, tspan, u_0, [], para);
```

**Parameter File**

```
function [tspan, u_0, para, speciesname,
paramname] = _parameterset()
%Parameter File for

%Time Span
tspan = [0,1000];

%Initial Conditions
```

**Equation File**

```
function du = (t,u,para)
%Equation File for

%State Variables
CaCyto = u(1);
CaExtra = u(2);
CaER = u(3);
IP3 = u(4);
IP3R000 = u(5);
IP3R001 = u(6);
IP3R010 = u(7);
IP3R011 = u(8);
IP3R100 = u(9);
IP3R101 = u(10);
IP3R110 = u(11);
IP3R111 = u(12);
C ...
```

Alternatively you can download the resulting Fortran files, upload the model to the Proteus server (as an registered user) or save the model as SBML file:



The screenshot shows the Proteus software interface. On the left, there is a sidebar with the following options: Design, Model Name, Redef. Values, Matlab, Fortran, SBML File (highlighted), and Upload. The main window is titled "SBML" and displays the following XML content:

```
<?xml version="1.0" encoding="UTF-8"?>
<sbml level="2" version="4" xmlns="http://www.sbml.org/sbml/level2/version4" xmlns:xhtml="http://www.w3.org/1999/xhtml">
<model name="" id="">
<notes>
<body>

Proteus Overview:

Compartments:
Cytosol
ExtraCell
ERMembrane
ER
Mitochondria

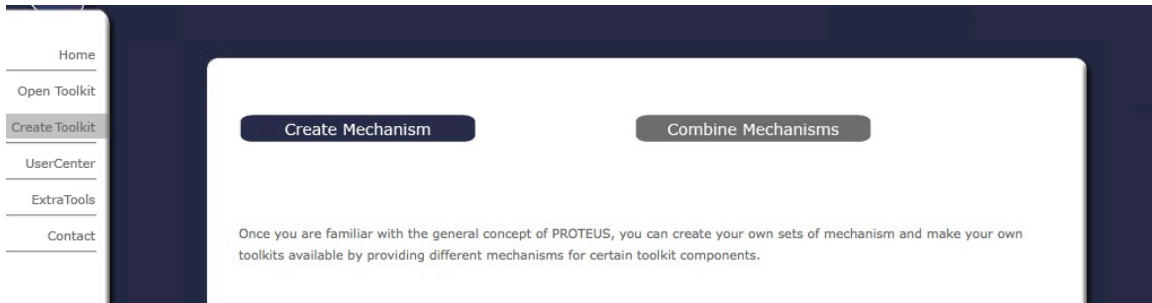
Species:
CaCyto
CaExtra
CaER
IP3
IP3R000
IP3R001
IP3R010
IP3R011
IP3R100
IP3R101
IP3R110
IP3R111
CaMito

Reactions:
JLeak
```

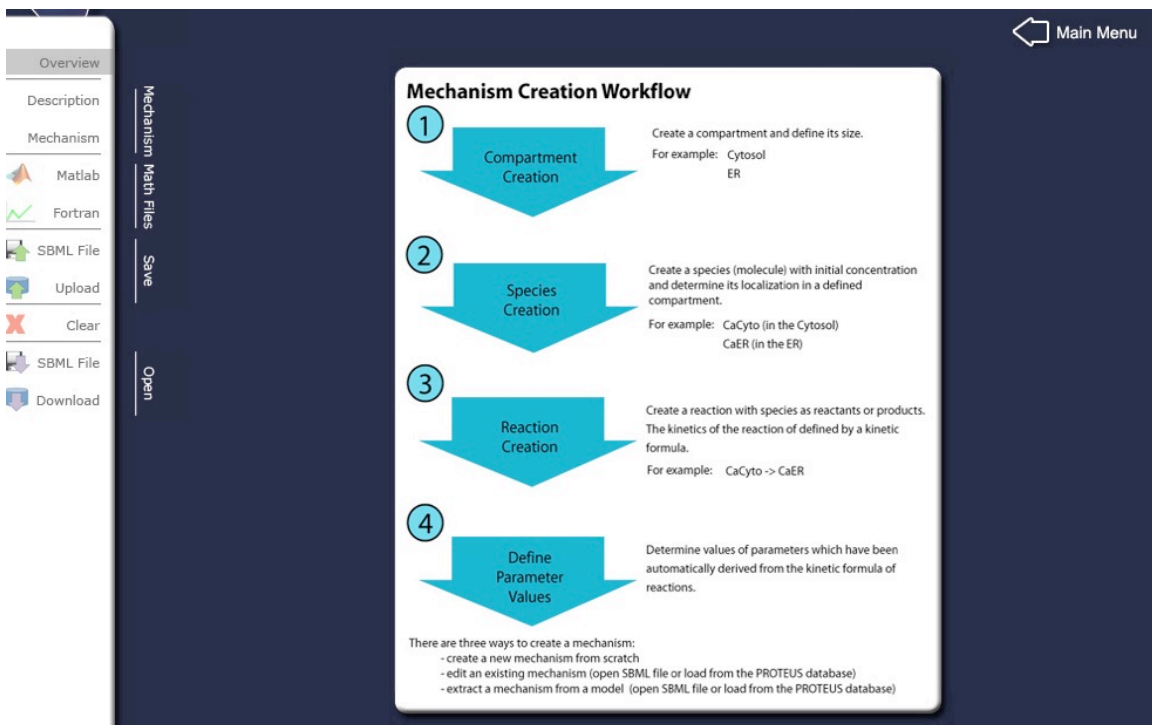
In summary, picking and choosing components and associated mechanisms is all you have to do, to create a model.

## 2. How to create a mechanism

To create a toolkit, you have to create a set of mechanisms via the "Create Mechanism" section (under "Create Toolkit") first.



The initial section of the Mechanism Creation section illustrates an overview:



You can create a mechanism from scratch or open an existing mechanism by downloading it from the Proteus server or loading a SBML formatted model.

A unique identifier has to be assigned to each mechanism and the provision of an optional description is highly recommended.

The screenshot shows a web interface for creating a mechanism. On the left is a sidebar with navigation options: Overview, Description, and Mechanism. Under Mechanism, there are buttons for Matlab, Fortran, SBML File, Upload, Clear, SBML File, and Download. The main content area is titled "Mechanism Naming" and contains two input fields: "Unique ID:" with the value "DeYoung\_Phosphatase" and "Description:" with the value "DeYoung and Keizer, 1992, Biophysics Phosphatase (optional)". A "Main Menu" button is in the top right corner.

The "Mechanism" section allows the creation of compartments, species, reactions, and parameters. The main page lists already created instances. Corresponding buttons enables the user to edit or create new instances.

The screenshot shows the "Mechanism" section of the software interface. It displays four lists of created instances, each with a "+ Create New" button. Each instance has an "Edit/Delete" button.

Compartments			
Unique ID	Biological Name	Size	Edit/Delete
Cytosol	Cytosol	1	
<a href="#">+ Create New</a>			

Species			
Unique ID	Biological Name	Compartment	Edit/Delete
CaCyto	CaCyto	Cytosol	
IP3	IP3	Cytosol	
<a href="#">+ Create New</a>			

Reactions			
Unique ID	Biological Name	For Kinetic Formula:	Edit/Delete
IP3flux02	IP3flux02	<input type="checkbox"/> Include Compartment Sizes	
<a href="#">+ Create New</a>			

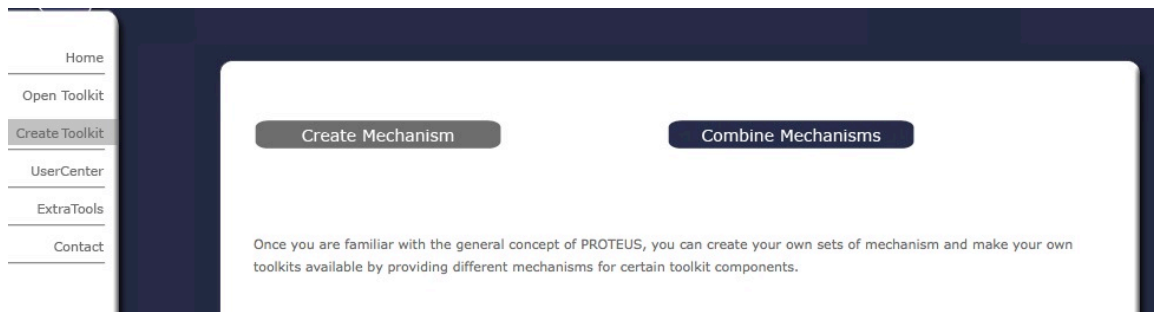
  

Parameters			
Unique ID	Unit	Value	Edit/Delete
Ir	dimensionless	1	
<a href="#">+ Create New</a>			

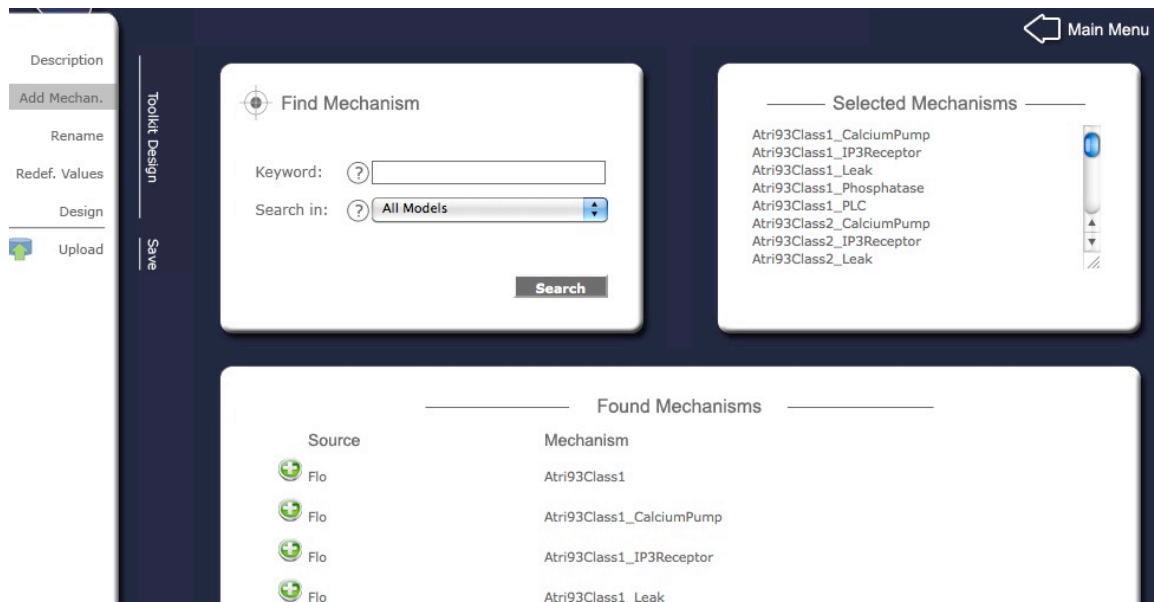
Once a mechanism has been created, the user can save the mechanism in SBML, Fortan, or Matlab format. In addition, registered users can upload the mechanism to the Proteus server, which is required to create a toolkit.

### 3. How to combine mechanisms to create a toolkit

To create a toolkit, you have to combine already created mechanisms (see chapter 2) and assign them to toolkit components. In the "Combine Mechanisms" section, a subsection of the "Create Toolkit" section, you can create toolkits from scratch or modify an existing one. This is the only section that requires to be a registered user, so that created toolkits can be uploaded to the server.



The first step is to upload a set of mechanisms in the "Add mechanisms" section. You can search mechanisms and add them to your "cart".



Once you have selected a number of relevant mechanisms, you can create toolkit components. For each toolkit component, you can upload an associated image that illustrates the given component and assign the corresponding mechanisms that you have uploaded to your cart.

Unique ID	Biological Name		
IP3Receptor	IP3Receptor		
CalciumPump	CalciumPump		
PLC	PLC		

That's actually all you have to do to create a toolkit: Upload a number of mechanisms, create toolkit components and assign the corresponding mechanisms to each component.

The "Rename" and "Redefine Values" sections allow to rename compartment, species, and parameter terms, and to change species concentrations, compartment sizes or parameter values, if required.

Finally you can upload the toolkit to the server.